Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Victoria A. Mah Date

Does Experience Matter? Examining the Relationships between Disease Experience and Perceptions of Research in Emergency Settings

By

Victoria A. Mah
MPH

Hubert Department of Global Health

_____

Rebecca Pentz, PhD

Committee Chair

_____

Mohammed K. Ali, MBChB, MSc

Committee Member

Does Experience Matter? Examining the Relationships between Disease Experience and Perceptions of Research in Emergency Settings

By

Victoria A. Mah

B.A., Vanderbilt University, 2008

Thesis Committee Chair: Rebecca Pentz, PhD

An abstract of
A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of Master of Public Health in Hubert Department of Global Health
2011

Abstract

Does Experience Matter? Examining the Relationships between Disease Experience and Perceptions of Research in Emergency Settings
By Victoria A. Mah

Objective: To determine how attitudes towards emergency research, exception from informed consent (EFIC) and a specific proposed clinical trial using EFIC (ProTECT™ III) are shaped by an individual's experience with illness.

Methods: ProTECT™ III is a randomized trial of progesterone for the treatment of traumatic brain injury (TBI). Data was collected from over 2,000 participants attending ProTECT™ III community consultation events hosted by 12 academic and medical centers around the country. Participants answered a survey during community consultations that gathered demographic data as well as opinions on specific consent circumstances in emergency research. Analysis was performed using chi-square test for proportions, t-test for means, and stratification to determine the impact of personal experience with TBI on attitudes towards ProTECT™ III and whether additional participant characteristics modulated the effect of personal experience.

Results: Among those participants who have either experienced a TBI themselves or have had a family member or friend suffer a TBI, there was a slightly higher level of acceptance of ProTECT™ III and EFIC than among those who did not have personal TBI experience. Age, race, and knowledge of ProTECT™ III all influenced the way in which personal TBI experience affected attitudes toward ProTECT™ III and EFIC. Among those participants who were 35 years and older, identified with a race other than Black, and had an incomplete understanding of the risks and benefits of ProTECT™ III, personal TBI experience appeared to be associated particularly strongly with favorable attitudes toward EFIC and the ProTECT™ III study.

Conclusion: These findings of differences in attitudes between those with personal TBI experience and those without may guide institutional review boards and investigators in setting standards or guidelines for the community consultation component of emergency research. Further studies on this relationship between disease experience and views of EFIC are needed to deepen our understanding of how different types of experience with a disease influence participants' attitudes towards emergency research.

Does Experience Matter? Examining the Relationships between Disease Experience and Perceptions of Research in Emergency Settings

By

Victoria A. Mah

B.A., Vanderbilt University, 2008

Thesis Committee Chair: Rebecca Pentz, PhD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of Master of Public Health in
Hubert Department of Global Health
2011

Acknowledgments

First of all, I would want to say how grateful I am to Dr. Neal Dickert for the many hours he spent helping me on this project during his personal time. He was truly invaluable and although he is not an official member of the thesis committee, I could not have completed this thesis without his help. I would also like to express my gratitude to my thesis advisor, Rebecca Pentz, PhD, for all the editing and brainstorming that she helped me do. She always made time for me among the many projects that she has and her input on the big picture of the thesis kept me focused. Lastly, I would like to thank Professor Ali for his incredible patience and dedication to helping me finish this project on time. He has been supportive of this thesis from the beginning and I appreciate the role he has played in my academic career at Rollins as a professor and mentor.

Table of Contents

Chapter 1: Introduction

Emergency medical care is a major issue in the United States (US). The Centers for Disease Control and Prevention (CDC) reports that each year, more than 400,000 people die of unexpected sudden cardiac death either in an emergency department or before reaching a hospital.[1] In addition, about 137,000 Americans die of stroke every year.[2] Unfortunately, cardiovascular events are not the only area where we have room for improvement in emergency medical care. The CDC estimates that about 1.7 million people sustain a traumatic brain injury (TBI) annually and of those, 52,000 die and 275,000 are hospitalized.[3] TBI is a contributing factor to a third of all injury-related deaths in the US which makes it a very significant cause of mortality. TBI is also a very costly problem; direct and indirect medical costs of TBI totaled an estimated $60 billion in the United States in 2000.[3] Emergency medical care of TBI and other critical health events can and should be improved not only to decrease morbidity and mortality, but also to lower the cost of long-term care for victims.

Best practices in medicine which help to keep morbidity and mortality rates low are typically determined through large clinical trials. Although most medical care providers aim to practice evidence-based medicine, not all standard treatments today are rooted in evidence. A solid foundation of evidence is critical, especially in the case of emergency medicine given the urgent and life-threatening nature of emergency situations. A recently released government guidance document prepared by the Office of Good Clinical Practice in the Office of the Commissioner, Food and Drug Administration (FDA), in consultation with FDA's Center for Biologics Evaluation and Research, Center

for Devices and Radiological Health, and the Center for Drug Evaluation and Research, affirms that much of what has become standard, accepted medical therapy for use in emergency settings has not been evaluated by adequate and well-controlled trials demonstrating that the treatment is safe and effective.[4] Conducting trials in urgent situations where obtaining consent is not possible will help to address the existing issues of high mortality and morbidity burdens from health emergencies.

In 1996 the FDA created the Exception From Informed Consent (EFIC) requirements for emergency research to allow the implementation of clinical trials without informed consent in very specific situations; titled 21 CFR 50.24. The rules that govern the use of the exception from informed consent are very strict. For a study to be eligible to be conducted under 21 CFR 50.24, all of the following conditions must be met:

- The participants are in a life-threatening situation that requires urgent intervention;
- Available treatments are unproven or unsatisfactory;
- Collection of valid scientific evidence is necessary to determine the safety and effectiveness of the intervention;
- Obtaining informed consent is not feasible because the subjects are not able to give their informed consent as a result of their medical condition;
- The intervention must be administered before consent can be obtained from the subject's legally authorized representative;
- There is no reasonable way to prospectively identify individuals that are likely to become eligible for participation;

- Participation in the research has the potential for direct benefit to the participants; and
- The clinical investigation could not practicably be carried out without the waiver.[4]

The rules that allow research in emergencies without consent also require researchers to monitor the results of their study through an independent data monitoring committee, to publicly disclose information regarding the study, and to carry out a process called community consultation (CC) before the institutional review board (IRB) will approve the investigation. Community consultation means providing the opportunity for discussions with, and soliciting opinions from, the community in which the study will take place as well as the community from which the study participants will be selected.[4, 5] As defined by the FDA guidance document, the goals of CC are to ensure the fulfillment of the principle of respect for persons contained within the Belmont Report through the following actions:

- Informing the community about the study in advance to provide a means for affected communities to give meaningful input to the IRB before the board makes its decision to approve, require modifications to, or disapprove the study;
- Allowing representatives of the community to identify potential community-level concerns and effects of the research; and
- Including in CC activities individuals who may have, or be at risk for, the condition under study and thereby obtain input from a group that is expected to be similar to the eventual study subjects.[4]

The CC portion of EFIC regulations has been one of the least understood and variably implemented portions of the requirements. It is a major source of frustration and confusion for reserachers[6-8] and perhaps one of the reasons that many important emergency research studies are not often initiated or completed[9]. EFIC research regulations are not specific about the CC methods they require and decisions regarding appropriateness have been the responsibility of the local IRB for a given study. Not to mention, CC is required for no other type of research; therefore, IRBs and investigators have little familiarity with the conduct and interpretation of CC. Much like the emergency treatments that EFIC seeks to improve and validate, CC methods are not yet evidence-based. It remains unknown what methods produce the highest levels of understanding and satisfaction among participants of CC events, as well as which groups to target as the best consultants.

Due to this lack of clarity and direction, the ProTECT™ III trial included a community consultation sub-study in the research design entitled "Assessing Community Consultation in Research Using the Exception from Informed Consent for Research in Emergency Settings in ProTECT™ III". ProTECT™ III is a large, phase III clinical trial conducted through the Neurological Emergencies Treatment Trials (NETT) Network that was created by the National Institutes of Health (NIH) to conduct large clinical trials with the goal of reducing the burden of very acute injuries and illnesses affecting the brain, spinal cord, and peripheral nervous system.[10] The Progesterone for Traumatic Brain Injury: Experimental Clinical Treatment (or ProTECT™) trial will evaluate whether progesterone, a hormone normally found in our bodies, is useful in limiting the amount of brain damage sustained from a TBI. Investigators of ProTECT™ III are testing whether

the addition of progesterone to standard medical care is incrementally more effective than standard medical care alone for the treatment of TBI and reduction of damage associated with TBIs. If progesterone is found to have a positive impact, this would be a major advancement in the treatment of TBIs.[11] The CC component of ProTECT™ III seeks to identify the best practices for community consultation in order to inform the research community and their respective IRBs. It also serves as another way to increase understanding of public perceptions of EFIC research.

Due to the distinct nature of research in emergency settings, the public perception of this type of research appears to be less favorable than perceptions of medical research in general.[12-14] Past investigations into public perceptions of non-EFIC medical research have found that attitudes towards research are generally positive.[15, 16] Among these studies, the factors contributing to willingness to participate that are typically identified are altruistic motives like advancing medical knowledge and considerations for self such as the possibility of getting better medical care and preferential treatment through participation.[17, 18] To a lesser extent, studies have identified an additional factor that affects participation and perceptions of research- an individual's personal experience or the experience of loved ones, including family members and friends, with the illness.[19-23] This phenomenon is not well-documented in the existing studies of perceptions of medical research and has never been directly evaluated with regard to perceptions of EFIC research.

Nonetheless, there are hints in the literature that personal experience correlates with a more positive view of emergency research. One study done during CC events for an EFIC trial on seizures collected information not only on participant's attitudes toward

EFIC and the specific seizure study, but also asked whether or not respondents knew anyone (including themselves) who had experienced seizures. This study showed that there is a correlation between knowing someone with the illness that is being studied and a positive perception of the research.[24] A qualitative study conducted among people who had recently survived a sudden cardiac death (SCD), also called sudden arrest, found that acceptance of a hypothetical emergency research study on SCD among individuals in this group with recent SCD experience was much more widespread than other studies had found among members of the general population.[25]

These and other studies indicate that personal experience may affect an individual's perceptions of emergency research, but this phenomenon has yet to be studied in detail in a large study with a diverse population. This is important to determine because if the level of acceptance and understanding among those who have personally experienced the disease in question differs from their unaffected peers, it may change the way that researchers and IRB committees think about and implement CC practices. These data may have important impact on which populations ought to be consulted in CC efforts, and how views of CC participants with or without experience with the disease ought to be interpreted. Additionally, it will help IRBs and investigators to better understand the potential impact of EFIC enrollment on different types of subjects.

Emergency research is necessary to advance the care of critically ill adults and children. Since the enactment of EFIC, clinical trials that have been conducted under this federal regulation have subsequently demonstrated that in some cases application of previously standard interventions in practice was ineffective, harmful or only beneficial

for a small portion of the population who is receiving the treatment.[4] Therefore, efforts to better execute and increase the implementation of emergency research should be made in order to collect evidence that may be used to change practices affecting the morbidity and mortality burden of trauma and emergency conditions in the US. The data from the community consultation portion of the ProTECT™ III trial may help to decrease confusion surrounding the implementation of the CC requirement of EFIC and also help researchers to understand attitudes toward of emergency research and how they are affected by characteristics of the population.

Chapter 2: Comprehensive Review of the Literature

Introduction

This literature review focuses on the perceptions of medical research, perceptions of emergency research, and influence(s) of illness experience on those perceptions. Articles and relevant information were found using the Pub Med search gateway and through the help of colleagues and mentors.

Perceptions of Medical Research

In general, medical research is thought to be very important and is well-accepted by the public. This positive attitude is shown in a 1998 study by Sugarman, et al. where 90% of patients interviewed in the waiting rooms of medical oncology, radiation oncology, and cardiology clinics had either a "very favorable" or "favorable" attitude about medical research.[15] This finding is not surprising in some ways because we live in a country where many research studies are being conducted. It is interesting to note, however, that although there have been historical failures in the research community such as the Tuskegee syphilis study, the vast majority of the population still holds a favorable opinion of medical research despite those ethical violations.

In many studies on opinions of medical studies, the variable of interest for researchers has not been how much participants like the idea of medical research, but whether or not they would be willing to participate in the research. This is an important outcome for researchers because they need to recruit participants in order to successfully study any topic of interest. In 2003, Comis, et al. completed a study on the attitudes of

American adults toward participation in cancer clinical trials. Interestingly, they used a hypothetical situation of being diagnosed with cancer to find out how people would react to being asked to participate in a clinical trial. It was estimated that 81% of participants, if diagnosed with a serious disease such as cancer, felt it would be very important or somewhat important to them to participate in a clinical trial. The percent of participants who would view participation in cancer clinical trials as very important or somewhat important increased to 87% in a different scenario where the patient's initial cancer treatment had failed.[20] This study confirms that the general perceptions of research are high, especially when participants are given a concrete example. It also highlights how the hypothetical situation of having personal experience with illness changes an individual's views on research.

The acceptability of medical research has also been studied in different US contexts. Pentz, Billot and Wendler investigated the acceptability of research on stored biological samples in two Atlanta clinics, comparing the views of African American and White American cancer patients. 95% of individuals in the study, regardless of ethnicity or socioeconomic status, were willing to provide a biological sample for future research.[26] Through this study we can infer that at least one form of non-invasive research is accepted across racial and socio-economic categories.

Several study questionnaires eliciting people's views on general medical research have included components that focus on what individuals would want done with regard to participation in research if they could not make decisions for themselves. For example, in a study by Karlawish, et al. in 2009, the authors investigated older adults' attitudes toward enrollment of non-competent subjects in Alzheimer's research. They found that

among older adults, the majority (83%) were willing to grant advance consent to a blood draw study, almost all (96%) were willing to identify a proxy for research decision making, and most (81% for the blood study) were willing to grant their proxy leeway over their advance consent.[27] These results suggest that older adults are willing to relinquish their rights if incapacitated to a consent process for some minimally invasive research. Consent issues did not appear to be the deciding factor in older adults' acceptance of research with subjects who have become non-competent due to Alzheimer's, but rather a favorable attitude about biomedical research and interest in the subject matter contributed to their willingness.[27]

Perner, Ibsen, and Bonde examined the attitudes to drug trials among relatives of unconscious intensive care unit (ICU) patients. This study showed that the majority (64.3%) of relatives of patients in the ICU would be okay with not having the option of giving consent if there was a limited time frame for initiation of treatment.[13] The idea of having a limited time frame for treatments is exactly the case in emergency research. The FDA refers to this time frame as the therapeutic window; the time period after onset of the given event within which the investigational product must be used or administered to have its potential clinical effect based on available scientific evidence.[4] This therapeutic window must be too short for it to be feasible for researchers to obtain consent from a surrogate in order for the given study to be approved under EFIC. This study by Perner, Ibsen, and Bonde, therefore, provides us with an idea of what people's perceptions of research in emergency settings would be in this case without directly asking participants about EFIC research.

Perceptions of Emergency Research

As Lecouturier, et al. puts forward, after a review of the evidence on perceptions of emergency research, one finds that we are still lacking in a clear picture of public opinion on this issue. However, among studies that exist, we find that usually a small majority of people are accepting of emergency research in general.[28] There is a great deal of variability in the statistics regarding acceptability of EFIC presented by researchers. Some of the variability can be attributed to the differences in the study populations and some of the inconsistencies are due to the differences in study designs and the ways that questions were asked.

Biros, Sargent, and Miller conducted a study in 2009 where the respondents were CC participants that were recruited while visiting the emergency medicine display at the Minnesota State Fair. This method of recruitment used in this study did not yield a demographically or geographically diverse group which may limit its applicability to the general US population. Findings from the study indicated that the vast majority of respondents supported research in emergency settings (88%). The concept of exception from informed consent was less well supported (35%). However, when a specific scenario of EFIC in a research study was presented to participants as it applied to their own potential participation, there was more acceptance (51%).[24] In their analysis, the authors also found that knowing someone that has seizures was significantly correlated with supporting EFIC enrollment in seizure trials for both themselves and for others when no surrogates were available.[24] Data was not collected on the type of relationship between the participant and the person they knew with seizures.

This trend of achieving higher rates of acceptance among people who are interviewed when they are presented with a specific situation applied to their own participation is supported by other studies. Lecouturier, et al. also found that people were more likely to accept EFIC research if the situation that was being presented to them was about personally being included rather than the abstract idea of the research itself.[28] Additionally, a study by McClure et al. showed that 49% of the interviewed emergency department patients and visitors believed enrolling patients without prior consent in an emergency situation would be acceptable, but a much higher 70% personally would be willing to be entered into a study prior to obtaining consent if it were important to learn about the treatment for a condition that currently has no good treatment.[12] Similarly, support for EFIC in the study by Longfield, et al. was found to be high (82%) when participants were giving approval specifically for the PolyHeme study in the local community; a trial designed to evaluate the safety and efficacy of Polymerized Human Hemoglobin (Poly-Heme) injection when used to treat patients in hemorrhagic shock following traumatic injuries. This is in contrast to the 64% of participants who responded favorably to the idea of research without prior consent in general with no specific study in mind.[29] The remaining 36% in the Longfield, et al. study consisted of 20% of participants who said they were unwilling and 16% of participants who said they were unsure about participation in emergency research.

Dickert and Kass' study from 2005 fills some of the gaps that were not addressed by previously mentioned studies (i.e. not eliciting opinions from participants in a forum that allowed them to consider the issues and discuss them in a more in-depth manner). This study on perceptions of EFIC was done among people who would have been

potential candidates for emergency research participation if a trial for SCD was available. Due to their recent emergency event and the fact that they are representative of those who would be included in EFIC research, their opinions are unique and potentially more important from an ethical standpoint than those that could be elicited from the general population. In this study, the authors found that the acceptance of EFIC research among a population of people who had survived a sudden cardiac death incident was higher than the previous reports from studies among the general population such as the Biros, Sargent, and Miller or Longfield, et al. studies.[25] Again, this is significant because the participants were people who are representative of a population that could be included in an EFIC study on cardiac arrest. The study was also unique in that it utilized qualitative methods which can enhance understanding and allow for deeper discussions of difficult and complex issues when compared to the quantitative surveys that have been used by other investigations.

Illness Experience and Perceptions

Given the results from the Dickert and Kass study, one can hypothesize that perhaps the personal experience of illness influences perceptions of participants on a particular study. Other research has pointed toward this association as well, including the Sugarman, et al. study where the authors listed locations from where patients were recruited as a potential limitation of the study given the population that would be present in those areas. The results may have been biased since the interviews were conducted in medical oncology, radiation oncology, and cardiology clinics, where a significant proportion of respondents had a serious disease.[15] Although this study included many

individuals with personal experience with serious diseases, it did not consider the experience of having family or friends with serious illnesses.

Sugarman, et al.'s briefly consideration of personal experience with illness as a potential source of influence on a patient's views of research in 1998 was followed by a study in 2000 by Trauth, et al. on public attitudes regarding willingness to participate in medical research studies. They used a random digit dial telephone survey method to collect information on persons in southwestern Pennsylvania. The results of the study indicated that 46% of those surveyed would be willing to take part in a medical research study focusing on a new treatment for a specific disease that was of concern to them; 29% were undecided and 25% were unwilling. However, the authors found that under certain hypothetical circumstances, such as having cancer, over half of those who were undecided said they would be willing to participate.[23] This finding suggests that the idea of being personally exposed to cancer has a strong influence on the opinions of participants and especially among those who were initially undecided.

Trauth, et al. also found that health status of the respondent's close family and friends had a significant impact on the respondent's willingness to participate; those with family or close friend with an illness were much more willing to participate (58%) than those who did not (39%), whether they were ill themselves or not ($p<0.001$). This study therefore supports the hypothesis that having a relative or friend who has an illness is a determinant in the willingness to participate in research and suggests that perhaps this is a stronger motivator than having the illness oneself. The authors postulate that the reason for personal experience with illness as a motivator is because experiencing the illness or

watching someone close go through the difficult experience serves to increase the perception of one's own vulnerability and therefore increases willingness to participate.[23]

Other evidence for the influence of illness experience on perceptions of research exists in non-EFIC situations such as the study by Burns, et al. that was carried out among patients and their significant others in clinics, intensive care unit waiting rooms, and public venues. Here, one of the variables significantly associated with willingness to participate included having an ongoing illness ($p=0.01$). The authors found that 58.7% of respondents, as compared to 46.0% in the study by Trauth et al, were willing to participate in a study focusing on a new treatment for a disease that was of concern to them.[19] Additionally, the authors identified clinical circumstances that have a significant positive effect on willingness to participate that included having an ongoing, non fatal disease with no known cure and being critically ill with a 50/50 chance of survival.[19]

On the qualitative side, there is evidence from Smith, et al. that personal experience with illness influences perceptions of research in focus groups of women in the African American community. If the research addressed an illness or disease that correlated with a personal or family medical problem, this encouraged participation.[21] These salient quotes represent the essence of the concepts we are trying to quantitatively understand and also points toward the value of qualitative studies to arrive at an in-depth understanding of opinions, allowing respondents to develop their thoughts and reasoning behind support or opposition to medical research:

> "When you're faced with a deadly disease, then it's a little easier to say, 'I don't have anything to lose,' you know, 'I don't have anything to lose. I have a shot in the dark that might work. So why not?'"
>
> "I think when you have something that touches you, you're more prone [to participate in research]. If you know your mother is suffering with breast cancer, you're going to likely help that cause because you know what your mother went through."[21]

Trauth, et al. found similar trends when attempting to identify the factors affecting older African American women's decisions to join a cancer screening trial. One of the factors that the women said influenced their willingness to participate was the experience of having a loved one with cancer. As one would expect, joiners were more likely than non-joiners to report having a close relative with cancer. According to Trauth, et al., among those who had a close relative with cancer, they were 2.31 (unadjusted OR) or 2.35 (adjusted OR) times as likely to join the trial as those who did not have a close relative with cancer. Women in the study made comments about how their loved ones' experiences with cancer forced them to be introspective, recognize that they too were at risk and pushed them to the realization that they should be getting screened for cancer.[22]

Summary and Study Relevance

These and other studies indicate that personal illness experience may affect a person's perception of EFIC. However, this hypothesis has yet to be studied in-depth with a large, diverse sample of individuals. It is important to study the influence of personal experience with illness on levels of acceptance and understanding of EFIC

because if there is a difference in opinions and knowledge, this may change the way that researchers and IRB committees think about and implement CC practices. These data may have important impacts on which populations ought to be consulted in CC efforts, and how views of CC participants with or without experience with the disease ought to be interpreted. Additionally, it will help IRBs and investigators to better understand the potential impact of EFIC enrollment on different types of subjects. Thoughtfully implemented emergency research is much needed to identify and confirm the best practices for treatment of emergency medical conditions in order to advance the care of critically ill adults and children.

Chapter 3: Project Content

Methods

The data used for this thesis was collected from the Emory IRB approved ethics component of the ProTECT™ III project described previously. The study population therefore includes participants of community consultation events for ProTECT™ III. A standardized, quantitative survey was developed to be implemented by all sites participating in ProTECT™ III. Responses to the survey were collected in an aggregate manner on a NETT database and individually using Excel.

The NETT EFIC working group's database, WebDCU, collected de-identified information on CC activities conducted as part of the ProTECT™ III study from 14 academic and medical centers around the country. The NETT database was used to centrally store data and track the progress of the ProTECT™ III study among others. Of the 16 hubs that were involved in the ProTECT™ III study, 14 of those hubs had entered data into the system by the time this analysis was completed. Data quality control and regulatory compliance with assurance activities were completed by NETT's data management team. The NETT EFIC working group and ProTECT™ leadership developed a standardized survey to be used at all of the different hubs with the option of small changes to customize the survey when needed. WebDCU was used to collect this information which pertained to the following major domains:

- Type of CC activity
- Community consulted

  - Number of participants
  - Intended audience
  - Demographic distribution of CC attendees
- Duration of the event
- Aggregated data from CC participants' responses to a survey assessing their views of and understanding of the ProTECT™ III study

The survey was cognitively pre-tested (under Emory protocol IRB00007665) to be sure that the questions were clear, communicated the right information and could be administered across a wide range of situations. Pre-testing involved both in-person and telephone interviews. Pre-test subjects were reflective of the populations that were to be encountered in the field. This iterative process of pre-testing was done by first administering the survey and then asking a set of questions to evoke how the subject arrived at their answers. They were asked about their thought process for each question with regard to: understanding the question, operative assumptions, the process of response construction, and their views on the sensitivity of questions. Problematic questions that did not convey the intended meaning or invoke the intended thought processes were identified, modified, and then tested again. After all the problems were identified and corrected, the survey was finalized and distributed for implementation at each site. The major domains of the survey instrument included the following:

- Attitudes of participants toward:
  - The importance and acceptability of the ProTECT™ III study
  - The use of the EFIC process
  - The CC process in which they participated

  - The opt-out process employed for ProTECT™ III
- Willingness to be enrolled in the ProTECT™ III study
- Understanding of relevant study details discussed in CC
- Demographic data

Demographic information including gender, ethnicity, race, and education was collected using multiple choice answers with a space for participants to write in a race for the "Other" category. Data on the attitudes towards ProTECT™ III and EFIC as well as willingness to be enrolled were collected using Likert scale questions on a 5 point scale ranging from strongly agree to strongly disagree. Data on study-specific understanding and EFIC understanding was collected using a series of multiple choice knowledge questions.

The surveys were administered at each individual site per the protocol. The sites were then asked to tally their total numbers for each of the given domains and enter this aggregate information in WebDCU. The total number of participants in WebDCU contributing to the ProTECT™ III aggregated data is 8585. However, not all of this data was collected using the exact standardized instrument that was developed by the NETT group. As previously mentioned there were circumstances that allowed for the use of a customized version of the survey (telephone random digit dialing surveys). Also, some of the hubs started their data collection before the finalized survey was developed. Of those hubs that used the finalized survey, there were 3300 participants.

Individual-level data from the CC surveys was necessary to connect demographics of a participant with their answers in order to see what associations

between the demographics and perceptions of EFIC and ProTECT™ III existed. Also, the research question about whether knowledge about the trial would affect perceptions of EFIC and ProTECT™ III could not be answered if the knowledge of each individual participant was not assessed with respect to their answers about perception. Due to the fact that the individual-level data was critical to the understanding of the research questions in analysis, the EFIC leadership asked each hub to submit either hard copies of the surveys collected from participants or an electronic copy of the individual responses (either in pdf or excel spreadsheet format) to Emory University's ProTECT™ III ethics study team.

After a series of requests, most of the sites that had used the specific format of questionnaire of interest and had data available at the time of analysis sent in their individual-level data. The data were then entered, cleaned, and streamlined into an excel spreadsheet. Importantly, the individual-level data was still not identifiable, as surveys were filled out anonymously; no identifiers were present on data sent to Emory investigators. This individual-level data was also linked to the aggregate data by the event name. Thus, the investigators could see not only what type of CC was done, but also look at the individual responses and correlations of demographic data and understanding of specific questions and answers.

Statistical analysis of the data was done using SAS 9.2. Analysis was mostly descriptive, but also included bivariate analyses with chi-square tests for proportions and t-test for comparing means when appropriate. The Likert scale questions of perception of EFIC and ProTECT™ III were initially collected on a 5 point scale with 1 being very important or strongly agree and 5 being not important at all or strongly disagree.

However, for analysis these responses were grouped together into three categories: agree, neutral, and disagree. The agree category contained responses of 1 and 2, the neutral category contained responses of number 3, and the disagree category included those responses of 4 or 5.

Understanding scores from the ProTECT™ III and EFIC-specific knowledge questions were developed after meetings with NETT EFIC group and consultation with a local Emory statistician. Each of the possible combinations of answers were explored and categorized into different levels of understanding based on group consensus deciding which answers were the most important to be correct. There were two questions related to knowledge about ProTECT™ III and each question was graded on a scale of 0 to 2 where those participants with the most complete understanding were given a 2 and those with little to no understanding were given a 0. Therefore, a participant who answered both of the knowledge questions correctly would get an overall understanding score of 4. A participant who did not answer any of the questions correctly would receive an understanding score of 0.

The ethics portion of the ProTECT™ III study was not specifically designed or powered to test any specific associations, but rather the intent was to use existing data to provide preliminary results that may be systematically tested in future EFIC studies. This study was included under the IRB approval of the CC component of the ProTECT™ III trial. The letter of approval from Emory University's IRB is located in the Appendix.

Results

Results are provided describing the study population, participants' attitudes toward EFIC research by their experience with illness, and factors that influence the relationship between attitudes toward EFIC and personal experience with TBI.

Study Population

Data from 12 out of the 14 sites were analyzed as these sites had used the finalized questionnaire and individual-level data from these areas were available at the time of analysis. Our study population included the 2620 individual surveys out of 3300, which is 79.4% of the total number of surveys available for this portion of the ProTECT™ III community consultation study. Those participants that were not included in analysis were either excluded per their request through checking a box that did not allow their information to be used for research or their surveys had not been received at the time of data analysis. The study population represents states from around the country (see Figure 1 and Table 1) and is therefore geographically diverse.

As seen in Table 2, the study population is composed of slightly more females (56%) than males (44%). About 27% of the population fell in the age range of 18-24, 16% in the 25-34 range, 24% in the 35-49 range, 25% in the 50-64 range, and 8% in the 65 and up category. With a mean age of about 40 years, about half of participants had completed 4 years or more of college education with another 35% having completed 1-3 years of college (some college or technical school). The racial and ethnic composition of

the participants was 77.9% White, 13.4% Black, 5.7% Asian, 0.6% Native Hawaiian or other Pacific Islander, 1.1% American Indian or Alaska Native, and 3.5% other.

Among participants in the study, 8.3% of them had suffered a TBI themselves (see Table 3). Another 17.9% knew family or friends who had experienced a TBI. Therefore, about a quarter of participants were categorized as having had personal experience with TBI either themselves or from family member and friend. Three quarters of the study population had no personal TBI experience which includes those persons who answered that they only knew someone else (not a family member or friend) who had suffered a TBI.

In Table 4, significant differences in demographic characteristics were found between those who had personal experience with TBI and those who did not. Specific differences were noted for were age ($p<0.0001$) and race, specifically being Asian ($p=0.0116$) or American Indian ($p=0.0003$). Additionally, the proportion of Blacks was close to being statistically different between the two groups ($p=0.0848$). Understanding scores were also found to be significantly different between those with personal TBI experience and those without ($p=0.0265$). Those participants with personal TBI experience were slightly older with a higher proportion of them being Blacks and American Indians or Alaska Natives. This group also had proportionally less Asians than the no experience group and the mean understanding of risks and benefits of ProTECT™ III was lower than the no TBI experience group.

Attitudes towards ProTECT™ III and EFIC Research

The questions on attitudes towards ProTECT™ III came from the standardized survey (see Appendix). The main questions of interest were:

Likert Scale Questions
6. The ProTECT study is an important study to do.
7. After hearing about the possible benefits and risks of the ProTECT study medication, you believe that it is acceptable to test this medication in traumatic brain injury patients.
8. Sometimes no family member can be found to make medical decisions for patients with traumatic brain injury. It is okay to include those patients in the ProTECT study without consent.
9. If you had a traumatic brain injury and no family member could be found to make decisions for you, you would be okay with being included in the ProTECT study without consent.
10. If you had a traumatic brain injury and a family member agreed to include you in the ProTECT study, you would be okay with being included.

On the whole, a very large majority (92.5%) of participants from the ProTECT™ III CC events agreed that the study was important to do (see Table 5). The bulk of respondents also agreed that ProTECT™ III was acceptable given the risks and benefits of participation (88.2%). Less favorable responses were found for the last three domains. When participants were asked if they thought that it was okay to include people in general without their consent when their surrogates cannot be found, 54.1% agreed. However, when the situation was personalized, a slightly higher percentage of people agreed that it was okay if they were included in the ProTECT™ III study if their family

members could not be found for consent (70.8%). An even larger percentage of people (86.4%) were agreeable to being included in ProTECT™ III study if their family members were consulted.

When analyzing the differences in responses between those who did have a personal experience (family, friends or self) with TBI and those who did not, the data showed no real differences between participants' responses on whether the ProTECT™ III study was important to do. Table 6 shows that participants in both groups strongly supported the ProTECT™ III study as more than 90% had favorable responses. Similarly, there was no significant difference in participants' views on whether it was acceptable to test the medication in TBI patients with more than 85% agreeing. For the question 10 on whether or not participants would be okay with personally being included in the ProTECT™ III study if their family members had consented for them, high levels of concurrence were found in both experience groups.

The differences between those with and those without personal TBI experience emerged in the questions related to consent in the ProTECT™ III study. Those participants who did have personal experience with the disease were significantly ($p=0.0007$) more likely to agree with the idea that it is okay to include TBI patients in the ProTECT™ III study without consent when no family member can be found to make medical decisions for the patient (59.8% concurrence versus 52.3%). It can also be seen in Table 6 that among those with personal TBI experience, participants were more likely to agree to being included personally in ProTECT™ III without consent (74.1% compared to 69.6%) even though this was not a statistically significant relationship ($p=0.0628$).

In order to examine the relationship between the type of personal TBI experience that participants had and their responses to the perception questions, analysis was done where each of the different combinations of experience were separated (see Table 7). The general trend in the data follows that those participants with both self and family/friend TBI experience have the highest rates of acceptance of emergency research, followed by those with family/friend TBI experience. Those that have only experienced a TBI themselves had the least favorable responses to the research. While most of these relationships were not statistically significant, the trends in the data are apparent. The comparisons that are closest to the significance level are those that compare both to self experience and family/friend to self experience, especially with respect to including patients without consent ($p=0.1968$ for both to self comparison) and approving family members as surrogates for consent ($p=0.1312$ for family to self comparison). An example of this trend is shown in Table 7 where participants were asked if it was okay to include patients without their consent (question 8). 69.2% of those who had both types of experience agreed with this statement as compared to 59.8% of those with only family/friend experience and 57.6% of those with only self experience. This same pattern applies to question 9 about being okay to be personally included in ProTECT™ III without consent; 76.9% of those with both experiences, 75.0% of those with family/friend experience, and 71.2% of those with self experience agreed.

In addition to looking at how the perceptions of emergency research were affected by the different types of personal experience, the relationship between knowledge about the ProTECT™ III study and types of TBI experience was examined. Knowledge of the risks of the study and overall knowledge of ProTECT™ III were both statistically

different between the various combinations of TBI experience. Those participants who had either family/friend experience or both types of experience were more likely to score well on the knowledge questions than those participants who had only experienced TBI themselves (see Table 8 and 9). The comparisons between both and self experience and family and self experience were statistically different for risks knowledge ($p=0.0191$ and $p<0.0001$ respectively) and for overall knowledge ($p=0.0194$ and $p=0.0001$ respectively). There was no statistical difference between the both and family/friend experience groups, however, the data suggested that the trend was such that the family/friend group scored higher than the group of individuals with both personal and family experience.

Factors That Influence the TBI Experience and EFIC Attitudes Relationship

As previously mentioned, the factors that were statistically different between the groups of those with TBI experience and those without were age, race (specifically being Asian, or American Indian) and understanding of risks and benefits. Since the percentage of American Indians and Asians was low, these two groups were not deemed to likely affect the overall results and were not further analyzed. The difference in proportions of Black participants was almost significant and as they were a rather large group, this characteristic as well as age and ProTECT™ III knowledge were further explored to examine the relationship between personal TBI experience and attitudes towards emergency research.

Age

In looking at the breakdown of age groups, the major change in proportions of those who have personal TBI experience and those who do not happens around age 35.

Therefore, the strata used were 35 and up and under 35 as shown in Table 10. Among those who were under 35 years of age, personal experience with TBI did not have as large of an effect on the perceptions of ProTECT™ III and EFIC as is evidenced by the lack of statistically significant differences between the two groups in this age bracket for question 8 (okay to include patients without consent), question 9 (okay to be personally included without consent) and question 10 (okay to be included if family member agreed); p=0.1641, p=0.5287, and p=0.5067 respectively. The percentage of participants under 35 years of age who responded favorably to including patients in ProTECT™ III without consent was 50.7% for the personal TBI experience group and 47.3% for the no experience group; this was a small and non-significant difference (3.4%). However, in the older population (35 and up), the percentage of participants with TBI experience who agreed to inclusion of patients in ProTECT™ III without consent was 65.2% compared to 56.4% of those without TBI experience; a significant difference of 9.4% in concurrence (p=0.0038).

Race

The stratification of the data into non-Black and Black participant groups produced some results that are distinct from the non-stratified data trends. Among those who were non-Black, more statistically significant differences were seen in the last three questions about consent between the personal TBI experience group and the no personal experience group (see Table 12). Interestingly, in the Black stratum, a non-significant paradoxical relationship was found between personal TBI experience and perceptions of ProTECT™ III. Those with personal experience with TBI that were Black were less likely to have a favorable response to all five of the questions. Most notably, there was

an 8.5% difference in responses to the question regarding whether patients would personally be okay with being included in ProTECT™ III without their consent.

ProTECT™ III Knowledge

The last stratification was done based on understanding scores. Those participants who demonstrated complete understanding of the risks and benefits of the ProTECT™ III study were placed in one stratum and those with any lower levels of knowledge on ProTECT™ III were positioned to the other. Among those in the complete understanding stratum, only one question yielded statistically significant differences between the personal TBI experience groups (see Table 13); among those participants who had a complete understanding of the study, those who had personal TBI experience were still more likely to answer favorably to the question of whether or not it was okay for people to be included in ProTECT™ III without their consent (p=0.0449). In the strata of participants with an incomplete understanding of the emergency research study, the same question 8 had significant difference between experience groups (p=0.0130), but favorable response rates to question 10 were also statistically different.

Summary of Mediating Factors

Table 11 summarizes the effects of personal TBI experience on favorable responses to question 8 about the acceptability of including TBI patients in general in ProTECT™ III without consent. The percentage difference in agreement with question 8 between those participants with TBI experience and those without is shown in decreasing order for both the non-stratified data and then within each of the stratum used during analysis. The stratum where personal TBI experience appeared to influence perceptions

of emergency research the most strongly was among those who belonged to a race other than Black (9.64% difference). This stratum is followed by the 35 and over group (8.81% difference) and the group with an incomplete understanding of the risks and benefits of pro (8.31% difference). This information in Table 11 gives us an idea of the extent to which each of the factors analyzed using stratification had an effect on the relationship between personal TBI experience and attitudes towards ProTECT™ III.

Chapter 4: Discussion, Conclusion and Recommendations

Discussion

The hypothesis that an individual's experience with TBI, whether from their own TBI or with family and friends, would affect their perceptions and attitudes towards EFIC research and the ProTECT™ III study was supported in our data to a limited extent. The differences found were not as large as predicted even though there were some consistent trends. No significant differences were found in the questions presented to participants about whether or not they thought that ProTECT™ III was an important study to do and whether they thought that it was okay to test progesterone in TBI patients (questions 6 and 7). Both questions received very high levels of support consistent with the Sugarman, et al. paper that found 90% support for medical research in general.[15]

The areas where the biggest differences between the experience and non-experience groups were found were the questions that examined participants' attitudes towards the exception from consent aspect of EFIC; questions 8, 9, and 10. The aggregate responses showed that a small majority of people, a little more than 50%, concurred with the use of exception from informed consent in an emergency situation (question 8). This is consistent with the rate found by McClure, et al. in a study with emergency room patients.[12] Question 9 asked about exception from consent in a slightly different way; participants were asked, "If you had a traumatic brain injury and no family member could be found to make decisions for you, would you be okay with being included in the ProTECT™ III study without consent?" Similar to what was found in the Lecouturier, et al. and Biros, Sargent, and Miller papers, there was a relationship in the

data to the way in hypothetical situations that people were presented with and their respective attitudes.[28 24] People were more likely to accept the premise of EFIC research if the hypothetical situation presented to them is about personally being included rather than considering the acceptability of the research abstractly. The rate of responding favorably to being personally included in ProTECT™ III without consent was much higher (70.8%) than the rate of concurrence with the idea of patients in general being included in ProTECT™ III without consent (54.1%). As one might expect, when participants were asked if it was okay to be included in ProTECT™ III if their family had given consent for them, there was even higher favorable response rate than the question where the scenario was personal inclusion without consent; more than 85% of participants answered favorably to having their family members be surrogates for consent in emergency research. This level of acceptance is similar to the rate of acceptance that one finds for medical research in general which makes sense since prospective consent would still be obtained in the hypothetical situation presented. Therefore, participants may feel more comfortable with this answering favorably since prospective consent is a process that they accustomed to experiencing.

Interestingly, the main shifts in acceptability of ProTECT™ III and EFIC associated with personal TBI experience seems to happen in the proportion of those individuals with neutral opinions. The data from this study shows that rather comparable rates of disapproval of EFIC exist among those with and without personal TBI experience. This is the case with question 8 which asks if it is okay to include patients in ProTECT™ III without consent; 21.4% of those with personal TBI experience and 21.9% of those without disagree. The higher proportion of favorable responses among those

with TBI experience appears to be attributed to a decrease in the neutral group. This finding is supported in the literature by the Trauth, et al. study where they found that under certain hypothetical circumstances like having cancer, over half of those who were originally undecided about participation in a clinical trial said they would be willing to participate.[23]

There are many explanations for how these small, but detectable differences in the attitudes towards EFIC and ProTECT™ III of those who had personal experience with the illness and those who did not have personal experience emerged. One theory is that individuals begin to feel more vulnerable when they or a loved goes through a serious disease like TBI.[22, 23] This vulnerability leads them to feel more eager to assist in research projects in hopes that treatment will be better if they ever need it. When participants have repeated exposure to these consequences of TBI, it may heighten their perceptions of the intensity of the illness. They may begin to have an appreciation for the gravity of TBIs. For example, one participant from this study wrote, "I think that a study like this could be beneficial. I think people would strongly disagree simply because they've never seen how bad a TBI can be. If they realized how bad it can be, they might be more accepting to the project because they would want everything possible to be done." Another participant commented, "More research and treatments are desperately needed for TBI patients. TBI is a devastating, heartbreaking epidemic in this country. I'll never get over what I've seen the man I love endure from his TBI 8 months ago- and his life has been ruined." Alternatively, a person who has experienced or know someone who has experienced a TBI may just appreciate the importance of the study or research question and act entirely altruistically. Individuals may also join support groups or other

disease-related organizations that advocate for research while dealing with their TBI or helping friends and family recover from TBI, and therefore they are more favorable toward conducting research on TBI regardless of whether there is consent.

A small difference also emerged in the data between the different types of personal TBI experience and the attitudes towards research. Although not statistically significant, it seems there is a somewhat cumulative effect of having additional personal TBI experience. Those persons with both self and family/friend experience are the most accepting of EFIC in the data, followed by individuals who have had only a family member or friend experience a TBI. Somewhat counter intuitively, those who have had the TBI themselves actually gave the least favorable opinions of ProTECT™ III. The stronger influence of having a family member or friend suffer a TBI may be due to this exposure to the consequences of TBI previously discussed. It would then make sense that if a person who had seen a family member or friend suffer a TBI and also had experienced their own TBI, they would be even more conscious of the problems that can happen from TBI as well as the likelihood of getting a TBI. This may motivate them to want to promote research in the area of TBI to improve care for the condition. This relationship between family/friend TBI experience and more positive views of emergency research is supported in the literature through a study done by Trauth, et al. that found that health status of the respondent's close family and friends had a significant impact on the respondent's willingness to participate, whether they were ill themselves. In fact, the study found that the respondent's own illness did not increase the likelihood of his/her willingness to participate in research.[22] Trauth, et al.'s study therefore suggests that

perhaps having a relative or friend suffer through an illness is a stronger motivator than having the illness oneself to be involved in research activities.

The type of personal TBI experience that an individual had was also correlated with the level of knowledge about ProTECT™ III that was achieved. The data from this study suggest that having had a family member or close friend suffer a TBI is associated with having higher levels of knowledge about ProTECT™ III, and more specifically the risks of the study. This may be due to the fact that participants who have had family/friends experience a TBI have been in the caregiver role for them and therefore may have been in charge of managing medical treatments for the loved one. This increased exposure to the health care system in a situation may have caused an increase in health literacy and awareness of risks. These participants with personal family/friend TBI experience and greater knowledge of the risks were even more willing to be included than their counterparts with less knowledge and only self TBI experience.

The difference in responses found between those who did have personal TBI experience and those who did not was smaller than anticipated. These unexpected results may be related to the demographic and other characteristics of participants that were analyzed in the results; age, race and knowledge. The fact that the responses of the older age group were more likely to be affected by the individual's personal experience with TBI could be explained by the fact that this older group has had more time to be exposed to the harsh consequences of TBI and are now more interested in advancing medical knowledge and treatment of TBI or are more prone to feeling vulnerable. As a Trauth, et al. study among older women found that participants in the study made comments about how their loved ones' experiences made them realize that they were getting older and

were more vulnerable to the illness.[22] Perhaps when a younger person sees a loved one have a fall or accident that causes a TBI, they think that it would never happen to them. However, as people get older, perhaps have witnessed more people with TBIs and really have more to lose as far as leaving their families uncared for, their opinions become more affected by the personal illness experience.

Another potential effect modifier of the results of the relationship between personal TBI experience and views on EFIC was being Black or African American. Among participants who were not Black, the relationship between attitudes toward ProTECT™ III and personal experience with TBI followed the non-stratified trend, but was much stronger. Among the non-Black study population, each of the last three questions (8, 9 and 10) which asked about participation in emergency research were found to have significant differences between those with and those without personal TBI experience. Unexpectedly, the relationship between attitudes toward ProTECT™ III and personal experience with TBI among those who were Black was the inverse of the trend discovered in the non-stratified data. Blacks with personal TBI experience actually had less favorable views of ProTECT™ III than those without. This relationship holds for all five questions. These findings contradict some studies such as those by Trauth, et al. and Smith, et al. that posit that personal experience motivates participation in clinical trials among African Americans. [21, 22] However, both of these studies were conducted using in-depth interviews and focus group discussions which provide a more intimate and deep discussion forum for participants; whereas in this study, the type of community consultation activity did not always allow for these types of in-depth discussions. Conversely, a study by Hull, et al. supports the findings in this study. Hull, et al. found

that patients were more likely to support having the opportunity to give permission (versus being notified) in a research scenario that involved use of non-identifiable information or samples if they were Black.[30]

Potential explanations of this unexpected result include the possibility that the experiences with TBI treatment among Blacks were unpleasant clinical interactions. According to a Richardson, et al. article, which found significant support and occasional adamant opposition to conducting emergency research, participants often spoke about specific personal experiences with medical care or research as the basis for both positive and negative opinions. For example, one participant of the Richardson, et al. study who believed that no medical research should be conducted without the expressed consent of the individual, relayed a story about a medical procedure done on his family member without the knowledge or consent of the patient or his next of kin.[31] Perhaps the African Americans in this study were victims of poor health care interactions and, therefore, increased personal experience with TBI actually meant more opportunities for the health care system to fail them. Furthermore, there is some historical mistrust between the African American community and medical researchers due to events such as the Tuskegee Syphilis Study. One Black CC participant from this study wrote in the comments section, "I do not like the way this was presented to me. This seems like yet another scheme at black genocide. I'm personally offended to be completely honest." Mistrust among Blacks of the medical community could be adding to the negative feelings toward research in emergency settings which requires an exception from informed consent. It is also possible that among Blacks, having personal TBI experience

for leads people to feel they are in a position to provide a more informed consent and therefore they are less willing to relinquish that opportunity.

The last potential effect modifier analyzed in this study is knowledge or understanding of the risks and benefits of ProTECT™ III. We found those individuals with TBI experience tend to have lower knowledge scores than those without. This finding is not supported by the literature which suggests that either there is no effect of experience with illness on knowledge or that there is a positive effect. Usually, people who have personal illness experience tend to be more knowledgeable about the illness disease event that has affected them or their loved one. This has been shown in the literature on TBI showing that people with personal experiences appear to be better-informed about brain injury than other subgroups.[32, 33] It would not be surprising that people who have experienced brain injury themselves or have observed someone close to them struggle with the aftermath of brain injury are better informed than other people in the lay public,[32] however, that is not the case in this study. Reasons for this discrepancy may be related to the fact that the understanding questions of this survey are not specifically linked to the everyday knowledge of TBI that the literature tested. The discrepancy may also be related to the decline in neurological function of those participants who had suffered a TBI themselves. People who have had a TBI often experience long-term difficulty remembering or recalling information.[3] As one participant of this study wrote on the survey, "My memory was affected that's why I wrote I don't know on all questions on front [related to risks and benefits]. I can't remember."

Upon stratification of our data based on knowledge scores, we find that the effect of personal experience among those who have a complete understanding of the study risks and benefits is diminished. However, the effect of personal TBI experience was slightly more pronounced in the stratum of those with an incomplete understanding of the study. In general, the acceptance of ProTECT™ III and EFIC is higher among those who do have the complete understanding. It is somewhat intuitive that the participants who really understand the study's risks and benefits would respond more favorably to a study such as ProTECT™ III with low risk and potential for direct benefit. On the other hand, acceptance is lower among those who do not have a complete understanding of risks and benefits of the study, but personal TBI experience increases favorable responses among those with an incomplete understanding. This finding suggests that personal experience may really be a motivating factor for these participants.

This study does not make a strong claim about the relationship between personal TBI experience and attitudes towards an emergency research study on TBI. There is some evidence that consent issues are more favorably viewed by those with personal TBI experience, but it does not appear that there is a large difference. Some trends are suggested but it does not always go in the direction one would expect as is the case with the Black population. The differences in attitudes towards ProTECT™ III are not nearly as dramatic as anticipated. The lack of strong associations is not viewed as a failure, but rather has important implications in that perhaps it is not as important to focus on recruiting participants from survivor or support groups for a particular illness as previously thought since their knowledge on the subject is not superior to other groups

and they do not appear to have radically different attitudes towards EFIC as compared those individuals with no personal experience.

Strengths

According to the 2010 US Census reports, the racial and ethnic composition of the United States as a whole was as follows among those who claim only one race: 72.4% White, 12.6% Black, 4.8% Asian, 0.2% Native Hawaiian or other Pacific Islander, 0.9% American Indian or Alaska Native and 6.2% Other.[34] Therefore, our study population is fairly representative racially of the general US population, but has less Hispanics than reported in the 2010 census. This racial representativeness of the US population is one of the strengths of this study over previous investigations. Others include a large sample size and the use of a standardized tool to collect data that was extensively pre-tested before implementation.

Limitations

One of the main limitations of this study is that it was not specifically designed or powered to test any specific associations. The sampling was determined by the participants that each hub recruited for their CC events. The intent of this study was to use existing data to provide preliminary results that may be systematically tested in future EFIC studies. Other limitations include the use of a closed ended survey. Since a survey such as the one used here does not allow for in-depth discussions, often the rationale behind a participant's nature of the objections is not clear. There may be differences in points of view and reasoning behind people's choices to select a given category of the Likert scale, but that is not shown in the data. Also, the survey was not necessarily

designed to collect detailed information on participants' experience with TBI and could maybe elicit more detailed information if more questions and survey space were dedicated to collecting information on personal TBI experience. Not to mention, the study was limited in that the final version of the survey was lacking questions which asked about the presence of permanent disability a person has experienced or their family member or friends with TBI have experienced.

Conclusion

Among those participants who have either experienced a TBI themselves or have had a family member or friend suffer a TBI, there was a slightly higher level of acceptance of ProTECT™ III and EFIC than those who did not have the same TBI experience. Age, race, and knowledge of the study were all factors that influenced the ways in which personal TBI experience affected attitudes toward ProTECT™ III and EFIC. Notably, among African Americans, having personal TBI experience actually decreased the positive response to ProTECT™ III and EFIC. These findings of small differences in attitudes may guide institutional review boards and investigators in community-consultation strategies for future waiver of or exception from informed consent studies as well as deepen our understanding of how participants decide to participate in emergency research.

Recommendations

Medical emergencies such as heart attack, stroke, seizures, and TBIs remain serious public health problems.[2, 3, 35, 36] The lack of effective and evidence-based treatments for these emergencies is a cause for concern. More research needs to be done

to find out what best practices are in these serious situations. This research will most likely need to be done under exception from informed consent regulations. Therefore, we need to improve practices of EFIC and understanding of patients' attitudes surrounding EFIC.

There does appear to be some trend in the relationship between personal TBI experience and attitudes toward EFIC, but further studies are needed to confirm these trends and verify the magnitude of difference in opinions between the two experience groups. This future research will need to expand the amount of information they collect on illness experience history in order to get a clearer picture of the relationship with attitudes. Also, it there may be some benefit to a qualitative component to future research as the qualitative methods can help tease out these deeper issues like reasons for objection to EFIC that could not be captured in a survey. Participants may also be able to more fully develop opinions about EFIC given the increased time and attention given to participants in in-depth interviews and focus groups.

Given the results of this study, those individuals with personal TBI experience do not have views on emergency research that are radically different from those without. This may mean that IRBs will decide it is not as high of a priority to include this group in CC activities. However, further studies are recommended to verify this finding. Every effort to better implement and increase participation in this kind of research should be made to reduce the burden of trauma and emergency conditions in the United States and hopefully this data from this study will help to assuage some of the current reluctance among the research community to take part in EFIC trials, which is partly attributed to lack of clear direction on how best to conduct the required community consultation

component. Emergency research is much needed to identify and confirm the best practices for treatment of emergency medical conditions. Thoughtfully implementing these clinical trials of emergency medicine may advance the care of critically ill adults and children.

References

1. CDC. State-Specific Mortality from Sudden Cardiac Death --- United States, 1999. *MMWR* 2002; http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5106a3.htm. Accessed April 9, 2011.

2. CDC. Stroke Facts and Statistics. *Stroke* 2010; http://www.cdc.gov/stroke/facts_statistics.htm. Accessed April 9, 2011.

3. CDC. Injury Prevention & Control: Traumatic Brain Injury. 2010; http://www.cdc.gov/TraumaticBrainInjury/statistics.html#3. Accessed April 9, 2011.

4. FDA. Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent Requirements for Emergency Research. In: DHHS, ed2011.

5. FDA. 21CFR50.24 Exception from informed consent requirements for emergency research1996.

6. Biros M. Struggling with the rule: the exception from informed consent in resuscitation research. *Acad Emerg Med.* Apr 2007;14(4):344-345.

7. Ragin DF, Ricci E, Rhodes R, Holohan J, Smirnoff M, Richardson LD. Defining the "community" in community consultation for emergency research: findings from the community VOICES study. *Soc Sci Med.* Mar 2008;66(6):1379-1392.

8. Richardson LD, Quest TE, Birnbaum S. Communicating with communities about emergency research. *Acad Emerg Med.* Nov 2005;12(11):1064-1070.

9. Halperin H, Paradis N, Mosesso V, Jr., et al. Recommendations for implementation of community consultation and public disclosure under the Food and Drug Administration's "Exception from informed consent requirements for emergency research": a special report from the American Heart Association Emergency Cardiovascular Care Committee and Council on Cardiopulmonary, Perioperative and Critical Care: endorsed by the American College of Emergency Physicians and the Society for Academic Emergency Medicine. *Circulation.* Oct 16 2007;116(16):1855-1863.

10. Barsan B. NETT: Neurological Emergencies Treatment Trials. http://www.nett.umich.edu/nett/welcome. Accessed April 9, 2011.

11. Emory. ProTECT Overview. *ProTECT Progesterone for the Treatment of Traumatic Brain Injury* http://sitemaker.umich.edu/protect/home. Accessed April 9, 2011.

12. McClure KB, DeIorio NM, Gunnels MD, Ochsner MJ, Biros MH, Schmidt TA. Attitudes of emergency department patients and visitors regarding emergency exception from informed consent in resuscitation research, community consultation, and public notification. *Acad Emerg Med.* Apr 2003;10(4):352-359.

13. Perner A, Ibsen M, Bonde J. Attitudes to drug trials among relatives of unconscious intensive care patients. *BMC Anesthesiol.* 2010;10:6.

14. Triner W, Jacoby L, Shelton W, et al. Exception from informed consent enrollment in emergency medical research: attitudes and awareness. *Acad Emerg Med.* Feb 2007;14(2):187-191.

15. Sugarman J, Kass NE, Goodman SN, Perentesis P, Fernandes P, Faden RR. What patients say about medical research. *IRB.* Jul-Aug 1998;20(4):1-7.

16. Treweek S, Doney A, Leiman D. Public attitudes to the storage of blood left over from routine general practice tests and its use in research. *J Health Serv Res Policy.* Jan 2009;14(1):13-19.

17. McCann SK, Campbell MK, Entwistle VA. Reasons for participating in randomised controlled trials: conditional altruism and considerations for self. *Trials.* 2010;11:31.

18. Tosounidis TI, Kontakis GM. Clinical research: the patients' perspectives. *Injury.* Jun 2008;39(6):631-635.

19. Burns KE, Magyarody N, Jiang D, Wald R. Attitudes and Views of the General Public Toward Research Participation. *Intern Med J.* Jan 17 2011.

20. Comis RL, Miller JD, Aldige CR, Krebs L, Stoval E. Public attitudes toward participation in cancer clinical trials. *J Clin Oncol.* Mar 1 2003;21(5):830-835.

21. Smith YR, Johnson AM, Newman LA, Greene A, Johnson TR, Rogers JL. Perceptions of clinical research participation among African American women. *J Womens Health (Larchmt).* Apr 2007;16(3):423-428.

22. Trauth JM, Jernigan JC, Siminoff LA, Musa D, Neal-Ferguson D, Weissfeld J. Factors affecting older african american women's decisions to join the PLCO Cancer Screening Trial. *J Clin Oncol.* Dec 1 2005;23(34):8730-8738.

23. Trauth JM, Musa D, Siminoff L, Jewell IK, Ricci E. Public attitudes regarding willingness to participate in medical research studies. *J Health Soc Policy.* 2000;12(2):23-43.

24. Biros MH, Sargent C, Miller K. Community attitudes towards emergency research and exception from informed consent. *Resuscitation.* Dec 2009;80(12):1382-1387.

25. Dickert NW, Kass NE. Patients' perceptions of research in emergency settings: a study of survivors of sudden cardiac death. *Soc Sci Med.* Jan 2009;68(1):183-191.

26. Pentz RD, Billot L, Wendler D. Research on stored biological samples: views of African American and White American cancer patients. *Am J Med Genet A.* Apr 1 2006;140(7):733-739.

27. Karlawish J, Rubright J, Casarett D, Cary M, Ten Have T, Sankar P. Older adults' attitudes toward enrollment of non-competent subjects participating in Alzheimer's research. *Am J Psychiatry.* Feb 2009;166(2):182-188.

28. Lecouturier J, Rodgers H, Ford GA, et al. Clinical research without consent in adults in the emergency setting: a review of patient and public views. *BMC Med Ethics.* 2008;9:9.

29. Longfield JN, Morris MJ, Moran KA, Kragh JF, Jr., Wolf R, Baskin TW. Community meetings for emergency research community consultation. *Crit Care Med.* Mar 2008;36(3):731-736.

30. Hull SC, Sharp RR, Botkin JR, et al. Patients' views on identifiability of samples and informed consent for genetic research. *Am J Bioeth.* Oct 2008;8(10):62-70.

31. Richardson LD, Wilets I, Ragin DF, et al. Research without consent: community perspectives from the Community VOICES Study. *Acad Emerg Med.* Nov 2005;12(11):1082-1090.

32. Hux K, Schram CD, Goeken T. Misconceptions about brain injury: a survey replication study. *Brain Inj.* May 2006;20(5):547-553.
33. Guilmette TJ, Paglia MF. The public's misconception about traumatic brain injury: a follow up survey. *Arch Clin Neuropsychol.* Mar 2004;19(2):183-189.
34. U.S.CensusBureau. Overview of Race and Hispanic Origin: 2010. *2010 Census Briefs* 2011; http://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf.
35. CDC. Heart Disease Fact Sheet. 2010; http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm. Accessed April 9, 2011.
36. CDC. Epilepsy: Basics. 2010; http://www.cdc.gov/epilepsy/basics/faqs.htm#4. Accessed April 9, 2011.

Tables and Figures

Figure 1: NETT Hubs and Centers[10]

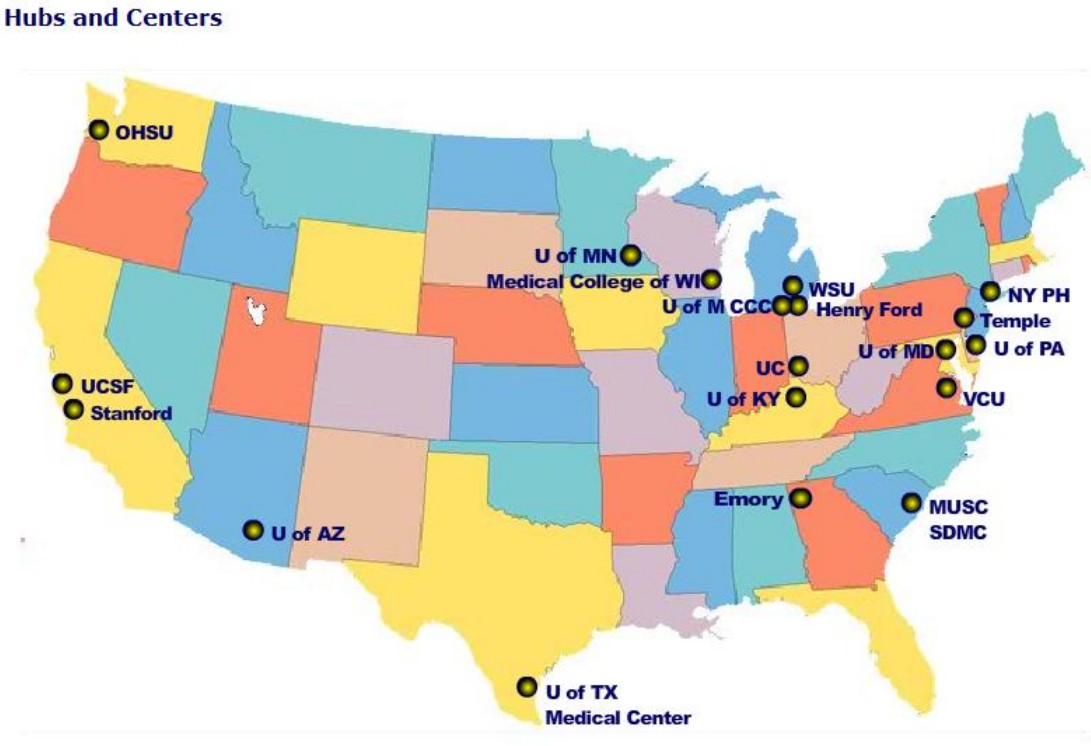

Table 1: Geographic Distribution of Participants (n= 2620)

Hub	n	% n
Arizona	26	0.99%
Cincinnati	248	9.47%
Emory	241	9.20%
HFHS	97	3.70%
Kentucky	904	34.50%
Maryland	85	3.24%
OHSU	75	2.86%
Stanford	216	8.24%
Temple	263	10.04%
Texas	324	12.37%
UCSF	93	3.55%
Wayne	48	1.83%
TOTAL	**2620**	**100%**

Table 2: Study Population Characteristics

		n	%
Gender (n= 2578, 42 missing)			
	Male	1135	44.03%
	Female	1443	55.97%
Age Distribution (n=2567, 53 missing)			
	Mean (Std Dev)	40.08	(16.63)
	15-17	8	0.31%
	18-24	688	26.80%
	25-34	407	15.86%
	35-49	620	24.15%
	50-64	639	24.89%
	≥ 65	205	7.99%
Highest Education Level Completed (n=2566, 54 missing)			
	Never attended school or only attended Kindergarten	3	0.12%
	Grades 1-8 (Elementary)	13	0.51%
	Grades 9-11 (Some high school)	41	1.60%
	Grade 12 or GED (High school graduate)	299	11.65%
	College 1-3 years (Some college or technical school)	920	35.85%
	College 4 years or more (College graduate)	1290	50.27%
Ethnicity (n=2506, 114 missing)			
	Hispanic	136	5.43%
	Not Hispanic	2355	93.97%
	Unsure/Don't know	15	0.60%
Race (n=2538, missing 82)			
	White	1977	77.90%
	Black or African American	340	13.38%
	Asian	145	5.71%
	Native Hawaiian or Other Pacific Islander	16	0.63%
	American Indian or Alaska Native	28	1.10%
	Other	79	3.50%

Table 3: Personal Experience with TBI among Participants (n= 2578, 42 missing)

TBI Experience	n	% (≠100%)
Who do you know that has experienced a TBI?		
Self	214	8.30%
Family or Friend	461	17.88%
Someone else	731	28.36%
No	1317	51.09%
Personal Experience		
Yes (If answered yes to self or family/friend)	636	24.67%
No	1942	75.33%

Table 4: Characteristics Analyzed for Differences between Those with Personal TBI Experience and Those Without

		Personal Exp n (%)	No Personal Exp n (%)	Difference	P-Value
GENDER		n=2540 (80 missing)			
	Male	264 (42.58%)	856 (44.58%)	Chi Square= 0.7625	0.3825
	Female	356 (57.42%)	1064 (55.42%)		
AGE		n=2529 (91 missing)			
	Mean (SD)	42.14 (16.12)	39.67 (16.71)	Satter T-test= 3.25	0.0012*
	15-17	4 (0.65%)	3 (0.16%)	Chi Square= 28.2660 MH Chi Square= 10.0973	<.0001* 0.0015*
	18-24	131 (21.16%)	531 (27.80%)		
	25-34	80 (12.92%)	323 (16.91%)		
	35-49	178 (28.76%)	438 (22.93%)		
	50-64	180 (29.08%)	458 (23.98%)		
	≥ 65	46 (7.43%)	157 (8.22%)		
EDUCATION		n= 2530 (90 missing)			
	Never attended or only Kindergarten	0 (0.00%)	2 (0.10%)	Chi Square= 8.3636 MH Chi Square= 3.7201	0.1373 0.0538
	Grades 1-8 (Elementary)	3 (0.48%)	10 (0.52%)		
	Grades 9-11 (Some high school)	16 (2.58%)	24 (1.26%)		
	Grade 12 or GED (High school graduate)	75 (12.08%)	216 (11.31%)		
	College 1-3 years (Some college or technical school)	232 (37.36%)	670 (35.10%)		
	College 4 years or more (College graduate)	295 (47.50%)	987 (51.70%)		
ETHNICITY		n= 2468 (152 missing)			
	Hispanic	38 (6.28%)	95 (5.10%)	Chi Square= 3.2662	0.1953
	Not Hispanic	561 (92.73%)	1759		

			(94.42%)		
	Unsure/Don't know	6 (0.99%)	9 (0.48%)		
RACE		n= 2502 (118 missing)			
	White	468 (76.97%)	1495 (78.93%)	Chi Square= 1.0459	0.3065
	Black	93 (15.27%)	238 (12.55%)	Ch Square= 2.9699	0.0848
	Asian	21 (3.45%)	116 (6.12%)	Chi Square= 6.3675	0.0116*
	Pacific Islander	3 (0.49%)	11 (0.58%)	Chi Square= 0.0636	0.8009
	American Indian	15 (2.47%)	13 (0.69%)	Chi Square= 13.2134	0.0003*
	Other	25 (4.11%)	60 (3.16%)	Chi Square= 1.2439	0.2647
UNDERSTANDING SCORE		n= 2489 (131 missing)			
	Mean (SD)	2.85 (1.21)	2.97 (1.18)	Satter T-test= -2.22	0.0265*
	0	40 (6.54%)	126 (6.71%)	Chi Square= 13.4174	0.0094*
	1	51 (8.33%)	106 (5.65%)		
	2	110 (17.97%)	260 (13.85%)		
	3	171 (27.94%)	583 (31.06%)		
	4	240 (39.22%)	802 (42.73%)		

*significance was determined at a p-value of <0.05

Table 5: Attitudes toward ProTECT™ III

	n	%
6. Important Study to Do (n=2533, 87 missing)		
Agree	2344	92.54%
Neutral	174	6.87%
Disagree	15	0.59%
7. Acceptable to test in TBI (n=2536, 84 missing)		
Agree	2237	88.21%
Neutral	260	10.25%
Disagree	39	1.54%
8. OK to include patients without consent (n=2538, 82 missing)		
Agree	1372	54.06%
Neutral	612	24.11%
Disagree	554	21.83%
9. You would be OK being included w/o consent (n=2550, 70 missing)		
Agree	1805	70.78%
Neutral	368	14.43%
Disagree	377	14.78%
10. You would be OK being included if family member agreed (n=2543, 77 missing)		
Agree	2198	86.43%
Neutral	254	9.99%
Disagree	91	3.58%

Table 6: Attitudes toward ProTECT™ III by Personal TBI Experience

Personal Experience	Yes [n(%)]	No [n(%)]	Exp vs. No Exp
6. Important Study to Do (n= 2521, 99 missing)			
Agree	567 (91.30%)	1765 (92.89%)	Chi Square= 4.5806 (p= 0.1012)
Neutral	47 (7.57%)	127 (6.68%)	
Disagree	7 (1.13%)	8 (0.42%)	
7. Acceptable to test in TBI (n=2524, 96 missing)			
Agree	541 (87.26%)	1686 (88.55%)	Chi Square= 0.7746 (p= 0.6789)
Neutral	69 (11.13%)	189 (9.93%)	
Disagree	10 (1.61)%	29 (1.52%)	
8. OK to include patients without consent (n=2526, 94 missing)			
Agree	372 (59.81%)	1087 (52.31%)	Chi Square= 14.4058 (p= 0.0007)*
Neutral	117 (18.81%)	491 (25.79%)	
Disagree	133 (21.38%)	417 (21.90%)	
9. You would be OK being included w/o consent (n=2538, 82 missing)			
Agree	461 (74.12%)	1334 (69.62%)	Chi Square= 5.5346 (p= 0.0628)
Neutral	74 (11.90%)	294 (15.34%)	
Disagree	87 (13.99%)	288 (15.03%)	
10. You would be OK being included if family member agreed (n=2531, 89 missing)			
Agree	538 (86.77%)	1651 (86.39%)	Chi Square= 4.5477 (p= 0.1029)
Neutral	53 (8.55%)	199 (10.41%)	
Disagree	29 (4.68%)	61 (3.19%)	

*significance was determined at a p-value of <0.05

Table 7: Types of Personal TBI Experience and Attitudes towards ProTECT™ III

Types of Experience	Both [n(%)]	Family [n(%)]	Self [n(%)]	Statistics
6. Important Study to Do (n=621)				
Agree	38 (97.44%)	377 (91.95%)	152 (88.37%)	Chi Square= 6.1327 (p= 0.1895)
Neutral	0 (0.00%)	29 (7.07%)	18 (10.47%)	
Disagree	1 (2.56%)	4 (0.98%)	2 (1.16%)	
7. Acceptable to test in TBI (n=620)				
Agree	37 (94.87%)	354 (86.34%)	150 (87.72%)	Chi Square= 9.0728 (p= 0.0593)
Neutral	0 (0.00%)	49 (11.95%)	20 (11.70%)	
Disagree	2 (5.13%)	7 (1.71%)	1 (0.58%)	
8. OK to include patients without consent (n=622)				
Agree	27 (69.23%)	246 (59.85%)	99 (57.56%)	Chi Square= 2.7388 (p= 0.6024)
Neutral	4 (10.26%)	80 (19.46%)	33 (19.19%)	
Disagree	8 (20.51%)	85 (20.68%)	40 (23.26%)	
9. You would be OK being included w/o consent (n=622)				
Agree	30 (76.92%)	310 (75.06%)	121 (71.18%)	Chi Square= 1.7617 (p= 0.7795)
Neutral	3 (7.69%)	49 (11.86%)	22 (12.94%)	
Disagree	6 (15.38%)	54 (13.08%)	27 (15.88%)	
10. You would be OK being included if family member agreed (n=620)				
Agree	34 (87.18%)	363 (88.11%)	141 (83.43%)	Chi Square= 11.8769 (p= 0.0183)*
Neutral	2 (5.13%)	38 (9.22%)	13 (7.69%)	
Disagree	3 (7.69 %)	11 (2.67 %)	15 (8.88%)	

*significance was determined at a p-value of <0.05

Table 8: Types of Personal TBI Experience and Knowledge about ProTECT™ III

Knowledge	Both	Family	Self	Statistics
Risks (n=615)				
0	4 (10.26%)	55 (13.41%)	37 (22.29%)	Chi Square= 31.4116 (p<0.0001)*
1	12 (30.77%)	85 (20.73%)	61 (36.75%)	
2	23 (58.97%)	270 (65.85%)	68 (40.96%)	
Benefits (n=615)				
0	1 (2.63%)	45 (10.95%)	20 (12.05%)	Chi Square= 6.7903 (p=0.1474)
1	17 (44.74%)	140 (34.06%)	69 (41.57%)	
2	20 (52.63%)	226 (54.99%)	77 (46.39%)	
Overall (n=612)				
0	0 (0.00%)	28 (6.86%)	12 (7.23%)	Chi Square= 32.6354 (p<0.0001)*
1	2 (5.26%)	23 (5.64%)	26 (15.66%)	
2	12 (31.58%)	61 (14.95%)	37 (22.29%)	
3	9 (23.68%)	118 (28.92%)	44. (26.51%)	
4	15 (39.47%)	178 (43.63%)	47 (28.31%)	

*significance was determined at a p-value of <0.05

Table 9: Types of Personal TBI Experience and Knowledge about ProTECT™ III Using Means

	Both	Family	Self	Both vs. Family	Both vs. Self	Family vs. Self
Risks (n=615)						
Mean (SD)	1.49 (0.68)	1.52 (0.72)	1.19 (0.78)	T-test= -0.32 (p=0.7478)	T-test= 2.41 (p=0.0191)*	T-test= 4.83 (p<0.0001)*
Benefits (n=615)						
Mean (SD)	1.50 (0.56)	1.44 (0.68)	1.34 (0.69)	T-test= 0.62 (p=0.5397)	T-test= 1.49 (p= 0.1403)	T-test= 1.54 (p=0.1243)
Overall (n=612)						
Mean (SD)	2.97 (0.97)	2.97 (0.06)	2.53 (1.25)	T-test= 0.03 (p=0.9739)	T-test= 2.39 (p=0.0194)*	T-test= 3.85 (p=0.0001)*

*significance was determined at a p-value of <0.05

Table 10: Stratification on Age Groups of Under 35 and 35 and Up

UNDER 35 YEARS n=1103			
Personal Experience	**Yes [n(%)]**	**No [n(%)]**	**Difference Exp vs. No Exp**
6. Important Study to Do (43 missing)			
Agree	194 (91.08%)	767 (90.55%)	Chi Square= 0.4681 (p= 0.7913)
Neutral	17 (7.89%)	75 (8.85%)	
Disagree	2 (0.94%)	5 (0.59%)	
7. Acceptable to test in TBI (41 missing)			
Agree	177 (83.10%)	723 (85.16%)	Chi Square= 1.3015 (p= 0.5217)
Neutral	33 (15.49%)	109 (12.84%)	
Disagree	3 (1.41%)	17 (2.00%)	
8. OK to include patients without consent (43 missing)			
Agree	108 (50.70%)	401 (47.34%)	Chi Square= 3.6148 (p= 0.1641)
Neutral	46 (21.60%)	237 (27.98%)	
Disagree	59 (27.70%)	209 (24.68%)	
9. You would be OK being included w/o consent (37 missing)			
Agree	139 (65.26%)	539 (63.19%)	Chi Square= 1.2748 (p= 0.5287)
Neutral	32 (15.02%)	156 (18.29%)	
Disagree	42 (19.72%)	158 (18.52%)	
10. You would be OK being included if family member agreed (36 missing)			
Agree	177 (83.10%)	709 (83.02%)	Chi Square= 1.3597 (p= 0.5067)
Neutral	25 (11.74%)	114 (13.35%)	
Disagree	11 (5.16%)	31 (3.63%)	

35 YEARS AND UP **n=1464**			
6. Important Study to Do (37 missing)			
Agree	364 (91.92%)	979 (94.96%)	Chi Square= 6.1457 (p= 0.0463)*
Neutral	28 (7.07%)	49 (4.75%)	
Disagree	4 (1.01%)	3 (0.29%)	
7. Acceptable to test in TBI (36 missing)			
Agree	356 (90.13%)	946 (91.58%)	Chi Square= 1.1360 (p= 0.5667)
Neutral	32 (8.10%)	75 (7.26%)	
Disagree	7 (1.77%)	12 (1.16%)	
8. OK to include patients without consent (32 missing)			
Agree	259 (65.24%)	584 (56.43%)	Chi Square= 11.1566 (p= 0.0038)*
Neutral	66 (16.62%)	248 (23.96%)	
Disagree	72 (18.14%)	203 (19.61%)	
9. You would be OK being included w/o consent (24 missing)			
Agree	317 (79.65%)	780 (74.86%)	Chi Square= 4.1199 (p= 0.1275)
Neutral	38 (9.55%)	135 (12.96%)	
Disagree	43 (10.80%)	127 (12.19%)	
10. You would be OK being included if family member agreed (31 missing)			
Agree	355 (89.65%)	924 (89.10%)	Chi Square= 3.1712 (p= 0.2048)
Neutral	24 (6.06%)	83 (8.00%)	
Disagree	17 (4.29%)	30 (2.89%)	

*significance was determined at a p-value of <0.05

Table 11: Non-Stratified and Stratified Differences in Favorable Response to Inclusion of Patients in General in ProTECT™ III without Consent between Those with and Those without Personal TBI Experience

Strata	% Difference Bet Experience Group
Non-stratified	7.50%
Under 35	3.36%
35 and Over	8.81%
Non-Black	9.64%
Black	0.27%
Complete Understanding	6.63%
Incomplete Understanding	8.31%

Table 12: Stratification on Race by Black and Non-Black

BLACK PARTICIPANTS n=2201			
Personal Experience	**Yes [n(%)]**	**No [n(%)]**	**Difference Exp vs. No Exp**
6. Important Study to Do (65 missing)			
Agree	468 (92.31%)	1517 (93.12%)	Chi Square= 4.6005 (p= 0.1002)
Neutral	33 (6.51%)	106 (6.51%)	
Disagree	6 (1.18%)	6 (0.37%)	
7. Acceptable to test in TBI (61 missing)			
Agree	456 (89.76%)	1461 (89.52%)	Chi Square= 0.2355 (p= 0.8889)
Neutral	45 (8.86%)	152 (9.31%)	
Disagree	7 (1.38%)	19 (1.16%)	
8. OK to include patients without consent (55 missing)			
Agree	316 (61.96%)	856 (52.32%)	Chi Square= 17.5140 (p= 0.0002)*
Neutral	91 (17.84%)	423 (25.86%)	
Disagree	103 (20.20%)	357 (21.82%)	
9. You would be OK being included w/o consent (47 missing)			
Agree	393 (77.21%)	1151 (69.97%)	Chi Square= 11.6081 (p= 0.0030)*
Neutral	52 (10.22%)	256 (15.56%)	
Disagree	64 (12.57%)	238 (14.47%)	
10. You would be OK being included if family member agreed (50 missing)			
Agree	449 (88.39%)	1432 (87.16%)	Chi Square= 12.3427 (p= 0.0021)*
Neutral	34 (6.69%)	169 (10.29%)	
Disagree	25 (4.92%)	42 (2.56%)	

NON- BLACK PARTICIPANTS **n= 340**			
6. Important Study to Do (14 missing)			
Agree	81 (88.04%)	216 (92.31%)	Chi Square= 3.0074 (p= 0.2223)
Neutral	11 (11.96%)	16 (6.84%)	
Disagree	0 (0.00%)	2 (0.85%)	
7. Acceptable to test in TBI (15 missing)			
Agree	68 (75.56%)	194 (82.55%)	Chi Square= 2.7678 (p= 0.2506)
Neutral	19 (21.11%)	32 (13.62%)	
Disagree	3 (3.33%)	9 (3.83%)	
8. OK to include patients without consent (19 missing)			
Agree	47 (52.22%)	120 (51.95%)	Chi Square= 2.1238 (p= 0.3458)
Neutral	18 (20.00%)	61 (26.41%)	
Disagree	25 (27.78%)	50 (21.65%)	
9. You would be OK being included w/o consent (14 missing)			
Agree	55 (60.44%)	162 (68.94%)	Chi Square= 2.1334 (p= 0.3441)
Neutral	17 (18.68%)	35 (14.89%)	
Disagree	19 (20.88%)	38 (16.17%)	
10. You would be OK being included if family member agreed (17 missing)			
Agree	73 (81.11%)	193 (82.83%)	Chi Square= 0.6100 (p= 0.7371)
Neutral	13 (14.44%)	27 (11.59%)	
Disagree	4 (4.44%)	13 (5.58%)	

*significance was determined at a p-value of <0.05

Table 13: Stratification on Levels of Understanding

COMPLETE UNDERSTANDING (SCORE=4) n=1062			
Personal Experience	**Yes [n(%)]**	**No [n(%)]**	**Difference Exp vs. No Exp**
6. Important Study to Do (30 missing)			
Agree	227 (95.78%)	764 (96.10%)	Chi Square= 0.1953 (p= 0.9069)
Neutral	9 (3.80%)	29 (3.65%)	
Disagree	1 (0.42%)	2 (0.25%)	
7. Acceptable to test in TBI (29 missing)			
Agree	218 (91.98%)	751 (94.35%)	Chi Square= 1.8692 (p= 0.3927)
Neutral	17 (7.17%)	39 (4.90%)	
Disagree	2 (0.84%)	6 (0.75%)	
8. OK to include patients without consent (29 missing)			
Agree	154 (64.44%)	459 (57.81%)	Chi Square= 6.2058 (p= 0.0449)*
Neutral	36 (15.06%)	178 (22.42%)	
Disagree	49 (20.50%)	157 (19.77%)	
9. You would be OK being included w/o consent (25 missing)			
Agree	189 (79.41%)	610 (76.35%)	Chi Square= 1.1675 (p= 0.5578)
Neutral	20 (8.40%)	84 (10.51%)	
Disagree	29 (12.18%)	105 (13.14%)	
10. You would be OK being included if family member agreed (25 missing)			
Agree	226 (94.56%)	726 (90.98%)	Chi Square= 4.5989 (p= 0.1003)
Neutral	6 (2.51%)	48 (6.02%)	
Disagree	7 (2.93%)	24 (3.01%)	

PARTIAL OR NO UNDERSTANDING (SCORE<4) n=1453			
6. Important Study to Do (43 missing)			
Agree	321 (88.67%)	950 (90.65%)	Chi Square= 4.0743 (p= 0.1304)
Neutral	35 (9.67%)	92 (8.78%)	
Disagree	6 (1.66%)	6 (0.57%)	
7. Acceptable to test in TBI (40 missing)			
Agree	305 (84.49%)	888 (84.41%)	Chi Square= 0.1651 (p= 0.9208)
Neutral	48 (13.30%)	144 (13.69%)	
Disagree	8 (2.22%)	20 (1.90%)	
8. OK to include patients without consent (40 missing)			
Agree	205 (56.79%)	510 (48.48%)	Chi Square= 8.6862 (p= 0.0130)*
Neutral	76 (21.05%)	293 (27.85%)	
Disagree	80 (22.16%)	249 (23.67%)	
9. You would be OK being included w/o consent (31 missing)			
Agree	258 (71.07%)	686 (64.78%)	Chi Square= 5.7272 (p= 0.0571)
Neutral	51 (14.05%)	202 (19.07%)	
Disagree	54 (14.88%)	171 (16.15%)	
10. You would be OK being included if family member agreed			
Agree	293 (81.39%)	876 (83.03%)	Chi Square= 8.4017 (p= 0.0150)*
Neutral	45 (12.50%)	149 (14.12%)	
Disagree	22 (6.11%)	30 (2.84%)	

*significance was determined at a p-value of <0.05

Appendices

IRB Approval

EMORY UNIVERSITY | Institutional Review Board

TO: Rebecca Pentz, MD
Principal Investigator

CC: Dixon Margie Hematology and Medical Oncology
Dickert Jr Neal RTP

DATE: June 1, 2010

RE: **Notification of Continuing Review Expedited Approval**
CR3_IRB00007665
IRB00007665
ASSESSING COMMUNITY CONSULTATION IN THE CONTEXT OF THE EMERGENCY RESEARCH EXCEPTION FROM INFORMED CONSENT

This is your notification that your above referenced Continuing Review was reviewed and APPROVED under the Expedited review process per 45 CFR 46.110 and 21 CFR 56.110. The approval is valid from 5/29/2010 until 5/28/2011. Thereafter, continued approval is contingent upon the submission of a continuing review request that must be reviewed and approved by the IRB prior to the expiration date of this study.

Any reportable events (serious adverse events, breaches of confidentiality, protocol deviation or protocol violations) or issues resulting from this study should be reported immediately to the IRB and to the sponsoring agency (if any). Any amendments (changes to any portion of this research study including but not limited to protocol or informed consent changes) must have IRB approval before being implemented.

Approved Consent Documents
Consent, community members: *version 3/16/2009*
Consent, formative interview: *version 8/7/2009*
Consent, IRB Chairs: *version 8/7/2009*
Consent, pre-test: *version 8/7/2009*
Consent, verbal: *version 3/16/2009*
Consent, web survey – IRB chair: *version 5/3/2009*
Consent, web survey – investigator: *version 5/3/2009*

Sincerely,

Sarah K. Clark, CIP
Senior Research Protocol Analyst
This letter has been digitally signed

Emory University
1599 Clifton Road, 5th Floor - Atlanta, Georgia 30322
Tel: 404.712.0720 - Fax: 404.727.1358 - Email: irb@emory.edu - Web: http://www.irb.emory.edu/
An equal opportunity, affirmative action university

Finalized ProTECT™ III Community Consultation Survey

Informed Consent Statement.

You are being asked to participate in a study of community consultation for the emergency exception of informed consent. The purpose of the study is to better understand community consultation with the goal of designing a method of evaluating community consultation. You are being asked because you have come to a community consultation meeting. The study will include about 300 people in the Atlanta area, depending on how many community members come to community consultation meetings. Your participation is filling out the attached survey containing 21 questions. It will take about 10 minutes to complete. There will be no personal identifiers on the survey. We ask that you put the survey in the box at the exit door when you leave so no one will know who filled it out. The only risk is that someone beside the research team will find out your answers. That risk is very small since there are no names or other identifiers on the survey. There are no benefits to you in participating. Your option is to refuse to fill out the survey. Your participation is entirely voluntary. You may refuse to answer any (or all) of the questions. If you have questions about this research, you may call Rebecca Pentz, 404 778 5694 or ask her now. If you have questions about your rights as a research participant you can call the Chair of the Emory IRB at 404 712 0720, or toll-free at 877 503 9797.

We would like to hear from you anonymously. We want to know about what you heard and find out what you think and how you feel about what we have shared with you today. There are no known risks involved in participating in this survey. Your participation in this survey is completely voluntary. You may refuse to participate, and not to answer any questions that you do need feel comfortable answering.
To start, five questions have been listed below related to the ProTECT study information that was shown and talked about today. Your answers will help us improve how we present this information to others at future community events.

---

1. The PROTECT study involves testing a new medication for treatment of traumatic brain injury. What is the study medication being tested? (Check only one)

__Estrogen __Progesterone __Steroids
__ I don't know

2. **In addition to standard medical care for TBI, which one of the following statements below is true about what type of treatment patients will receive if they are enrolled in the ProTECT study?** (Check only one)

__All patients in this study will be treated with the study medication.

__Patients in this study will be treated with **EITHER** the study medication **OR** a solution that looks like the study medication but it is not (it is a placebo).

__ I don't know

3. Which of the following are possible risks, or side effects, of receiving the ProTECT study medication?
(Check all that apply)

__ Blood clots

__ Hair growth

__ Changes in liver function /liver enzymes

__ Seizures

__ I don't know

4. Which of the following statements are true about the ProTECT study? (Check all that apply)

__ Some patients who are treated with the study medication might have reduced brain damage

__ No patient in this study will benefit directly

__ This study may result in improved treatment for future traumatic brain injury patients

__I don't know

5. Not all patients included in the ProTECT study will be treated with the study medication. How is it decided which treatment patients receive? (Check only one)

__Study doctors choose which patients need the study medication.

__ It is decided at random, like in a coin toss.

__ I don't know

Next, we would like to know your feelings and opinions about the ProTECT study. Please tell us how much you agree with each of the following six statements.

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
6. The ProTECT study is an important study to do.					
7. After hearing about the possible benefits and risks of the ProTECT study medication, you believe that it					

is acceptable to test this medication in traumatic brain injury patients.					
8. Sometimes no family member can be found to make medical decisions for patients with traumatic brain injury. It is okay to include those patients in the ProTECT study without consent.					
9. If you had a traumatic brain injury and no family member could be found to make decisions for you, you would be okay with being included in the ProTECT study without consent.					
10. If you had a traumatic brain injury and a family member agreed to include you in the ProTECT study, you would be okay with being included.					

11. Do you think that ProTECT researchers will seriously consider what community members like you have to say about this study before starting it?

__Yes __No __ I Don't know

12. Do you feel that you have been given enough information to give your informed opinion about whether you think it is ok for researchers to do the PROTECT study?

__Yes __No

12a. If you answered No, to question 12 above, what information would you still like to know?

_____
_____
_____

13. Have you or has anyone you know ever experienced a traumatic brain injury? (Check all that apply)

__Me __A family member or loved one __Someone else I know __No

14. A bracelet is available ahead of time that you can wear to tell doctors that you do NOT want to participate in this study. The bracelet says "PROTECT STUDY DECLINED." Doctors will not include eligible brain injury patients wearing these bracelets in the ProTECT study. Do you want to wear one of these bracelets?

__ Yes (Pick up a ProTECT brochure and contact the study team listed to get a bracelet sent to you)

__ No

14a. Can you tell us why you do or else do not want to wear a bracelet?

_____

Lastly, so that we can make sure we are hearing from a wide range of <<city, county, state>> residents, please complete the following final six questions about yourself.

15. What is your age: __ __ __ (years old):

16. Are you: __Male __Female

17. Are you Hispanic or Latino? __Yes __No __I don't know

18. Which one or more of the following would you say is your race: (Check all that apply)

__White

__Black or African American

__Asian

__Native Hawaiian or Other Pacific Islander

__American Indian or Alaska Native

__Other [specify]_____

19. What is the highest grade or year of school you completed?

__Never attended school or only attended kindergarten

__Grades 1 through 8 (Elementary)

__Grades 9 through 11 (Some high school)

__Grade 12 or GED (High school graduate)

__College 1 year to 3 years (Some college or technical school)

__College 4 years or more (College graduate)

20. **In addition to learning your thoughts and feelings about the ProTECT study, researchers would also like to use your answers to this survey to learn more about how best to talk with communities about studies like ProTECT. Because your name is not on this survey, nobody will be able to identify you with the answers you gave, they will be anonymous. Is it ok if researchers use your survey answers for this research purpose?**

__Yes __No

21. Please provide below, any additional comments, concerns or questions you would like to share with the ProTECT study team:

_____

_____

_____

_____

_____

Be sure to ask for a copy of the ProTECT research teams contact information on your way out if you would like to contact them further.

Return this survey to a study team member. ***Thank You!***