Published in final edited form as:

Resuscitation. 2013 June ; 84(6): 825–830. doi:10.1016/j.resuscitation.2013.01.030.

Why Persons Choose to Opt Out of an Exception from Informed Consent Cardiac Arrest Trial

Maria J. Nelson, MD, MCR, Nicole M. Delorio, MD, Terri A. Schmidt, MD, MS, Dana M. Zive, MPH, Denise Griffiths, BS, and Craig D. Newgard, MD, MPH

Center for Policy and Research in Emergency Medicine, Oregon Health and Science University, Portland, Oregon

Abstract

Background—We sought to characterize persons who requested to opt out of an exception from informed consent (EFIC) cardiac arrest trial and their reasons for opting out.

Methods—At one site of a multi-site, out-of-hospital, cardiac arrest EFIC trial (September 2007 – June 2009), persons who did not want to participate in the study could request an opt-out “NO STUDY” bracelet to prevent trial enrollment. We surveyed all persons who requested a bracelet by phone interview, web or mail. Opt-out bracelets were advertised in all public communication about the study, including community consultation and public disclosure efforts. Survey questions included demographics, Likert scale items about attitudes toward the trial and research in general, plus open-ended questions. We used descriptive statistics for standardized questions and qualitative analysis to identify common themes from open-ended questions.

Results—Sixty bracelets were requested by 50 individuals. Surveys were completed by 46 persons (92% response rate). Seventy percent of respondents agreed emergency research is important, but 87% objected to any research without consent. In the qualitative analysis, 5 overlapping themes emerged: questioning the ethics of EFIC research; concerns about how the study would impact end-of-life preferences; subjective emotions including sarcasm, anger, and allusions to past unethical research; negative reference to unrelated public health controversies; and objections to the study protocol based on misinformation.

Conclusions—A primary reason for opting out from this EFIC trial was opposition to all research without informed consent, despite stated support for emergency research. Understanding the demographics and beliefs of persons opting out may aid researchers planning EFIC studies and help provide clarity in future EFIC-related community education efforts.

Keywords

exception from informed consent; resuscitation research; research ethics; opt-out

© 2013 Elsevier Ireland Ltd. All rights reserved.

For correspondence: Craig D. Newgard, MD, MPH, Center for Policy and Research in Emergency Medicine, Department of Emergency Medicine, Oregon Health & Science University, 3181 SW Sam Jackson Park Road, mailcode CR-114, Portland, OR 97239, (503) 494-1668, newgardc@ohsu.edu.

Conflict of interest statement

No conflicts of interest to declare.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Informed consent is one of the basic tenets of protection for human subjects in clinical research. However, there are important, unanswered questions about the optimal treatment of people with emergent, time-sensitive conditions such as cardiac arrest and serious traumatic injuries. Because informed consent is not possible for patients with certain acute medical conditions or requiring time-sensitive interventions, the Food and Drug Administration (FDA) developed regulations creating safeguards for potential subjects in these trials, including requirements for community consultation and public disclosure.^{1, 2} While resuscitation research using the exception from informed consent (EFIC) regulations has become more common, researchers and regulatory bodies continue to struggle with both the ethics and logistics involved in conducting this type of research.⁹ IRB members have often found the community consultation and public disclosure regulations vague and difficult to implement; the most appropriate form of community consultation has not been defined.^{3, 4} The American Heart Association (AHA) has outlined steps to be taken in planning community consultation and public disclosure to allow flexibility among different communities.⁵ Studies have shown that the majority of people support resuscitation research using the EFIC, but some individuals seriously object to any interventional research without informed consent.^{6, 7}

Although federal regulations do not specifically require investigators to provide a mechanism for people to refuse potential enrollment in EFIC studies, some local IRBs require the provision of an opt-out option.⁸ Community characteristics of persons opting out of EFIC studies have been detailed,¹⁰ yet description of individuals opting out of EFIC trials and their reasons for doing so have not been previously published. Since an important component of EFIC research is building and maintaining a level of trust between the research community and the public, characterizing this population and understanding their reasons may aid researchers and regulatory bodies in addressing community concerns about this type of research.

The purpose of this study was to characterize persons opting out of an EFIC out-of-hospital cardiac arrest trial at one site of a multi-site resuscitation network and to detail common themes cited as reasons for opting out.

METHODS

Study design

This was a mixed-methods study using a structured survey (discrete quantitative questions and open-ended qualitative questions) administered either by phone, mail or internet. The sample included persons requesting an opt-out bracelet at a single-site participating in the Resuscitation Outcomes Consortium (ROC) Prehospital Resuscitation using an Impedance valve and Early vs. Delayed analysis (PRIMED) multi-center, out-of-hospital, cardiac arrest trial.^{11, 12} The study was approved by the Oregon Health & Science University IRB.

Setting

The ROC is a 10-site consortium in the United States and Canada funded by the National Institutes of Health (NIH) to conduct resuscitation trials in the out-of-hospital setting. The ROC PRIMED trial compared two interventions during out-of-hospital resuscitation from cardiac arrest: an impedance threshold device and duration of CPR prior to rhythm analysis. We conducted the current study at one ROC site (Portland, OR). ROC PRIMED, like other studies using the exception from informed consent, was evaluated by multiple IRBs at each ROC site. In Portland, 7 separate IRBs oversaw the local process of community consultation and public disclosure as part of the study's final IRB approval (specifically, there were five

hospital IRBs, one EMS agency IRB, and one public health IRB). Prior to ROC PRIMED, Portland-area investigators had conducted two previous EFIC studies in this community (the Public Access to Defibrillation [PAD] Trial and the ROC Hypertonic Saline Trial).^{13,14}

For the ROC PRIMED study, local investigators conducted community consultation followed by public disclosure using a variety of venues and methods. Over a 6-month period, the study team contacted 54 community organizations in the study region to arrange community consultation meetings and sent 413 IRB-approved letters to city officials, state representatives, senators, and neighborhood associations briefly explaining the project and offering to meet with them. Of the 54 community organizations approached, we were able to schedule and complete 13 presentations, with 296 attendees. IRB representatives attended all of the community presentations. We were unable to schedule a community presentation with the additional 41 organizations due primarily to: inability to find a time for the presentation, lack of response or lack of interest. We also sent a news release to regional media outlets (newspapers, radio, television, and newsletters), including multiple materials related to the study. The media release resulted in three newspaper articles (including the Associated Press) and multiple news stories on 3 local radio stations (including Oregon Public Broadcasting). We also sent articles in English and Spanish regarding the study to approximately 30 community newsletters. Furthermore, the study team created a public website to provide additional information about the study, answers to frequently asked questions, links to the national ROC website, and contact information to allow the direct communication between the public and the study team. Overall, the community response was positive (as interpreted by IRBs overseeing the project) and the study was approved. The public disclosure process followed the completion of community consultation and final IRB approval and included follow-up letters to all groups (54) and individuals (413) initially contacted about the study. We also created an additional press release for public disclosure that resulted in 10 additional newspaper and newsletter articles over the course of the study.

During each community consultation event and for all press releases, local IRBs mandated publicizing the opportunity for objectors to opt out of the trial by calling a specified phone number or visiting the study website. Information about opting out of the trial (phone number, email, and local study website) was provided in all public disclosure efforts. We distributed stainless steel opt-out bracelets stating “NO STUDY” to all interested persons (up to 4 per requesting party) to wear throughout the duration of the trial. During EMS training for the study, paramedics were specifically trained to look for an opt-out bracelet as part of the study exclusion criteria. At the conclusion of the study, all patients who had requested an opt-out bracelet were sent a letter letting them know that the study had been completed.

Subjects

All individuals who contacted the Portland ROC PRIMED investigators requesting to opt out of the study were approached for the survey. The survey was administered during the public disclosure phase (in conjunction with initiating opt-out bracelet distribution) and throughout the first 12 months of the clinical trial (September 2007 through June 2009). At the time of opt-out bracelet request, we asked the person to complete a voluntary, standardized survey administered by phone, in writing (by mail) or on-line, depending on the method of contact used by persons seeking to opt out of the study. All phone surveys were conducted by one investigator (MJN). For all persons requesting opt-out bracelets, the survey was optional and requesters received the bracelet(s) regardless of whether or not a survey was completed. All media coverage and written public disclosure described the process for opting out of the trial, but did not mention the survey.

Survey Design

The survey (Appendix) was developed by the investigative team based on extensive experience with survey research, medical ethics, EFIC regulations, previous EFIC trials and research assessing the process of conducting EFIC studies. The survey consisted of Likert scale questions, demographic questions and free-text responses. Survey content focused on opinions about the ethics and importance of medical research in general, specific to EFIC studies and regarding the ROC PRIMED trial. The majority of questions had been developed and used for a previous EFIC survey of visitors to the emergency department¹⁵ and have been used elsewhere.¹⁶ The survey was pilot tested using a group of volunteer research assistants (primarily college students, none of whom had prior or current involvement in EFIC research) as a surrogate group of community members, with minor resulting modifications to the survey.

When a call for an opt-out bracelet request was received, callers provided their mailing address, the number of bracelets requested (they were allowed to request bracelets for themselves and/or immediate adult family members, but not for general distribution) and were asked to complete the optional survey about their reasons for opting out. Those who left a message about opting out were contacted later by phone to gather pertinent information and administer the survey. In the event that the caller was not reached by phone or preferred to complete the survey in written form, a paper copy of the survey was included with the opt-out bracelet mailing. Callers requesting two or more bracelets by phone who completed the phone survey were sent additional surveys with a written invitation for other family members to complete the survey. Alternatively, bracelets could be requested via a web link from the Portland ROC website. Persons requesting bracelets through the web site were encouraged to access an electronic version of the survey. The phone, written and on-line surveys were identical.

Surveys completed by phone were transcribed directly to a paper version of the survey using the answers provided by the respondent during the interview. Web responses were transferred to paper versions of the survey for ease of comparison and consistency. Written surveys completed directly by persons receiving an opt-out bracelet were compiled with the other written surveys. Quantitative responses (Likert scale responses and demographic information) were entered into a Microsoft Access database and imported into a Microsoft Excel spreadsheet for tabulation.

Data Analysis

Descriptive statistics were used to characterize the sample and to report Likert scale responses. The five-point Likert scale (strongly agree, agree, neutral, disagree, strongly disagree) was collapsed to agree, neutral and disagree for analysis. Two authors (MJN and NMD) reviewed, coded and analyzed the free-text survey responses using standard qualitative methods.^{17,18} It was not possible to blind coders to the method used for survey completion (phone, paper or web). Investigators coded all free-text responses, identifying and annotating key ideas, phrases and recurring themes describing respondent's opinions. Each investigator independently compared the frequency of certain codes, associated phrases and representative quotes. They then worked together to compare and contrast precipitating themes for opting out of EFIC studies, including how they interacted with and influenced each other.

RESULTS

During the 18-month study period, 60 bracelets were requested by 50 individuals. Forty-six surveys were completed and analyzed (response rate 92%). No bracelets were requested

after the first year of trial enrollment and all persons requesting to opt out of the trial were approached about participation in the survey. The majority of respondents were Caucasian, female, highly educated, religious and over 50 years of age (Table 1).

Quantitative Results

Responses to the Likert scale questions are depicted in Figure 1. Respondents generally supported medical research in emergency medicine (70%), but objected to all research using EFIC, regardless of the study question, protocol or subject matter (87%). Most (82%) favored the rights of the individual over public health interests.

When asked to choose discreet reasons for opting out of the study (Table 2), 91% stated they would opt out of any study performed without prospective consent. Smaller proportions of respondents reported prior negative experience with medical research or preferred not to participate in any clinical research. A minority of persons objected to the institution (hospital) coordinating the research and any research with U.S. government sponsorship. Seventy-six percent reported unwillingness to participate in the ROC PRIMED study, in particular. When asked about the mechanism for learning about the study, 84% of respondents reported the newspaper, 11% listed TV and 16% stated “word of mouth.”

Qualitative Results

In the qualitative analysis, five overlapping themes emerged: (1) questioning the ethics and processes of EFIC research; (2) concerns about how this particular study would impact end-of-life preferences; (3) emotionally charged protests to EFIC research; (4) negative references to other public health controversies; and (5) objections to the study protocol based on misinformation. These themes are detailed below, with illustrative quotes included in Table 3.

The first theme focused on concerns about the ethics of EFIC research. A majority of persons opting out of the trial expressed strong concerns about the EFIC regulations. Many respondents emphasized the rights of the individual over the needs of the community. Several persons stated that it would be more ethical if the community were able to opt in, rather than opt out. Subjects endorsed a lack of faith in the public disclosure system and expressed concerns that many in the community could have missed the announcements and be unaware of the on-going trial. Some suggested that information should be distributed to everyone in the community (e.g. by mass mailing).

The second theme was the potential adverse impact of the trial on end-of-life preferences. Respondents commonly confused enrollment in the study with involuntarily being put on life-support. Many identified poor experiences with family members “on life support” or expressed concerns about “the quality of life” after implementation of the trial intervention, worrying that this intervention may “save people at the expense of who they are.” Others confused participation in the study with choosing a life-prolonging measure versus no resuscitation. Two respondents, in addition to opting out of the survey, specifically asked where they could get information about a DNR order or advance directives.

The third theme involved emotionally charged responses to the study and EFIC research. The topic of medical research without informed consent elicited a strong emotional outpouring from many respondents, often including inflammatory, emotionally-charged language. Several respondents did not want to reveal the media source where they learned of the trial because they thought researchers would “stop” the sources from advertising the study, not understanding that study investigators had issued press releases in order to inform the public. There was a common belief that every patient should receive standard, approved treatment as the default and that research-based treatment should only be provided by

individual request. Respondents indicated that being exposed to investigational treatment makes them feel like “lab rats”. The strength of individual emotions and tone used was noteworthy for strong elements of anger, fear, sarcasm, and distrust of institutions and government.

The fourth theme focused on negative references to previous public health controversies. Many respondents (particularly those responding through the web site) referenced previous public health controversies as support for their disagreement with the trial. Respondents cited water fluoridation, medical experiments in Nazi concentration camps, organ donation and previous EFIC studies conducted in this community.

The final theme involved objections to the study protocol based on misinformation about the trial. The misinformation involved both the PRIMED study and the process of medical research. Multiple persons requesting opt-out bracelets seemed to prefer no resuscitation in the event of cardiac arrest or were concerned that the study interventions would lead to inappropriate resuscitation. Other respondents cited personal medical conditions (e.g., a pacemaker/defibrillator) as reasons for not wanting to participate in the cardiac arrest trial. This theme had substantial overlap and interaction with theme two (adverse impact of the trial on end-of-life preferences).

DISCUSSION

To our knowledge, this is the first study to characterize persons opting out of an EFIC study and to elucidate reasons for opting out. The views represented by this small group of respondents are unlikely to represent the views of the larger community, as evidenced by the 7 involved IRBs independently interpreting community responses as supportive of the study and allowing the trial to proceed, as well as previous studies demonstrating general support for EFIC research.^{15,19} However, this group of dissenters, although modest in number, represents an important population who deserve special consideration. We found that persons opting out value emergency research but prioritize the interests and rights of the individual over those of the general community. Support for emergency care research, while opposing EFIC, suggests an under-appreciation of the challenges involved with conducting resuscitation research for patients with highly time-dependent conditions who are unable to provide prospective consent (e.g., out-of-hospital cardiac arrest). This may indicate a role for further community education about the ethics and challenges of resuscitation research and its potential for added value to community health. The strong emotional reaction by many of the respondents also suggests that there will be a group of people who strongly oppose this research, no matter the potential for benefit. Richardson similarly found that personal experiences often formed the basis for both positive and negative opinions about an EFIC study.²⁰

Although the FDA regulations regarding EFIC research do not preserve the right of self-determination of the research participant, they do create other protections while preserving a means to advance the science of resuscitation.²¹ In our sample of persons opting out of the trial, many expressed beliefs that EFIC studies are never acceptable and most cited objection to EFIC research as a primary reason for wanting to opt out. These findings suggest ideological differences and concerns about this type of research, rather than concern or opposition to specific details of the trial. Previous studies of attitudes toward EFIC research drew similar conclusions.^{15,16}

A number of persons in our study expressed concern about the processes involved in the federal regulations guiding EFIC research, specifically community consultation and public disclosure. Respondents also indicated mistrust of the primary institution conducting the

trial and the federal government. A substantive portion of our sample reported prior negative experiences with medical research, possibly a reflection of the select sample of community respondents. Additionally, nearly half of respondents admitted that they would want the new treatment if proven effective, though were unwilling to share in the equitable distribution of risk when testing the potential benefit. These findings suggest that certain people in a community may not agree with certain types of research or with public health efforts that prioritize community health over individual rights. In the context of planned research, they may disagree with certain principles of medical ethics (e.g., justice). The opt-out mechanism in this trial allowed these community members a mechanism to assert their individual beliefs and avoidance of potential study enrollment, while still allowing the study to proceed. Respecting a variety of beliefs and opinions, while still attempting to improve health outcomes through rigorous resuscitation science, remains challenging but feasible.

Two of the themes focused on misconceptions about the research protocol, including potential effects on end-of-life preferences and individual medical conditions. These findings highlight the complexity of educating the public about specific research studies, medical topics and details of research protocols. A portion of respondents held the misguided belief that study enrollment would interfere with existing Do Not Resuscitate (DNR) orders (an exclusion criterion for the trial) or that their end-of-life wishes would not be honored. It is possible that additional community education and two-way communication may have reduced such misconceptions about the study and reduced the number of persons opting out. However, the rigor of local community consultation and public disclosure processes for this trial were similar to those of other ROC sites and to other multicenter EFIC trials.²² Our results suggest that with current community consultation and public disclosure processes, there is a portion of the community who will not understand a given study or will receive misinformation about the project. In a previous study assessing the influence of media on opting out from an EFIC study, 23% of media reports contained errors about the research protocol.²³ Future efforts to reduce misinformation and improve community education about EFIC studies under consideration are greatly needed.

LIMITATIONS

Public perception of the PRIMED trial may have been influenced by previous press about a trauma resuscitation trial done by the same research network in this community. The trauma trial had significantly higher numbers of persons requesting to opt out, possibly because persons objecting to the PRIMED study already had a bracelet from the previous EFIC trial.^{23,24} However, the same team of investigators fielded all opt-out requests from the previous EFIC trial and felt that the themes identified in this study were similar to phone conversations with persons previously requesting opt-out bracelets.

Our findings may not be generalizable to all EFIC studies or to communities in other regions. Racial and ethnic minorities, particularly African Americans, have historically had greater mistrust of medical research,^{25–28} but these groups were not well-represented in our sample. Furthermore, our study site had the highest rate of opt-out requests among the 10 ROC sites involved in PRIMED, which could reflect ideals of a region known for rugged individualism, personal rights and strong efforts in end-of-life decision making. However, it is also possible that differing community consultation and disclosure efforts, broad publicizing of the opportunity to opt-out (including phone and web contact information) and more extensive media coverage also contributed to this finding. It will be important to replicate similar investigations in other regions and among broader populations to assess whether our findings are generalizable.

Finally, the majority of respondents in this study stated that they learned about the study through media sources (primarily newspaper, but some by television news), which only provided a one-way mechanism for communication. This scenario is common in community consultation processes for EFIC studies in the U.S., as two-way communication (interaction, discussion, opportunity to have questions directly answered) is not feasible with large populations. Nonetheless, our findings may reflect an emotional response by persons learning about the study without the opportunity to fully understand the research and propelled by inaccurate media reporting on the study (as demonstrated in a previous EFIC study²³).

CONCLUSION

Persons opting out of an EFIC trial on cardiac arrest at one site prioritized the rights of the individual over public health and the needs of the community. Respondents had concerns about the ethics of research without informed consent, regardless of subject matter or the study intervention. Additional attitudes and beliefs included concerns about infringement on end-of-life preferences and emotional responses of anger, fear and mistrust of the medical/research community. Many respondents cited inaccurate information about the study protocol as reasons for opting out. In better understanding the beliefs and attitudes of persons opting out of an EFIC trial, resuscitation researchers and regulatory bodies guiding EFIC studies may be able to improve the community-based processes guiding such research and to ensure an appropriate balance between individual rights and community/public health efforts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

FUNDING

This publication was made possible with support from the following sources: Oregon Clinical and Translational Research Institute (#UL1 RR024140, the National Center for Research Resources, a component of the NIH, and NIH Roadmap for Medical Research); and the Resuscitation Outcomes Consortium (ROC) Training Grant (#U01/HL-04-001, National Heart, Lung and Blood Institute), and the ROC cooperative grants. The ROC is supported by a series of cooperative agreements to 10 regional clinical centers and one data Coordinating Center (5U01 HL077863, HL077881, HL077871 HL077872, HL077866, HL077908, HL077867, HL077885, HL077885, HL077863) from the National Heart, Lung and Blood Institute in partnership with the National Institute of Neurological Disorders and Stroke, U.S. Army Medical Research & Material Command, The Canadian Institutes of Health Research (CIHR) - Institute of Circulatory and Respiratory Health, Defense Research and Development Canada, the Heart and Stroke Foundation of Canada, and the American Heart Association.

References

1. Adams JG, Wegener J. Acting without asking: An ethical analysis of the Food and Drug Administration waiver of informed consent for emergency research. *Ann Emerg Med.* 1999; 33(2): 218–223. [PubMed: 9922420]
2. Health and Human Services policy for protection of human subjects research--HHS. Final rule. *Fed Regist.* 1994; 59(104):28276. [PubMed: 10135123]
3. McClure KB, DeIorio NM, Schmidt TA, Chiodo GT, Gorman P. A qualitative study of Institutional Review Members' experience with reviewing proposals for exception from informed consent in resuscitation research. *J Med Ethics.* 2006; 33:298–293.
4. Nelson M, Schmidt TA, DeIorio NM, McConnell KJ, Griffiths DE, McClure KB. Community consultation methods in a study using exception to informed consent. *Prehosp Emerg Care.* 2008; 12(4):417–425. [PubMed: 18924003]

5. Halperin H, Paradis N, Mosesso V, Nichol G, Sayre M, Ornato JP, Gerardi M, Nadkarni VM, Berg R, Becker L, Siegler M, Collins M, Cairns CB, Biros MH, Vanden Hoek T, Peberdy MA. 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.
6. Sachs GA, Hougham GW, Sugarman J, Agre P, Broome ME, Geller G, Kass N, Kodish E, Mintz J, Roberts LW, Sankar P, Siminoff LA, Sorenson J, Weiss A. Conducting empirical research on informed consent: challenges and questions. *Irb*. 2003; (Suppl 25)(5):S4–S10. [PubMed: 14870730]
7. Smithline HA, Gerstle ML. Waiver of informed consent: A survey of emergency medicine patients. *Am J Emerg Med*. 1998; 16(1):90–91. [PubMed: 9451323]
8. <http://www.fda.gov/oc/ohrt/irbs/except.html>.
9. Mosesso VN Jr, Brown LH, Greene HL, Schmidt TA, Aufderheide TP, Sayre MR, Stephens SW, Travers A, Craven RA, Weisfeldt ML. Conducting research using the emergency exception from informed consent: The Public Access Defibrillation (PAD) Trial experience. *Resuscitation*. 2004; 61(1):29–36. [PubMed: 15081178]
10. Nelson MJ, Warden C, Griffiths DE, Zive D, Schmidt TA, Hedges JR, Daya M, Newgard CD. A Geospatial Analysis of Persons Opting Out of an Exception from Informed Consent Out- of- Hospital Clinical Trial. *Resuscitation*. 2009; 80:89–95. [PubMed: 19010580]
11. Aufderheide TP, Nichol G, Rea TD, Brown SP, Leroux BG, Pepe PE, Kudenchuk PJ, Christenson J, Daya MR, Dorian P, Callaway CW, Idris AH, Andrusiek D, Stephens SW, Hostler D, Davis DP, Dunford JV, Pirralo RG, Stiell IG, Clement CM, Craig A, Van Ottingham L, Schmidt TA, Wang HE, Weisfeldt ML, Ornato JP, Sopko G. A trial of an impedance threshold device in out-of-hospital cardiac arrest. *N Engl J Med*. 2011; 365(9):798–806. [PubMed: 21879897]
12. Stiell IG, Nichol G, Leroux BG, Rea TD, Ornato JP, Powell J, Christenson J, Callaway CW, Kudenchuk PJ, Aufderheide TP, Idris AH, Daya MR, Wang HE, Morrison LJ, Davis D, Andrusiek D, Stephens S, Cheskes S, Schmicker RH, Fowler R, Vaillancourt C, Hostler D, Zive D, Pirralo RG, Vilke GM, Sopko G, Weisfeldt M. Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest. *N Engl J Med*. 2011; 365(9):787–797. [PubMed: 21879896]
13. Hallstrom AP, Ornato JP, Weisfeldt M, Travers A, Christenson J, McBurnie MA, Zalenski R, Becker LB, Schron EB, Proschan M. Public-access defibrillation and survival after out-of- hospital cardiac arrest. *N Engl J Med*. 2004; 351(7):637–646. [PubMed: 15306665]
14. Bulger EM, May S, Kerby JD, Emerson S, Stiell IG, Schreiber MA, Brasel KJ, Tisherman SA, Coimbra R, Rizoli S, Minei JP, Hata JS, Sopko G, Evans DC, Hoyt DB. ROC investigators. Out of hospital hypertonic resuscitation after traumatic hypovolemic shock: a randomized, placebo-controlled trial. *Ann Surg*. 2011; 253(3):431–441. [PubMed: 21178763]
15. McClure KB, DeIorio NM, Gunnels MD, Ochsner MJ, Biros MH, Schmidt TA. Attitudes of ED patients and visitors regarding exception from informed consent in resuscitation research, community consultation, and public notification. *Acad Emerg Med*. 2003; 10:352–9. [PubMed: 12670849]
16. Triner W, Jacoby L, Shelton W, Burk M, Imarenakhue S, Watt J, Larkin G, McGee G. Exception from informed consent enrollment in emergency medical research: attitudes and awareness. *Acad Emerg Med*. 2007; 14(2):187–191. [PubMed: 17267533]
17. Miles, MB.; Huberman, M. *Qualitative Data Analysis: An Expanded Sourcebook*. 2. SAGE Publications; Thousand Oaks, CA: Sage; 1994.
18. Giacomini MK, Cook DJ. User's guides to the medical literature XXIII. Qualitative Research in Health Care, A Are the results of the study valid? *JAMA*. 2000; 284:357–362. [PubMed: 10891968]
19. Biros MH, Sargent C, Miller K. community attitudes towards emergency research and exception from informed consent. *Resuscitation*. 2009; 80(12):1382–1387. (i.e. the community generally supports EFIC rsch). [PubMed: 19818546]
20. Richardson L, Wilets I, Fish Ragin D, Holohan J, Smirnoff M, Rhodes R, Winkel G, Rodriguez M, Ricci E. Research without Consent: Community Perspectives from the *Community VOICES* Study. *Acad Emerg Med*. 2005; 12(11):1082–1090. [PubMed: 16264079]

21. Morris MC. An ethical analysis of exception from informed consent regulations. *Acad Emerg Med*. 2005; 12(11):1113–1119. [PubMed: 16264082]
22. Silbergleit R, Biros MH, Harney D, Dickert N, Baren J. Implementation of the exception from informed consent regulations in a large multicenter emergency clinical trials network: the RAMPART experience. *Acad Emerg Med*. 2012; 19:448–454. [PubMed: 22506949]
23. Nelson MJ, DeIorio NM, Schmidt TA, Griffiths DE, Daya M, Haywood L, Zive D, Newgard CD. Media Influence on Opting Out from an Exception to Informed Consent Out-of-Hospital Clinical Trial. *Annals of Emergency Medicine*. 2010; 55(1):1–8. [PubMed: 19682770]
24. Bulger EM, May S, Brasel KJ, Schreiber M, Kerby JD, Tisherman SA, Newgard C, Slutsky A, Coimbra R, Emerson S, Minei JP, Bardarson B, Kudenchuk P, Baker A, Christenson J, Idris A, Davis D, Fabian TC, Aufderheide TP, Callaway C, Williams C, Banek J, Vaillancourt C, van Heest R, Sopko G, Hata JS, Hoyt DB. Out-of-hospital hypertonic resuscitation following severe traumatic brain injury: a randomized controlled trial. *JAMA*. 2010; 304(13):1455–1464. [PubMed: 20924011]
25. Corbie-Smith G. The continuing legacy of the Tuskegee Syphilis Study: Considerations for clinical investigation. *American Journal of the Medical Sciences*. 1999; 317(1):5–8. [PubMed: 9892266]
26. Corbie-Smith G, Thomas SB, Williams MV, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. *Journal of General Internal Medicine*. 1999; 14(9):537–546. [PubMed: 10491242]
27. Fouad MN, Partridge E, Green BL, Kohler C, Wynn T, Nagy S, Churchill S. Minority recruitment in clinical trials: A conference at Tuskegee, researchers and the community. *Annals of Epidemiology*. 2000; 10(8 Suppl):S35–40. [PubMed: 11189091]
28. Freimuth VS, Quinn SC, Thomas SB, Cole G, Zook E, Duncan T. African Americans' views on research and the Tuskegee Syphilis Study. *Social Science & Medicine*. 2001; 52(5):797–808. [PubMed: 11218181]

Figure 1.

Likert scale survey responses assessing attitudes about medical and exception from informed consent research among persons opting out of an exception from informed consent cardiac arrest trial.

Table 1

Demographic characteristics of persons opting out of an exception from informed consent cardiac arrest trial.

Age–median (IQR)	62	(52.5–65.5)
Gender		
Female	31	(74%)
Race:		
White	32	(94%)
Educational Level:		
High School	7	(18%)
Some College	12	(30%)
College Degree	9	(23%)
Graduate Degree	12	(30%)
Religion:		
Catholic	7	(21%)
Protestant	12	(36%)
Other	9	(27%)
No preference	5	(15%)
Religious degree:		
Very or Somewhat	25	(64%)
Survey type:		
Phone	36	(78%)
Web	8	(17%)
Mail	2	(4%)

Table 2

Survey responses assessing specific reasons for requesting to opt out of an exception from informed consent cardiac arrest trial.

I am not willing to be involved in any study <i>without my consent</i> .	42	(91%)
I have had a previous negative experience with medical research.	13	(28%)
I am not willing to <i>ever</i> be a subject in any medical research.	13	(28%)
I object to the hospital or institution coordinating the research.	6	(13%)
I object to any research sponsored by the U.S. government.	6	(13%)
I am not willing to be involved in <i>this particular</i> study (PRIMED).	35	(76%)

Table 3

Themes and illustrative quotes from persons opting out of an exception from informed consent cardiac arrest trial regarding attitudes about medical and exception from informed consent research.

1. Concerns about the ethics and processes of EFIC research.

"I do not like the option of the study enrolling people automatically."

"No one should automatically be in a study, ever."

"It's not this study. It's the idea of people not knowing – research without consent."

"Lots of people didn't see the article—that's terrifying to me"

"You need to notify better—maybe public mailing?"

"Unless people read the papers and small fine print—people miss it— it's not well-advertised"

"Media articles are not enough to constitute public notification—what if I hadn't read the paper?"

2. Concerns about how this particular study would impact end-of-life preferences.

"I'm ready to go home; I know the Lord."

"I don't want to live and be brain dead."

"I'm not interested in prolonging life in any circumstance."

"It's the cycle of life" ... "when it's my time."

"I watched my grandfather get put on life-support against his will; it's my body, my life, please let me have the choice."

3. Strong subjective, emotionally charged protests to this type of research, including fear, anger and sarcasm.

"I am infuriated with liars and frauds ... I am a daughter of the founders of this nation, and I don't like invasion of privacy."

"If they get away with this, what's next?"

"The right of the intelligent individual outweighs the right of the stupid minority."

"[Hospital] is a terrible place and serves only to create products for drug companies to make profits."

"[Hospital] shot themselves in the foot with this one; they are really out of favor with the community ... this hospital is underhanded."

"I don't want to be a guinea pig."

"Are we expected to wear these bracelets like Jews in a concentration camp for the rest of our lives?"

4. Negative references to other public health controversies.

"Water fluoridation doesn't work and poisons people"

"It is not ethical for an obscure medical review board to make decisions that determine the type of treatment a trauma victim will receive."
(reference to a previous EFIC study in this community)

"Organ donation in our country is an opt-in system, as participation in medical research should be."

"Government has proven it can't be trusted evidenced by history. Right of intelligent individual outweighs right of stupid majority."

5. Objections to the study based on misinformation.

"I'm not willing to participate because of my medical condition – I have a pacer/defibrillator."

"I have concerns about people who get the placebo treatment – that doesn't seem fair."

(many quotes from theme 2 were also closely related to theme 5)