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Systematic Review and Meta-summary of Attitudes Toward Research in Emergency Medical Conditions

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SYSTEMATIC REVIEW AND META-SUMMARY OF ATTITUDES TOWARD RESEARCH IN EMERGENCY MEDICAL CONDITIONS

ABSTRACT

Emergency departments are challenging research settings truly informed consent can be difficult to obtain. A deeper understanding of emergency medical patients' opinions about research is needed. We conducted a systematic review and meta-summary of quantitative and qualitative studies on which values, attitudes, or beliefs of emergent medical research participants influence research participation. We included studies of adults that investigated opinions toward emergency medicine research participation. We excluded studies focused on the association between demographics or consent document features and participation and those focused on non-emergency research. In August 2011, we searched the following databases: MEDLINE, EMBASE, Google Scholar, Scirus, PsycINFO, AgeLine, and Global Health. Titles, abstracts, and then full manuscripts were independently evaluated by 2 reviewers. Disagreements were resolved by consensus and adjudicated by a third author. Studies were evaluated for bias using standardized scores. We report themes associated with participation or refusal. Our initial search produced over 1800 articles. A total of 44 articles were extracted for full-manuscript analysis and 14 were retained based on our eligibility criteria. Among factors favoring participation, altruism and personal health benefit had the highest frequency. Mistrust of researchers, feeling like a "guinea pig", and risk were leading factors favoring refusal. Many studies noted limitations of informed consent processes in emergent conditions. We conclude that highlighting the benefits to the

participant and society, mitigating risk, and increasing public trust may increase research participation emergency medical research. New methods for conducting informed consent in such studies are needed.

Keywords: Emergency Medicine; Research; Informed Consent; Systematic Review; Clinical Trials

INTRODUCTION

Emergency departments are an increasingly important setting for conducting medical research(1). In the United States alone, there were approximately 123.8 million visits to emergency departments in 2008.(2) Emergency departments care for populations that are traditionally under-represented in medical research, such as minorities and those without other sources of medical care.(2) Interventions in a variety of time-sensitive diseases can reduce morbidity and mortality.(3, 4) However, in patients with emergent conditions, the effects of acute illness, time constraints, lack of access to family or physicians, and other challenges complicate the informed consent process.(5-7)

In order to rationally propose solutions to the difficulties in enrolling patients in emergency medical trials, it is necessary to synthesize a deeper understanding of the motivations and concerns of potential emergency medicine research participants. Such an understanding will allow us to make the process more patient-centered.(8) Prior work has primarily focused on attitudes toward research in patients with non-emergent conditions.(9, 10) Factors found to be associated with research participation in non-emergent conditions include, among others: demographics, patients' health beliefs, and disease severity.(11, 12) Prior work in emergency settings has examined the relationship between patient demographics or aspects of informed consent documents and research participation.(13-15) These studies have not been able to lead to implementable proposals for improving the informed consent process in emergency medicine research.

Some prior qualitative and survey studies have examined patients with specific emergency medical conditions and their attitudes toward research. We seek to collate

and synthesize the available literature to understand emergency medical patients' perspective without regard to specific medical conditions. This is due to the fact that there is some non-specificity of the symptoms of many emergent medical conditions(16) and many emergency medicine trials require enrollment based on symptoms, not diagnoses. The objective of this study, then, was to conduct a systematic review and meta-summary to evaluate what values, attitudes, or beliefs on the part of potential or actual research participants with emergent medical conditions influence participation in research.

METHODS

Study design

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement.(17)

Eligibility criteria

We considered studies with the following criteria: studies including patients over 18 years of age, and any study reporting on or investigating the values, attitudes, or beliefs toward emergency medical research (studies conducted in the emergency department or on emergency medical conditions) from participants' point of view. In addition, the following exclusion criteria were used: any study reporting the association of participant demographics (age, race/ethnicity, gender, economic, or education status) with research participation, any study primarily reporting the association of features of the consent process with research participation, and any study reporting on attitudes toward non-emergency research. We eliminated studies focused on demographics as they

were beyond the scope of the intended paper and we did not plan any subgroup analyses a priori.

Information sources

In August 2011, we searched the following electronic databases: MEDLINE (accessed by PubMed), EMBASE, Google Scholar, Scirus, PsycINFO (via EBSCO), AgeLine (by AARP) and Global Health. We did not use limits for date and language when conducting the search. In addition, we searched the references of the included articles manually. We also performed a citation analysis of the included studies using Google Scholar, and sought experts' suggestions.

Search

The initial search comprised the MeSH terms "Emergencies", "Patients", "Research", "Perception", "Values", "Culture", and related entry terms. The complete search strategy used for the PubMed database is shown in Appendix 1 (available online).

Study selection

Titles and abstracts of the retrieved articles were independently evaluated by 2 reviewers (A.P. and T.M.). Both reviewers have prior experience in performing systematic searches and reviews. Abstracts that did not provide enough information regarding the eligibility criteria were kept for full-text evaluation. Two reviewers (T.M. and L.L.H.O.) independently evaluated full-text articles and determined study eligibility. Disagreements were solved by consensus and if disagreement persisted, they sought the lead author's opinion (A.L.).

Risk of bias across studies

Risk of bias was evaluated by reviewers ranking each study according to items adapted from Bennett, et al.(18) for surveys and the online Joanna Briggs Institute-Qualitative Assessment and Review Instrument (JBI-QARI, (The Joanna Briggs Institute, University of Adelaide, Australia)) for qualitative studies.

Data extraction

Two reviewers (T.M. and L.L.H.O.) independently conducted initial data extraction. The lead author (A.L.) reviewed all final studies and iteratively generated the list of themes. Characteristics of the studies collected included year of publication, authors, geographic region of first author, objective, study design, setting, intervention studied (if any), participant sampling methods, inclusion and exclusion criteria, data collection and analysis methods, participants' characteristics, main results, and authors' conclusion(s).

Primary data analysis

Qualitative meta-summary(19) is a quantitatively oriented aggregation approach to research synthesis of both qualitative and survey studies. As opposed to traditional meta-analysis in which bivariate or multivariable research findings are combined, qualitative meta-summary uses descriptive findings from primarily quantitative and qualitative studies. The primary requirements for inclusion are that the findings are descriptive and can be seen as addressing the same question (in this case, "What factors are associated with participation in emergency medicine research?"). From the reports of qualitative research findings, we extracted themes or patterned responses from the results sections of the collected studies regardless of how many

participants endorsed the themes. When possible, we extracted sample quotations from participants. From the quantitative reports, we extracted descriptive information on the factors associated with participation, which were presented in survey format (i.e., proportion of participants reporting each factor). The lead author created a draft list of themes based on unstructured summaries of findings from each study created by the 2 independent article extractors. This framework was then iteratively refined through subsequent reviews of the results sections of final articles. These interim versions were reviewed by the lead author with one author who has experience with qualitative meta-summary and adjustments made accordingly. The final version was reviewed by a panel of 3 content experts for consensus: the aforementioned expert on qualitative meta-summary, one with expertise in bioethics, and a third with an expertise in clinical trials processes. The themes were grouped by similarity, and within each group, brief descriptions of the findings were generated.(19-21) We did not assume that the presence of a factor that favored participation implied that the absence of that factor favored refusal, unless specifically cited. For example, although previous experience with research favored participation, the lack of previous experience was not assumed as a reason for refusal.

To represent the magnitude of each finding, “frequency effect sizes” were generated by dividing the number of studies citing a particular theme by the total number of studies in our final list (14 studies). To represent the magnitude of each report, “intensity effect sizes” were calculated 2 ways. Specifically, for each study, the number of findings with a frequency effect size >25% was divided by the total number of findings with frequency

effect size >25%(16 themes). Additionally, for each study, the number of themes it cited was divided by the total number of themes overall (43 themes).

RESULTS

Study selection

Our initial search produced over 1800 articles from among the various databases. Of these, on the basis of title and abstract analysis, a total of 44 articles were extracted for full-manuscript analysis of appropriateness. Analysis of the references and citations of these articles produced an additional 9 articles for review. From among these 53 articles, 14 were retained based on our eligibility criteria (Figure 1. Study Workflow).

Study characteristics

Of the 14 articles that met eligibility criteria, 6 were qualitative studies, 8 included survey items, and 3 contained elements of both qualitative or open-ended questions and quantitative survey items (Table 1). Five studies examined suspected myocardial infarction patients, 3 focused on stroke patients, 1 focused on sudden cardiac near-death survivors, and the rest examined undifferentiated emergency department patients. The number of patients involved per study ranged from 11 to 40 in the qualitative studies and 103 to 1,901 in the quantitative survey studies. Although we did not set a language filter, our search produced publications exclusively in the English language and primarily in American and Western European research contexts.

Table 1: Study characteristics.

Reference	Study Design	No of Patients	Gender	Age *
Ågård A (2001)(22)	qualitative	31	29,03% female, 70,97% male	69 years

Mangset M (2008)(23)	qualitative	11	27,3% female, 72,7% male	69.9 years
Blixen CE (2005)(24)	qualitative	12	50% female, 50% male	55.2 years
Gammelgaard A (2004)(25)	qualitative	23	18,75% female, 81,25% female	aged from 43 to 78 ┼
Kasner SE (2010)(26)	qualitative	40	22,5% female, 77,5% male	60.0 years
Dickert NW (2009)(27)	qualitative	19	47,37% female, 52,63% male	60 years
Williams BF (2003)(28)	qualitative/ survey	367	20,71% female, 79,29% male	64 years
Biros MH (2009)(29)	survey	1901	65% female, 35% male	18-24 (247) 25-34 (171) 35-49 (532) 50-64 (627) >65 (324) ┼
Triner W (2007)(30)	cross sectional/ survey	497	56.2% female, 43.8% male	18–25 (109) 26–35 (104) 36–45 (104) 46–55 (89) 56–65 (54) >65 (37) ┼
McClure KB (2002)(31)	cross sectional/ survey	530	46% female, 54% male	41 years
Gammelgaard A (2004)(32)	survey	103	25% female, 75% male	61 years
Paradis C (2010)(33)	observational /survey	229	47.80% female, 52,20% male	>45 years=183 ┼
Wilets I (2003)(34)	cross sectional/ survey	240	62% female, 38% male	42 years
Yuval R (2000)(35)	cross sectional/ survey	580/50	-	-

* The data inserted on the "Age" column is the mean age of all participants in the study. However, some studies did not provide this information, and, for these studies, we inserted in this column the available non-standardized data.

┼ Non-standardized data, as explained above.

Risk of bias across studies

No studies were excluded on the basis of bias. Overall survey studies were of moderate quality. Almost all of the survey studies included a justification of the research question, instrument pre-testing, and description of sample; none provided clear evidence of reliability, validity or sample size calculation (Appendix 2, available online). Quality was high among the primarily qualitative studies. Nearly all demonstrated congruity between the research method and the question, data collection methods, representation and interpretation of the data. None, however, addressed the influence of the researcher on the research or vice versa (Appendix 3, available online).

Themes

The retained reports presented a number of themes influencing participant participation in research (Table 2 and Appendix 4). Among themes favoring participation, a sense of altruism and personal health benefit had the highest frequency effect sizes. Among the personal health benefits noted were access to better treatments, and access to more skilled care providers, follow up care, or other resources. Other common themes favoring participation included having a good understanding of the risks and benefits of the study, trust in their physician, and an awareness by the participant that there are no other effective treatments for their condition.

Table 2: Themes favoring participation.

Themes	No. of Studies (%)	Studies (% of study participants endorsing) *
Personal Health Benefit		
Think experimental treatment is better	11 (79%)	Ågård A (2001)(22); Blixen CE (2005)(24); Dickert NW (2009)(27); Gammelgaard A (2004)(25); Gammelgaard A (2004)(32) (12%); Mangset M (2008)(23); Williams BF (2003) (22%); Yuval R (2000)(35) (43%); Kasner SE

		(2010)(26); Paradis C (2010)(33); Wilets I (2003)(34) (26%)
Access to better physicians/institution/resources	4 (29%)	Wilets I (2003)(34) (18%); Gammelgaard A (2004)(25); Gammelgaard A (2004)(32) (26%); Yuval R (2000)(35) (12%)
Altruism		
Help society/others	9 (64%)	Ågård A (2001)(22); Blixen CE (2005)(24); Biros MH (2009)(29) (47%); Gammelgaard A (2004)(25); Mangset M (2008)(23); Paradis C (2010)(33); Williams BF (2003)(28) (12%); Kasner SE (2010)(26); Wilets I (2003)(34) (46%)
Gain scientific knowledge	7 (50%)	Ågård A (2001)(22); Biros MH (2009)(29); Dickert NW (2009)(27); Gammelgaard A (2004)(32) (2%); Paradis C (2010)(33); Yuval R (2000)(35) (35%); Triner W (2007)(30)
Improve future medical care	6 (43%)	Ågård A (2001)(22); Blixen CE (2005)(24); Dickert NW (2009)(27); Gammelgaard A (2004)(25); Gammelgaard A (2004)(32) (23%); Wilets I (2003)(34) (96%)
Existing treatment is inadequate	4 (29%)	Blixen CE (2005)(24); Dickert NW (2009)(27); Kasner SE (2010)(26); McClure KB (2002)(31) (75%)
Prognosis is otherwise bad for condition	3 (21%)	Blixen CE (2005)(24); Dickert NW (2009)(27); Kasner SE (2010)(26);
Financial incentives	3 (21%)	Biros MH (2009)(29) (15%); Paradis C (2010)(33); Wilets I (2003)(34) (17%)
Convenience	1 (7%)	Paradis C (2010)(33)
Participant Comfort with Research		
Trust in MDs/institution	6 (43%)	Ågård A (2001)(22); Dickert NW (2009)(27); Kasner SE (2010)(26); Mangset M (2008)(23); Paradis C (2010)(33); Williams BF (2003)(28) (7%)
Risks/benefits were well understood	7 (50%)	Blixen CE (2005)(24); Dickert NW (2009)(27); Gammelgaard A (2004)(25); Kasner SE (2010)(26); McClure KB (2002)(31); Yuval R (2000)(35); Williams BF (2003)(28)
Curiosity	3 (21%)	Biros MH (2009)(29) (54%); Wilets I (2003)(34) (11%); Yuval R (2000)(35)
Intervention is supported by prior research/compares two existing txs	3 (21%)	Blixen CE (2005)(24); Dickert NW (2009)(27); Kasner SE (2010)(26)

Understood voluntariness and ability to withdraw	2 (14%)	Paradis C (2010)(33); Gammelgaard A (2004)(25)
Previous participation in research	2 (14%)	Biros MH (2009)(29) (15%); Paradis C (2010)(33)
Small/minimal risk to participant	2 (14%)	McClure KB (2002)(31) (70%); Gammelgaard A (2004)(32)
Problems with Informed Consent		
Did not understand their ability to refuse or withdraw	6 (43%)	Ågård A (2001)(22); Wilets I (2003)(34) (26%); Gammelgaard A (2004)(25); Gammelgaard A (2004)(32) (5%); Mangset M (2008)(23); Yuval R (2000)(35) (8%)
Did not understand they were even participating in research	3 (21%)	Ågård A (2001)(22); Gammelgaard A (2004)(25); Williams BF (2003)(28) (19%)
Thought their doctor thought it would be best for them to participate	1 (7%)	Gammelgaard A (2004)(32) (9%)
Problems with information delivery		
Too much or too complex information-"gave up trying to understand"	2 (14%)	Ågård A (2001)(22); Gammelgaard A (2004)(25)
Effects of acute illness		
Did not want to delay treatment	6 (43%)	Ågård A (2001)(22); Gammelgaard A (2004)(25); Gammelgaard A (2004)(32) (15); Kasner SE (2010)(26); Mangset M (2008)(23); Williams BF (2003)(28) (22%)
Too little time- made a rushed decision	4 (29%)	Ågård A (2001)(22); Mangset M (2008)(23); Gammelgaard A (2004)(32) (40%); Mangset M (2008)(23)
Too sick/too much pain: "willing to sign anything"	4 (29%)	Ågård A (2001)(22); Gammelgaard A (2004)(25); Mangset M (2008)(23); Williams BF (2003)(28)
Effect of pain meds/sedatives: "not in my right mind"	2 (14%)	Ågård A (2001)(22); Gammelgaard A (2004)(25)

*Survey studies only.

Mistrust of researchers and fear of the actual risk of the research were two of the leading themes favoring refusal of participation. Coupled with mistrust of researchers was the specific use of the term "guinea pig". Use of a placebo arm and of randomization were also cited as deterrents from participation.

A number of the studies focused on participants' ability to comprehend the complexities of research. Some participants were not even aware that they were participating in (or had been asked to participate in) research. Others did not understand their ability to refuse participation. Many misunderstandings were attributed to limitations of informed consent processes in patients with emergent conditions (Table 3 and Appendix 5). Additionally, the format of information presentation (oral versus written) influenced some respondents' likelihood of participating. Many themes related to informed consent were associated with either participation or refusal depending on the respondent.

Table 3: Themes favoring refusal.

Themes	No. of Studies (%)	Studies (% of study participants endorsing *)
Not enough financial compensation	1 (7%)	Biros MH (2009)(29) (12%)
Too much of a time investment	2 (14%)	Biros MH (2009)(29) (53%); Wilets I (2003)(34) (6%)
Inconvenience	2 (14%)	Paradis C (2010); Biros MH (2009)(29) (25%)
Feeling like a "guinea pig"	8 (57%)	Ågård A (2001)(22); Blixen CE (2005)(24); Dickert NW (2009)(27); Gammelgaard A (2004)(25); Mangset M (2008)(23); Paradis C (2010)(33); Wilets I (2003)(34) (49%); Williams BF (2003)(28) (6%)
Drug companies involvement	3 (21%)	Dickert NW (2009)(27); Kasner SE (2010)(26); Wilets I (2003)(34) (74%)
Privacy	2 (14%)	Biros MH (2009)(29) (20%); Wilets I (2003)(34) (5%)
Government involvement	1 (7%)	Wilets I (2003)(34) (74%)
Risk was too great	6 (43%)	Biros MH (2009)(29) (23%); Dickert NW (2009)(27); Gammelgaard A (2004)(32) (37%); Mangset M (2008)(23); Wilets I (2003)(34) (38%); Williams BF (2003)(28) (6%)
Prefer non-experimental/control treatment	4 (29%)	Gammelgaard A (2004)(25); Mangset M (2008)(23); Gammelgaard A (2004)(32) (3%); Yuval R (2000)(35) (49%)
Didn't like possibility of receiving a placebo	3 (21%)	Kasner SE (2010)(26); Mangset M (2008)(23); Yuval R (2000)(35) (28%)

Didn't like the idea of randomization	4 (29%)	Ågård A (2001)(22); Dickert NW (2009)(27); Gammelgaard A (2004)(32) (18%); Kasner SE (2010)(26)
Not interested in research	1 (7%)	Wilets I (2003)(34) (24%)
Too much or too complex information	2 (14%)	Gammelgaard A (2004)(25); Paradis C (2010)(33)
Not enough information	3 (21%)	Biros MH (2009)(29) (21%); Paradis C (2010)(33) (29%); Gammelgaard A (2004)(32) (7%)
Written IC presentation	2 (14%)	Ågård A (2001)(22); Gammelgaard A (2004)(25)
Did not want to delay treatment	2 (14%)	Gammelgaard A (2004)(25); Gammelgaard A (2004)(32) (31%)
Too little time/felt rushed	2 (14%)	Biros MH (2009)(29) (53%); Paradis C (2010)(33) (29%)
Felt too sick	2 (14%)	Gammelgaard A (2004)(25); Paradis C (2010)(33)

*Survey studies only.

There was a trend toward qualitative studies having higher intensity effect scores, with several studies contributing to more than half of the themes with frequency effect sizes greater than 25% (Table 4 Intensity Score A, Columns A & B).

Table 4. Intensity Effect Sizes

Reference	**No of Themes with Frequency Effect Size >25%**	**Intensity Score A** (column A/total themes with Frequency Effect Size >25% (16))	**Total No of Themes**	**Intensity Score B** (column C/ Total themes(43))
Ågård A (2001)(22)	11	69%	15	35%
Biros MH (2009)(29)	3	19%	12	28%
Blixen CE (2005)(24)	6	38%	8	19%
Dickert NW (2009)(27)	10	63%	13	30%
Gammelgaard A (2004)(32)	10	63%	18	42%
Gammelgaard A (2004)(25)	11	69%	15	35%

Kasner SE (2010)(26)	8	50%	12	28%
Mangset M (2008)(23)	11	69%	12	28%
McClure KB (2002)(31)	2	13%	3	7%
Paradis C (2010)(33)	6	38%	15	35%
Triner W (2007)(30)	1	6%	1	2%
Wilets I (2003)(34)	8	50%	15	35%
Williams BF (2003)(28)	8	50%	9	21%
Yuval R (2000)(35)	6	38%	8	19%

However, there was considerable overlap between the themes contributed by qualitative versus quantitative survey studies. No single study contributed the majority of the overall findings, with all studies producing less than 50% of the total available themes (Table 4, Intensity Score B, Column C and D).

DISCUSSION

Understanding emergency patients' views of research will allow us to accommodate their unique needs. Several qualitative and quantitative survey studies have been conducted to examine participants' reasons for participating in emergency medical research. To our knowledge, these studies have not been synthesized across disciplines in a manner that informs researchers of emergent conditions. Use of qualitative meta-summary allows extraction of themes from both quantitative survey and qualitative work, recognizing that the differences between the two approaches are not as substantial as many suppose. This leverages the strengths of qualitative work (depth and greater possibility for unanticipated responses) with those of quantitative

survey studies (standardization of assessment, sample size sufficient for inferential testing). Another unique strength of our meta-summary was the identification of themes that both favored and disfavored participation dependent on the respondent. Such bi-directional findings may have been otherwise difficult to elucidate in individual qualitative studies or meta-analyses. Our analysis of intensity scores indicates that qualitative studies tended to have a high number of factors that were reported in several other studies and that no study contributed more than 50% of the total themes generated.

Among the most commonly reported motivators was personal health benefit and altruism, whereas the most commonly cited barriers were lack of trust and concern over risk. Some themes, such as time constraints, were reported to favor either participation or refusal, depending on the respondent. We also noted inadequacies of the informed consent process in emergency research. Several studies documented participant participation despite poor understanding of basic principles such as voluntariness, consent, randomization, or the risks and benefits of research.

Personal health benefit

Adam Smith posited in 1759 the “invisible hand” of self-interest as a driver of decisions.(36) Accordingly, it is not surprising that participants will participate in research that they feel is likely to benefit them. Self-interest was also noted in the influence of non-health benefits such as financial compensation, convenience, and access to specialists. This is consistent with prior research on this topic in other

fields.(37) In many cases, this belief in self-interest is held so strongly that it even overpowers directly conflicting information provided during informed consent. "Therapeutic Misconception" is the term used for the notion that participating in research is a means of providing the best care available as opposed to an attempt to further scientific knowledge. This phenomenon was present even in those with firm understanding of trial mechanics, as witnessed by the statement of one participant:

> "So, I reckoned that all things being equal it would be better to go to the angioplasty centre, I mean getting the chance to go; I'm aware of the drawing of lots and the existence of a control group and that."(25)

Another example occurred in the Paradis, et al.(33), study in which participants reported personal health benefit in a study for which they were explicitly informed that they would receive no direct benefit. Thus, highlighting the benefits of the study to the participant is likely to improve enrollment, but must be done in a measured fashion to avoid therapeutic misconception.

Altruism

Altruism has been found to be an important factor to research participation. This would appear to be somewhat inconsistent with the notion of personal health benefit until it is realized that altruism was expressed in many different ways, consistent with the academic literature on this topic.(38) While some participants expressed altruism in furthering scientific knowledge and helping others, another way it was expressed was a hope to improve future medical care. This implicitly would include future benefit for the participant as well. For some, the sense of altruism was tied to their sense of belonging

to a particular group that would benefit from the research, such as gender, race, nationality, or health condition. Still others might posit that merely appearing altruistic is a form of benefit. Thus, it would seem that highlighting a study's ability to help others would increase participation.

Mistrust

Previous studies have noted mistrust in medical researchers as a barrier to research participation. This finding has been noted in numerous settings of research and across cultures.(39, 40) Many associate a sense of mistrust to past research misconduct.(41) The connection between improper conduct of research and mistrust is also expressed by multiple participants' use of the specific term "guinea pig". The use of guinea pigs for medical research dates to the 17th century(42) and the term has a negative connotation of research experimentation in popular culture. In the studies we reviewed, participants universally used the term to describe their mistrust of medical research, indicating that they felt they would be placed in danger in order to further scientific knowledge. Others expressed concern over the protection of their privacy and over relationships between researchers and sponsors. Increasing public trust in research has been a longstanding national priority, however, it is not clear whether there are simple methods for doing so.

Risk

It is not surprising that patients with emergency conditions are sensitive to the risk involved in research. In an outpatient setting, participants who had a negative reaction to the informed consent language regarding risks were less likely to enroll into a

hypothetical trial.(43) Further evidence of this sensitivity is revealed in the studies by Dickert, et al.,(27) and McClure, et al.,(31) in which acceptance of studies is higher for diagnostic trials as opposed to interventional trials. As noted in the study by Blixen, et al.,(24) emergency medicine patients are particularly sensitive to any intervention that could result in death, even if the likelihood is remote. An important exception was noted among patients with known poor prognosis. While all studies attempt to mitigate risk, the manner in which this risk is communicated to patients may be more important than the actual level of risk. Risk communication remains a difficult challenge for researchers.(44) This aligns with prior research demonstrating poor comprehension and a lack of acceptance of common research concepts among lay people.(45)

Informed consent processes

The inherent difficulties in performing informed consent in patients with time-sensitive conditions were also made apparent. In a number of cases, limitations in time, inability to comprehend complex information, and the emotional aspects of acute illness resulted in either uninformed refusal or misguided participation in research. In some instances, a particular factor (e.g.s lack of time, pain) led to either increased likelihood of participation (albeit misguided) or decreased likelihood, depending on the patient. Other standard research methods such as randomization and use of placebo were also cited as deterrents to participation. This may be due to poor comprehension of such procedures and their rationale. The fact that some participants did not even understand that they were participating in research is alarming. This reinforces the fiduciary responsibility of the researcher in the emergency setting. Although these qualities are

not unique to emergency care research,(46-48) they do point to the need for improved methods of providing information to potential research participants. The preference of respondents for oral versus written information suggests that existing informed consent documents are a suboptimal means of communication. Additionally, assessment of patients' comprehension of information is poorly done (and poorly documented) in our current paradigm of informed consent.

The factors noted above point to several potential solutions to ensuring safe, ethical enrollment of patients with emergency medical conditions. Just as we must strive to improve the ways we provide medical care, so too must we strive to improve our research methods, including informed consent. The consensus of the research community is that informed consent documents are too long.(49) However, as noted above, patients do not view the documents as the optimal means of communication, suggesting the need for other methods. Innovative interventions might outperform traditional informed consent processes; for example, multimedia presentation or simple test-retest methods(50) have not been explored in emergency medicine research contexts. Given that that the critical factor in the consent process may be the human interaction between researcher and patient (50), technological advances will only aid the consent process if they can retain this factor.

Second, a public health education program highlighting research participants' rights and protections might be beneficial. This program could educate the public about the existing patient safeguards required for any research study, including the voluntariness of research participation. This would potentially reduce the amount of new information that potential research participants would face in the setting of acute illness.

Additionally, research study designs might be able to mitigate the effect of acute illness by waiting until stabilizing treatments are started before approaching participants.

Limitations

The present study is limited by its reliance on published literature. As such, it is constrained by bias by authors in interpreting data and publication bias. In particular, it is possible that preconceived notions of authors about factors influencing research participation are highlighted more frequently. Unlike quantitative meta-analysis, we cannot perform a forest plot to gain insight into any publication bias. We did perform a quality analysis, with evidence of high quality studies. A number of our studies focused on patients with cardiac and neurologic disease, potentially limiting their generalizability. However, we also extracted several articles performed on a general emergency department population.

We may have missed or inappropriately excluded some relevant studies. However, we used rigorous, standardized methods for identifying articles. Finally, we report in our basic quantitative analysis the number of studies citing a theme. The quantity of articles reporting a factor may not reflect its relative importance to respondents. Additionally, given the wide range in the number of respondents in any given study, an increasing number of studies citing a theme does not necessarily reflect more respondents.

CONCLUSIONS

Understanding emergently ill patients' views of research will allow us to adapt research processes to accommodate patients' needs. It will also guide Institutional Review Boards on how to conduct activities to prevent exploitation of emergently ill patients. In

this systematic review and meta-summary, we found several factors associated with research participation. New methods for conducting informed consent are needed to overcome inherent obstacles to information transmission in emergency settings. The relative importance of these factors should be prospectively tested in experimental fashion.

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Figure Legends

Figure 1. Study Workflow. A total of 1800 records were identified. After screening, 53 full text articles were assessed for eligibility. Ultimately, 14 articles were included.