

# Public opinion of a stroke clinical trial using exception from informed consent

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## Abstract

**Background** Acute stroke is a leading cause of morbidity and mortality. Clinical trials in stroke are challenging because victims often do not have the capacity to provide informed consent, excluding those patients most likely to benefit from the research.

**Aim** We evaluated patient willingness to participate in a hypothetical acute stroke trial using an exception from informed consent.

**Methods** Consecutive patients presenting to four emergency departments (EDs) underwent structured interviews regarding a hypothetical stroke trial using an exception from informed consent.

**Results** Of 461 (72% of eligible) participants, 55% (95% CI, 50%–59%) were willing to be enrolled in the hypothetical study without giving informed consent. After multivariable analysis, independent predictors of willingness to enroll included Catholic religion (OR 1.57, 95% CI 1.17–2.10) and belief that current therapy offers a >50% chance of full recovery (OR 1.29, 95% CI 1.05–1.57). There was no difference between the proportion willing to enroll in a cardiac arrest study vs. a stroke study (55% vs. 55%,  $p=0.83$ )

**Conclusions** Fifty-five percent of ED patients would be willing to be enrolled in a stroke trial using exception from informed consent.

**Keywords** Informed consent · Public opinion · Stroke

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## Introduction

Acute stroke is a leading cause of morbidity and mortality, and few interventions have proven to improve outcome [1]. Altered mental status among stroke victims limits their ability to give informed consent, which excludes those patients most likely to benefit, skewing the study population towards those with the least severe strokes [2–4]. Therefore, some have advocated for use of an exception from the standard informed consent procedure [5, 6]. While research using this exception is allowable under federal regulations, the process is both logistically and ethically complex, and typically applied to a narrow range of diseases.

When stroke survivors and caregivers are involved in stroke trial development, they have advocated for exception from consent [7]. The only study examining patient opinion of such an exception interviewed patients after their stroke had occurred, finding that 92% would be willing to participate [8]. These patients may be more aware of the

long-term morbidity of stroke and the limitations of current therapies, and thus be more supportive of such research than the general public.

To investigate public opinion, we interviewed a consecutive cohort of patients presenting to the emergency department (ED) for a variety of conditions [9]. Since it is impossible to discuss this issue with actual patients at the time of their stroke, we interviewed patients in the ED who would be more aware of the need for emergency evaluation and treatment, but be cognitively intact. The primary analysis examined the effect of an educational intervention on patient opinion of exception from consent in general and was published previously [9]. Here, we report a secondary analysis examining independent predictors of participants' willingness to participate in a stroke trial in particular.

## Methods

We described the study design previously, including the full questionnaire text [9]. Briefly, consecutive patients presenting to four EDs during selected 24-h periods were approached. Adults (aged >18) who were awake and responsive were eligible for enrollment. Subjects were excluded for medical instability, mental illness, intoxication, complaint of sexual assault, or if they were prisoners. The original study tested the hypothesis that an educational intervention would increase willingness to participate; subjects were randomized to receive the control survey or one with a paragraph discussing the ethical/legal requirements involved in using exception from informed consent [9]. The hypothetical stroke study is shown in Fig. 1; subjects were also asked about a hypothetical cardiac arrest study.

For analysis of the dichotomous variable "willing to enroll," we collapsed answers from a 5-point Likert scale into "agree" (the responses Strongly Agree and Agree), and

"do not agree" (Neutral, Disagree, and Strongly Disagree). We performed multivariable logistic regression to determine predictors of willingness to participate, with predictor variables chosen a priori based upon previously published data or suspected influence on willingness to participate in research. The model included a term for site, to account for within-ED clustering. We used Stata 9.0 (StataCorp, College Station, TX) for analysis. We also collected qualitative data using open-ended questions. The study was approved by the Institutional Review Boards of all participating sites.

## Results

Of 1,080 patients presenting to the four EDs during the study period, 640 were eligible, 473 participated, and 461 (72%) answered all questions including opinion on the hypothetical stroke study (Table 1). Fifty-five percent would be willing to participate in the hypothetical stroke study, a similar proportion to that willing to participate in a hypothetical cardiac arrest study (also 55%,  $p=0.83$ ). Univariate analysis identified no significant predictors of willingness to participate in the hypothetical stroke study. Multivariate analysis identified the following independent predictors of willingness to be enrolled: male sex, Catholic religion, and belief that current therapy offers >50% chance of full recovery (Table 2).

Qualitative comments were provided by 37 (15%) of those who were willing to participate, and by 50 (24%) who were neutral or unwilling. The most common statement was the belief that a surrogate is always immediately available ( $n=15$ ). Other common statements included that the risks were too high ( $n=10$ ); that the research should proceed in case it might help ( $n=6$ ); and that patients should only be enrolled if it were already known that the treatment would help ( $n=4$ ).

**Fig. 1** Case scenario

**Case Scenario:** When a person has an acute stroke, they can suddenly lose control of their arms, legs, or ability to speak with or understand other people. There is a new treatment for this but it must be given immediately. Doctors think that this medication will increase the chance of recovering brain function in some patients, but are worried that it may increase the risk of bleeding in the brain. They need to do a study to find out if this treatment helps people; however, people with a stroke may not be able to give their consent for such a study.

**Question:** If I had an acute stroke and could no longer understand or provide consent, I would be willing to be entered into this study without giving consent.

- |                      |            |                   |
|----------------------|------------|-------------------|
| 1. Strongly disagree | 3. Neutral | 4. Agree          |
| 2. Disagree          |            | 5. Strongly agree |

**Table 1** Demographic characteristics, by willingness to participate in a hypothetical stroke trial

	Disagree	Neutral	Agree	<i>P</i> value
Overall (n=461)	34%	11%	55%	
Age, median (IQR)	46 (27–63)	43 (29–59)	47 (31–59)	0.95
Income in \$1,000 s, median (IQR)	59 (47–79)	59 (47–68)	66 (47–79)	0.74
Sex				0.61
Male (n=214)	31%	9%	60%	
Female (n=241)	36%	12%	51%	
Race				0.69
White (n=290)	33%	11%	57%	
Black (n=80)	38%	11%	51%	
Other (n=77)	36%	14%	49%	
Ethnicity				0.25
Non-Hispanic (n=400)	34%	11%	55%	
Hispanic (n=18)	32%	12%	56%	
Religion				0.30
Protestant (n=100)	36%	15%	49%	
Catholic (n=192)	34%	7%	59%	
Other (n=85)	28%	20%	52%	
None (n=81)	37%	6%	57%	
Strong connection to religion				0.52
No (n=230)	33%	10%	56%	
Yes (n=148)	34%	14%	51%	
Education				0.62
<8th grade (n=22)	23%	14%	64%	
<12th grade (n=23)	30%	9%	61%	
High school (n=132)	34%	12%	54%	
Some college (n=109)	39%	7%	53%	
College (n=113)	34%	13%	53%	
Post grad. (n=62)	32%	11%	56%	
Insurance				0.84
Private (n=262)	33%	11%	56%	
Medicare (n=18)	17%	11%	72%	
Medicaid (n=62)	35%	11%	53%	
None (n=24)	33%	4%	63%	
Other (n=88)	39%	11%	50%	
“What do you think your chance of recovering ... is, based on current therapies?”				
<5% (n=27)	41%	4%	55%	
5–50% (n=94)	38%	10%	52%	
50/50 (n=176)	33%	14%	53%	
>50% (n=120)	32%	12%	57%	
>95% (n=30)	20%	7%	73%	0.30
Educational intervention				1.0
No (n=233)	34%	11%	55%	
Yes (n=228)	35%	11%	54%	

\*IQR, Interquartile range

## Discussion

We found that 55% of potential subjects would be willing to participate in a stroke trial without informed consent,

11% were neutral, and 34% would refuse. Prior research has shown 34–84% of respondents to be willing to participate in other studies such as cardiac arrest without informed consent [10].

**Table 2** Multivariable analysis of clinical features associated with willingness to participate in a hypothetical stroke trial

Clinical factor	Odds ratio (95% CI)
Age per decade	1.0 (0.8–1.2)
Household income (per US\$10,000)	1.0 (0.9–1.1)
Female sex	0.8 (0.7–0.9)
Race:	
White	Referent
Black	1.0 (0.7–1.6)
Other	0.7 (0.5–1.0)
Hispanic ethnicity	1.2 (0.5–2.7)
Education:	
<8th grade	Referent
Some high school	0.9 (0.4–2.0)
High school	0.8 (0.4–1.4)
Some college	0.8 (0.4–1.3)
College	0.8 (0.4–1.7)
Post graduate	1.1 (0.4–3.0)
Religion:	
Protestant	Referent
Catholic	1.6 (1.2–2.1)
Other	1.1 (0.6–2.0)
None	1.4 (0.7–2.8)
Insurance:	
Private	Referent
Medicare	2.1 (0.7–6.3)
Medicaid	0.9 (0.6–1.3)
None	1.3 (0.3–5.9)
Other	0.7 (0.2–2.7)
Belief that current therapies offer a >50% chance of full recovery	1.3 (1.1–1.6)
Educational intervention	1.0 (0.7–1.6)

Multivariable analysis revealed that patients with a more optimistic view of the benefits of current therapies were more willing to participate. It may be that those with more positive opinions of clinical care also have more faith in the ethical management of clinical trials or a greater belief that research carries clinical benefit for the participants. We also noted an effect of sex and religious affiliation on willingness to enroll; the reason for this is unclear. Future studies will be necessary to clarify whether these relationships are artifacts of multiple hypothesis testing, or whether there is a reason that males and Catholics are more willing to participate in research without consent.

Our study is limited by the fact that not all eligible subjects completed the survey; a response rate over 80% would be preferred. Also, by excluding the most severely ill patients, we may have missed those most likely to be enrolled in studies using an exception from informed consent and whose opinions are most critical. Unfortunately, while such patients who survive cognitively intact could be

interviewed after their clinical course has stabilized, such interviews would select for those who benefited most from standard therapy, and decision-making at the time of the stroke may be quite different from that made long afterwards. Finally, healthy people at risk for stroke could be interviewed to avoid any biases from being in the emergency department at the time of the survey. However, patients' opinions of research (and medical care) may be quite different when in close spatial and psychological proximity to a true medical emergency, and so such surveys may introduce a separate set of biases.

These data add to the growing body of evidence for patients' support of emergency research without informed consent. Clinical trials in stroke have not traditionally been considered candidates for exception from consent; however, our data support the concept that within the context of current federal regulations (including factors such as clinical equipoise, ethics board approval, and absence of a surrogate), the majority of patients would be willing to participate in clinical trials of novel stroke therapies without consent.

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