

Challenges in Enrollment of Minority, Pediatric, and Geriatric Patients in Emergency and Acute Care Clinical Research

Seth W. Glickman, MD

Kevin J. Anstrom, PhD

Li Lin, MS

Abhinav Chandra, MD

Daniel T. Laskowitz, MD

Christopher W. Woods, MD

Debra H. Freeman, RN

Monica Kraft, MD

Laura M. Beskow, MPH, PhD

Kevin P. Weinfurt, PhD

Kevin A. Schulman, MD

Charles B. Cairns, MD

From the Division of Emergency Medicine, Department of Surgery (Glickman, Chandra, Freeman, Cairns), Center for Clinical and Genetic Economics (Glickman, Schulman, Lin, Weinfurt), Duke Clinical Research Institute, the Duke Translational Medicine Institute (Beskow, Anstrom), the Department of Biostatistics and Bioinformatics (Anstrom), the Institute for Genome Sciences and Policy (Beskow), and the Divisions of Neurology (Laskowitz), Pulmonary, Allergy and Critical Care (Kraft), Infectious Diseases (Woods), Department of Internal Medicine, and General Internal Medicine (Schulman), Duke University Medical Center, Durham, NC.

Study objective: Emergency department (ED) –based clinical research has the potential to include patient populations that are typically underrepresented in clinical research. The objective of this study is to assess how emergency clinical care and research processes, informed consent, and patient demographic factors (age, sex, and ethnicity/race) affect enrollment and consent in clinical research in the ED.

Methods: This was an analysis of prospectively collected data of all patients (aged 2 to 101 years) eligible for one of 7 clinical research studies from February 2005 to April 2007 in an academic ED. We measured rates of enrollment and consent in the clinical studies.

Results: One thousand two hundred two of the 4418 patients screened for participation in 7 clinical studies were clinically eligible for enrollment. Of the 868 patients who were able to provide a voluntary decision regarding consent, 639 (73.6%) agreed to participate; an overall enrollment rate of 53.2%. The mean age of patients enrolled was 51.8 years (range 3 to 98 years). Black patients (49.2% enrollment) and Latino patients (18.4% enrollment) were less likely to be enrolled in comparison with white patients (58.3% enrollment) (adjusted odds ratio [OR] of enrollment for blacks=0.64; 95% confidence interval [CI] 0.50 to 0.82; adjusted OR of enrollment for Latinos=0.16; 95% CI 0.08 to 0.33). Enrollment rates were lower among pediatric (40.0%) and geriatric patients (49.1%) in comparison with adult patients ages 18 to 64 years (55.5%) (adjusted OR of enrollment for pediatric patients=0.70, 95% CI 0.34 to 1.43; adjusted OR of enrollment for geriatric patients=0.69, 95% CI 0.53 to 0.90). Unique issues contributing to underenrollment included challenges in consent among pediatric and elderly patients, language issues in Latino patients, reduced voluntary consent rates among black patients, and perhaps underuse of minimal risk waivers.

Conclusion: In a large academic ED, minority, pediatric, and geriatric patients were less likely to be enrolled in acute care clinical research studies than middle-aged whites. Enrollment and consent strategies designed to enhance research participation in these important patient populations may be necessary to address disparities in the development and application of evidence-based emergency and acute care. [Ann Emerg Med. 2008;51:775-780.]

0196-0644/\$-see front matter

Copyright © 2008 by the American College of Emergency Physicians.

doi:10.1016/j.annemergmed.2007.11.002

Editor's Capsule Summary*What is already known on this topic*

For a variety of reasons, clinical research in medicine has been disproportionately focused on white adult nongeriatric men.

What question this study addressed

How enrollment of 639 of 1,202 eligible subjects into 7 simple blood draw studies differed among sexes, races, and age groups, and why.

What this study adds to our knowledge

This novel study demonstrates that percentage of enrollment was lower in traditionally underrepresented groups (odds ratios 0.70 to 0.16) because of difficulty obtaining consent (altered mental status, language barrier, absence of a family member) or patient refusal.

How this might change clinical practice

Researchers might enhance participation by traditionally underrepresented populations by gaining waiver of informed consent from their institutional review board for appropriate studies or developing consent processes that overcome the problems identified in this article.

INTRODUCTION

The 2006 Institute of Medicine report on emergency care in the United States emphasized the need to develop clinical research to enhance the evidence base and quality of acute and disaster care.¹ Emergency departments (EDs) treated 115 million patients in 2005 and serve an inclusive patient population, including pediatric, geriatric, medically underserved, and minority populations. Thus, ED-based clinical research has the potential to include patient populations that are typically underrepresented in clinical research.

There are several major challenges that affect the ability to conduct clinical research in emergency settings. These challenges are multifactorial and include unique aspects of emergency care (ie, complex clinical environment consisting of patients with acute, undifferentiated disease), challenges in the consent process (including brief intervals for subject identification and recruitment and lack of preexisting relationships with patients), and the broad diversity of emergency patient populations.

There are few studies describing enrollment and consent experiences with emergency care research. We used prospectively collected data from 7 diagnostic clinical trials in acute and trauma care in the ED at a large academic medical center to identify how the process of ED informed consent and patient characteristics, including age, race/ethnicity, and sex, affected consent and enrollment.

MATERIALS AND METHODS

Between February 1, 2005, and April 5, 2007, 4,418 patients who sought treatment at an academic ED (annual census 65,000) at the only Level I trauma center in Durham County, NC (county demographics 46% white, 38% black, 11% Latino), were screened for eligibility to participate in 7 diagnostic clinical studies. Patient consent was required by the institutional review board before enrollment in each of these studies. Clinical studies were both industry and government sponsored and spanned a variety of clinical areas (including neurology, pulmonary, cardiology, and infectious diseases). Included were 7 different biomarker studies, each requiring an additional blood draw, and a single study also tested a noninvasive diagnostic approach for acute coronary syndromes. Prospectively collected study screening log data, including reasons for nonenrollment, for eligible and enrolled patients were kept for each study. All studies were approved by the institutional review board.

The patients were screened by one of 12 trained, dedicated research personnel. All study personnel completed both general training as required by the local institutional review board for participation in human clinical studies and protocol-specific acute care research training. Sex, age, race/ethnicity, study eligibility, and consent were recorded for all patients screened.

Reasons for nonenrollment were organized by the research team according to a priori categories: (1) the patient voluntarily declined enrollment; (2) the patient's family declined enrollment on behalf of the patient; (3) the treating nurse or physician did not allow the patient to be approached for consent; (4) the patient was not competent for consent (ie, altered mental status); (5) operational care and research system related issues, including nonenrollment of non-English-speaking patients (ie, research financial and personnel resource constraints related to regulatory Spanish-language consent procedures) and ED operational factors that prevented enrollment (ie, patient unavailable because of discharge, admission, or diagnostic processes); and (6) all other issues that could not be reliably categorized into one of the 5 areas.

Generalized linear mixed models (SAS Proc GLIMMIX) were used to model the likelihood of patient enrollment and refusal. There were a variety of reasons why an eligible patient was not enrolled in a clinical study (including operational issues, language barriers, patient refusal, and family and provider refusal). The first model (enrollment) incorporates all eligible patients (n=1,203), and captures the impact of all of these ED factors on the overall likelihood of an eligible patient ultimately being enrolled in a clinical study.

The second category (patient refusal) incorporates only patients who provided an individual decision about consent (n=868). The model was formulated to address consent by assessing the likelihood of a patient's refusing to participate in a clinical study. Therefore, the second model excludes patients (n=335) who did not provide an individual decision about consent (because of language barriers, altered mental status, etc).

Table 1. Enrollment rates and odds of overall enrollment (among all patients meeting clinical eligibility criteria) and refusal (among all patients who meet clinical eligibility criteria, were approached, and competent to provide consent) for participation in a clinical research study.

Characteristics	Eligible	Enrolled		Overall Enrollment if Eligible, N=1,202		Voluntary Refusal if Eligible and Able to Provide Consent, N=868	
		Yes	No	Adjusted Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Total, No. (%)	1,202	639 (53.2)	563 (46.8)				
Sex							
Male	573	306 (53.4)	267 (46.6)	Reference	Reference	Reference	Reference
Female	628	333 (53.0)	295 (47.0)	1.05	0.83–1.33	1.27	0.92–1.74
Race							
White	653	381 (58.3)	272 (41.7)	Reference	Reference	Reference	Reference
Black	457	225 (49.2)	232 (51.8)	0.64*	0.50–0.82	1.79*	1.30–2.48
Latino	49	9 (18.4)	40 (81.6)	0.16*	0.08–0.33	2.27	0.75–6.84
Other	43	24 (55.8)	19 (44.2)	1.42	0.59–3.43	0.70	0.20–2.48
Age, y							
Adult (18–64)	815	452 (55.5)	363 (44.5)	Reference	Reference	Reference	Reference
Pediatric (2–17)	40	16 (40.0)	24 (60.0)	0.63	0.34–1.43	1.69	0.70–4.07
Geriatric (≥65)	344	169 (49.1)	175 (50.9)	0.69*	0.53–0.90	1.18	0.82–1.69

Note: Percentages may not total to 100 because of rounding and occasional missing data. Odds ratios were adjusted for race, age, sex, and screener effects.

*Indicates statistical significance at the $P=.05$ level. Reference indicates the reference group for comparison. Data are presented as number (percentage).

The dependent variable was defined as a binary outcome for both enrollment and consent, either yes or no. Sex, race/ethnicity, and age categories were included in the model as fixed effects. The individual “screener” was included as a random effect to account for correlation in the data among patients.

All analyses were conducted with SAS statistical software, version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

Between February 13, 2005, and April 3, 2007, 4,418 patients were screened for eligibility to enroll in one of 7 ED-based clinical studies; 1,202 patients met clinical eligibility criteria for enrollment, and 639 were enrolled (Table 1 and also Table E1, available online at <http://www.annemergmed.com>). The distribution of enrollment between male and female patients was similar.

White patients had the largest percentage (58.3%; 381/653) of successful enrollment, followed by black (49.2%) and Latino patients (18.4%). The adjusted odds of enrollment were lower among black (0.64; 95% confidence interval [CI] 0.50 to 0.82) and Latino patients (0.16, 95% CI 0.08 to 0.32) in comparison with white patients.

The mean age of patients who enrolled was 51.8 years (range 3 to 98 years). Adult patients (aged 18 to 64 years) had the highest enrollment rate (55.5%), followed by geriatric (49.1%) and pediatric patients (40.0%). The adjusted odds of enrollment were lower among pediatric (0.63; 95% CI 0.34 to 1.43) and geriatric patients (0.69; 95% CI 0.53 to 0.90) in comparison with adult patients aged 18 to 64 years.

The most common reason for nonenrollment was patient refusal (40.7% of patients not enrolled), followed by research-

or care system-related issues (24.4%) and inability to obtain consent because of patient altered mental status (20.3%) (Table 2 and also Table E2, available online at <http://www.annemergmed.com>). Clinical provider refusal (6.6%) and family refusal (4.4%) were less frequent. The reasons for nonenrollment differed according to patient demographics. For example, most of the Latino patients (77.5%) were excluded because of language barriers and associated financial and personnel research resource constraints related to Spanish-language consent procedures, including forward and backwards Spanish-English translations of consent documents and hiring of additional Spanish-speaking personnel.

Of the 1,202 eligible patients who met clinical eligibility criteria, 868 were able to provide a voluntary decision about consent. The remaining patients were unable or unavailable to be approached for voluntary consent. Of the 868 patients, 639 (73.6%) gave consent and were enrolled in a research study. A greater percentage of patients who refused participation were women (29.3%) versus men (22.9%) (adjusted odds ratio of refusal for women=1.27; 95% CI 0.92 to 1.74). Blacks (32.8% refused) and Latinos (40.0% refused) were more likely than whites (22.1% refused) to decline participation in a clinical study. The adjusted odds of refusal were higher among black (1.79; 95% CI 1.30 to 2.48) and Latino patients (2.27; 95% CI 0.75 to 6.84) in comparison with white patients.

LIMITATIONS

There are several issues that should be considered in the interpretation of the results of this study. This study was conducted at a single, large, academic medical center. Research

Table 2. Reasons for nonenrollment among those patients who are eligible but are not enrolled (n=563).

Characteristics	Patient Declines, N=229	Family Declines, N=25	Provider Declines, N=37	Not Consentible (Altered Mental Status), N=114	System-Related Issues,*N=137	Other, N=20
Sex						
Male	91 (34.1)	16 (6.2)	18 (6.7)	59 (22.1)	73 (28.0)	10 (3.7)
Female	138 (46.8)	9 (3.1)	19 (6.4)	55 (18.6)	64 (21.7)	10 (3.4)
Race						
White	108 (39.7)	10 (3.7)	19 (7.0)	72 (26.5)	58 (21.3)	5 (1.8)
Black	110 (47.4)	14 (6.0)	16 (6.9)	36 (15.5)	42 (18.1)	14 (6.0)
Hispanic	6 (15.0)	0	1 (2.5)	2 (5.0)	31 (77.5)	0
Other	5 (26.3)	1 (5.3)	1 (5.3)	4 (21.1)	7 (36.8)	1 (7.1)
Age, y						
Pediatric (2–17)	9 (37.5)	4 (16.7)	0	0	10 (41.7)	1 (4.2)
Adult (18–64)	158 (43.4)	7 (1.9)	25 (6.7)	63 (17.3)	99 (27.2)	12 (3.3)
Geriatric (≥65)	61 (34.7)	15 (8.5)	12 (6.8)	51 (29.0)	29 (16.5)	8 (4.5)

*System-related issues include mainly language barriers and ED operational factors (patient admitted, discharged, or out of department) when approached for consent. Data are presented as number (percentage).

subjects and personnel may not be fully representative of those at other institutions. However, our team of study recruitment personnel was diverse, and large proportions of patients were screened by male, female, black, and Latino screeners. We also tested and did not find any important interaction between screener and patient characteristics with regard to likelihood of enrollment or refusal. In addition, a recent study of survey responses by Durham county blacks compared with a national sample revealed generally similar perceptions of racial/ethnic discrimination in health care.² The studies used for this project were all diagnostic trials using blood draws. Additional studies of therapeutic, interventional clinical trials will also be necessary to determine whether disparities in enrollment apply to acute treatment trials.

DISCUSSION

The recent Institute of Medicine report on emergency care highlighted the need for more research on key issues related to acute and trauma care.¹ However, the ability to conduct clinical research in the emergency care setting, as well as the research challenges unique to the emergency setting, have not been adequately evaluated. Overall, we found that despite the difficulties inherent in emergency research, most eligible patients who were able to provide consent participated in one of these studies at a rate (73.6%) that compares favorably to those recently reported for other outpatient clinical settings, both noninterventional (ie, interview, examination) studies (74.9% to 82.4%) and interventional (ie, treatment, counseling) studies (41.8% to 55.9%).³ However, we identified a number of significant challenges that resulted in an inability to enroll a number of otherwise eligible patients, particularly among pediatric, geriatric, and minority patient populations.

The results of this study demonstrate an association between age and enrollment, with pediatric and geriatric patients having the lowest enrollment rates. Unique challenges in the consent process exist for each of these age

groups. Among geriatric patients, challenges included patients with altered mental status (neurologic status and the acuity of the presenting condition, ie, intubation, shock) coupled with the lack of availability of surrogate proxies for consent. It appears that high-acuity conditions associated with physiologic derangement and altered mental status (ie, sepsis) disproportionately affected the enrollment of elderly patients in comparison to that of other studies. Consent challenges among pediatric patients included requirements for parental permission (from 1 or 2 parents, depending on risk level) and assent from the child.

Several provisions of the federal regulations allow for research without informed consent, including waiver of the requirement of informed consent for minimal-risk studies and the exception from informed consent for emergency research.^{4,5} However, these provisions have not been widely used for the conduct of clinical research in emergency care settings. The American Heart Association has recently suggested that stratification of the required community consultation and public disclosure procedures for exception studies be based on study risk (minimal for low-risk studies, more extensive for high-risk studies).⁶ These requirements for community consultation and public disclosure can be cumbersome and sometimes lead to delays in obtaining approval for research studies using the emergency exception process.⁶ Because the diagnostic studies included in this analysis do not entail incremental risk to the patient (an additional low-volume blood draw), these types of studies should be considered for future conduct under either a minimal-risk waiver or a modified consultation and disclosure process under an exception from consent.

In this study, black patients were more likely to refuse participation in comparison to white patients. Although this difference was statistically significant, the absolute difference in refusal rates between blacks and whites was fairly modest (32.8% versus 22.1%). Previous research has demonstrated underrepresentation of minorities in clinical research in other

clinical settings.^{7,8} The reasons for higher rates of refusal among blacks in these studies are likely multifactorial. According to previous research, issues related to trust of health care providers and research in general may have played important roles in this study.⁹ Disparities in enrollment may have important implications for the interpretation and generalizability of clinical trial results. Therefore, additional studies need to be conducted in the acute care setting to assess racial/ethnic differences in patient enrollment. Future studies are also necessary to identify population and patient-specific reasons for nonenrollment and to develop intervention strategies to assess issues in minority consent.

A sizable proportion of eligible, non-English-speaking Latino patients was not enrolled in a clinical study. This finding also has important implications, considering that the Latino population is the fastest-growing ethnic group in the United States and is increasingly using the ED as a source of care. By far the most common reason for underenrollment (78% of all Latino patients not enrolled) was system-related regulatory issues, mainly a result of research financial and personnel resource constraints related to Spanish-language consent procedures.

Local institutional review board requirements for enrollment of these patients includes (1) foreign-language and back-translation versions of long-form consent documents and research protocols (and the associated translation fees) and (2) separate Spanish-speaking personnel for both oral presentation and witnessing of the consent process (which would have required hiring additional Spanish-speaking personnel).¹⁰ A review of institutional review board protocols at other major medical centers revealed similar personnel and translation requirements and costs for research with non-English-speaking subjects. Many sponsors were unwilling or unable to provide additional resources for these services. Recognition of these challenges by sponsors and institutional review board and research institutions, coupled with additional support services, will be vital to ensuring participation of this group in emergency care research studies.

In a large academic ED, minority, pediatric, and geriatric patients were less likely to be enrolled in acute care clinical research studies. Further studies of enrollment in ED-based acute care clinical research are needed. Enrollment and consent strategies to enhance research participation in these important patient populations may be necessary to address disparities in the development and application of evidence-based emergency and acute care. These strategies may include demographic-sensitive patient engagement, sponsorship, and institutional support for inclusion of non-English-language patients and increased use of minimal-risk waivers.

Supervising editor: David L. Schriger, MD, MPH

Author contributions: CBC had full access to all of the data in this study and takes responsibility for the integrity of the data and the accuracy of the data analysis. SWG, KJA, LMB, KW,

and CBC were responsible for study concept and design. SWG, AC, DHF, and CBC acquired data. SWG and CBC drafted the article. SWG, AC, CWW, MK, LMB, KW, KAS, and CBC were responsible for critical revision of the article for important intellectual content. SWG, KJA, LL, and CBC conducted statistical analysis. SWG, LMB, and CBC obtained funding. DTL, CWW, DHF, MK, KW, KAS, and CBC were responsible for administrative, technical, and material support. KAS and CBC supervised the study. CBC takes responsibility for the paper as a whole.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article, that might create any potential conflict of interest. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement. This publication was made possible by grant number 1 UL1 RR024128-01 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH. Drs. Anstrom, Schulman, and Weinfurt have made available detailed listings of disclosure information at <http://www.dcri.duke.edu/research/coi.jsp>. No other authors reported financial disclosures.

Publication dates: Received for publication July 25, 2007. Revisions received September 30, 2007, and October 17, 2007. Accepted for publication November 1, 2007. Available online January 11, 2008.

Address for reprints: Charles B. Cairns, MD, Duke Clinical Research Institute, Duke University Medical Center, 2400 Pratt Street, Durham, NC 27710; 919-668-8694, fax 919-668-7124; E-mail charles.cairns@duke.edu.

REFERENCES

1. Institute of Medicine of the National Academies. *Hospital-Based Emergency Care: At the Breaking Point*. Washington, DC: National Academies Press; 2006.
2. Friedman JY, Anstrom KJ, Weinfurt KP, et al. Perceived racial/ethnic bias in healthcare in Durham County, North Carolina: a comparison of community and national samples. *N C Med J*. 2005;66:267-275.
3. Wendler D, Kington R, Madans J, et al. Are racial and ethnic minorities less willing to participate in clinical research? *PLoS Med*. 2006;3:201-209.
4. Cairns CB. FDA public hearing on the conduct of emergency clinical research. *Acad Emerg Med*. 2007;14:e31-32.
5. Vaslef SN, Cairns CB, Falletta JM. Ethical and regulatory challenges associated with the exception from informed consent requirements for emergency research: from experimental design to IRB approval. *Arch Surg*. 2006;141:1019-1023.
6. Halperin H, Paradis N, Mosezzo V, 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. *Circulation*. 2007;116(16):1855-1863.

7. Institute of Medicine of the National Academies. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*. Washington, DC: National Academies Press; 2003.
8. Heiat A, Gross C, Krumholz H. Representation of the elderly, women, and minorities in heart failure clinical trials. *Arch Intern Med*. 2002;162:1682-1688.
9. Smith GC, Thomas S, George M. Distrust, race, and research. *Arch Intern Med*. 2002;162:2458-2463.
10. Duke University Health System Institutional Review Board Policy on research involving non-English-speaking subjects (version 10/10/04). Available at: <http://irb.mc.duke.edu/doc/transpolicy.100606.doc>. Accessed June 3, 2007.

Table E1. Enrollment rates (stratified by each clinical study). Data are presented as number (percentage)

	Suspected ACS			Abdominal Pain			Brain Injury			Suspected Venous Thromboembolism		
	Eligible	Enrolled		Eligible	Enrolled		Eligible	Enrolled		Eligible	Enrolled	
		Yes	No		Yes	No		Yes	No		Yes	No
Total, No. (%)	45	37 (82)	8 (18)	98	51 (52)	47 (48)	256	159 (62)	97 (38)	126	104 (83)	22 (17)
Sex												
Male	31	25 (81)	6 (19)	34	22 (65)	12 (35)	125	81 (65)	44 (35)	52	46 (88)	6 (12)
Female	14	12 (86)	2 (14)	64	29 (45)	35 (55)	131	78 (60)	53 (40)	74	58 (78)	16 (22)
Race												
White	30	24 (80)	6 (20)	52	31 (60)	21 (40)	150	104 (69)	46 (31)	65	59 (91)	6 (9)
Black	13	11 (85)	2 (15)	35	14 (40)	21 (60)	81	48 (59)	33 (41)	55	42 (76)	13 (24)
Hispanic	0			6	2 (33)	4 (67)	11	2 (18)	9 (82)	3	1 (33)	2 (67)
Other	2	2 (100)	0	5	4 (80)	1 (20)	14	5 (36)	9 (64)	3	2 (67)	1 (33)
Age, y												
Adult (18–64)	27	22 (81)	5 (19)	78	37 (47)	41 (53)	164	107 (65)	57 (35)	103	84 (82)	19 (18)
Pediatric (2–17)	0			0			1	1 (100)	0 (0)	0		
Geriatric (≥65)	18	15 (83)	3 (17)	20	14 (70)	6 (30)	91	51 (56)	40 (44)	23	20 (87)	3 (13)
	Suspected Pneumonia			Suspected Sepsis			Suspected Sepsis					
	Eligible	Enrolled		Eligible	Enrolled		Eligible	Enrolled		Eligible	Enrolled	
		Yes	No		Yes	No		Yes	No		Yes	No
Total, No. (%)	111	58 (52)	53 (48)	483	208 (43)	275 (57)	83	22 (27)	61 (73)			
Sex												
Male	65	34 (52)	31 (48)	219	91 (42)	128 (58)	41	10 (24)	31 (76)			
Female	46	24 (52)	22 (48)	263	117 (44)	146 (56)	42	12 (29)	30 (71)			
Race												
White	35	26 (74)	19 (26)	268	122 (46)	146 (54)	43	15 (35)	28 (65)			
Black	58	32 (55)	26 (45)	180	72 (40)	108 (60)	35	6 (17)	29 (83)			
Hispanic	7	0	7 (100)	20	4 (20)	16 (80)	2	0	2 (100)			
Other	1	0	1 (100)	15	10 (67)	5 (33)	3	1 (33)	2 (67)			
Age, y												
Adult (18-64)	73	40 (55)	33 (45)	317	143 (45)	174 (55)	54	19 (35)	35 (65)			
Pediatric (2-17)	13	4 (31)	9 (69)	26	11 (42)	15 (58)	0					
Geriatric (≥65)	25	14 (56)	11 (44)	140	54 (39)	86 (61)	29	3 (10)	26 (90)			

ACS, Acute coronary syndrome.

Table E2. Reasons for nonenrollment among patients (stratified by each clinical study). Data are presented as number (percentage).

	Suspected ACS						Abdominal Pain					
	Patient Declines, N=6	Family Declines, N=0	Provider Declines, N=0	Not Consentible, N=0	Systems Issues, N=2	Other, N=0	Patient Declines, N=23	Family Declines, N=0	Provider Declines, N=0	Not Consentible, N=6	Systems Issues, N=15	Other, N=3
Sex												
Male	4 (67)				2 (100)		4 (17)			0 (0)	8 (53)	
Female	2 (33)				0		19 (83)			6 (100)	7 (47)	3 (100)
Race												
White	5 (83)				1 (50)		13 (57)			2 (33)	6 (40)	3 (100)
Black	1 (17)				1 (50)		8 (35)			4 (67)	6 (40)	0
Hispanic	0				0		1 (4)			0	3 (20)	0
Other	0				0		1 (4)			0	0	0
Age, y												
Adult (18–64)	4 (67)				1 (50)		20 (87)			4 (67)	14 (93)	2 (67)
Pediatric (2–17)	0				0		0			0	0	0
Geriatric (≥65)	2 (33)				1 (50)		3 (13)			2 (33)	1 (7)	1 (33)
	Brain Injury						Suspected Venous Thromboembolism					
	Patient Declines, N=31	Family Declines, N=10	Provider Declines, N=12	Not Consentible, N=25	Systems Issues, N=19	Other, N=0	Patient Declines, N=6	Family Declines, N=0	Provider Declines, N=2	Not Consentible, N=1	Systems Issues, N=11	Other, N=2
Sex												
Male	13 (42)	5 (50)	8 (67)	14 (56)	13 (68)		1 (17)		0	0	3 (27)	2 (100)
Female	18 (58)	5 (50)	4 (33)	11 (44)	6 (32)		5 (83)		2 (100)	1 (100)	8 (73)	0
Race												
White	15 (48)	4 (40)	8 (67)	15 (60)	3 (16)		0		1 (50)	1 (100)	5 (45)	0
Black	13 (42)	5 (50)	3 (25)	7 (28)	5 (26)		5 (83)		1 (50)	0	5 (45)	1 (50)
Hispanic				1 (4)	8 (42)		1 (17)		0	0	1 (10)	0
Other	2 (7)	1 (10)	1 (8)	2 (8)	3 (16)		0		0	0	0	1 (50)
Age, y												
Adult (18–64)	21 (68)	2 (20)	7 (58)	16 (64)	12 (63)		4 (67)		2 (100)	0	11 (100)	2 (100)
Pediatric (2–17)	0	0 (100)	0	0	0		0		0	0	0	0
Geriatric (≥65)	10 (32)	8 (80)	5 (42)	9 (36)	7 (37)		2 (33)		0	1 (100)	0	0
	Suspected Pneumonia						Suspected Sepsis					
	Patient Declines, N=25	Family Declines, N=3	Provider Declines, N=1	Not Consentible, N=7	Systems Issues, N=15	Other, N=2	Patient Declines, N=106	Family Declines, N=10	Provider Declines, N=20	Not Consentible, N=67	Systems Issues, N=59	Other, N=13
Sex												
Male	14 (56)	2 (67)	0	5 (71)	10 (67)	1 (50)	40 (38)	7 (70)	9 (45)	34 (51)	31 (53)	7 (54)
Female	11 (44)	1 (33)	1 (100)	2 (29)	5 (33)	1 (50)	66 (62)	3 (30)	11 (55)	33 (49)	27 (47)	6 (46)
Race												
White	9 (36)	1 (33)	0	5 (71)	2 (13)	2 (100)	54 (51)	3 (30)	9 (45)	45 (68)	32 (54)	3 (23)
Black	14 (56)	2 (67)	1 (100)	2 (29)	7 (47)	0	48 (45)	7 (70)	10 (50)	19 (29)	14 (24)	10 (77)
Hispanic	1 (4)	0	0	0	6 (40)	0	3 (3)	0 (100)	1 (5)	1 (1)	11 (19)	0
Other	1 (4)	0	0	0	0	0	1 (1)	0 (100)		2 (2)	2 (3)	0
Age, y												
Adult (18–64)	19 (76)	1 (33)	1 (100)	2 (29)	9 (67)	1 (50)	69 (65)	4 (40)	13 (65)	41 (61)	42	7 (64)
Pediatric (2–17)	2 (8)	1 (33)	0	0	6 (33)	0	7 (7)	2 (20)	0	0	4	1 (8)
Geriatric (≥65)	3 (12)	1 (33)	0	5 (71)	0	1 (50)	30 (28)	4 (40)	7 (35)	26 (39)	13	5 (28)

Table E2. Reasons for nonenrollment among patients (stratified by each clinical study) (cont'd).

	Suspected Sepsis					
	Patient Declines, N=32	Family Declines, N=2	Provider Declines, N=2	Not Consentible, N=8	Systems Issues, N=17	Other, N=0
Sex						
Male	15(47)	2 (100)	1 (50)	6 (75)	7 (41)	
Female	17 (53)	0	1 (50)	2 (25)	10 (59)	
Race						
White	11 (34)	2 (100)	1 (50)	4 (50)	10 (59)	
Black	21 (66)	0	1 (50)	4 (50)	3 (18)	
Hispanic	0	0	0	0	2 (12)	
Other	0	0	0	0	2 (12)	
Age, y						
Adult (18–64)	21 (66)	0	2 (100)	2 (25)	10 (59)	
Pediatric (2–17)	0	0	0	0	0	
Geriatric (≥65)	11 (34)	2 (100)	0	6 (75)	7 (41)	