Published in final edited form as:
Acad Emerg Med. 2012 June ; 19(6): 664–672. doi:10.1111/j.1553-2712.2012.01364.x.

Risk Factors for Increased ED Utilization in a Multinational Cohort of Children with Sickle Cell Disease

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Abstract

Objectives—To identify clinical, social, and environmental risk factors for increased emergency department (ED) use in children with sickle cell disease (SCD).

Methods—This study was a secondary analysis of ED utilization data from the international multicenter Silent Cerebral Infarct Transfusion (SIT) trial. Between December 2004 and June 2010, baseline demographic, clinical, and laboratory data were collected from children with SCD participating in the trial. The primary outcome was the frequency of ED visits for pain. A secondary outcome was the frequency of ED visits for acute chest syndrome.

Results—The sample included 985 children from the US, Canada, England, and France, for a total of 2,955 patient-years of data. There were 0.74 ED visits for pain per patient-year. A past medical history of asthma was associated with an increased risk of ED utilization for both pain (RR = 1.28, 95% CI = 1.04 to 1.58) and acute chest syndrome (RR = 1.60, 95% CI = 1.03 to 2.49). Exposure to environmental tobacco smoke in the home was associated with 73% more ED visits for acute chest syndrome (RR 1.73, 95% CI = 1.09 to 2.74). Each $10,000 increase in household income was associated with 5% fewer ED visits for pain (RR 0.95, 95% CI = 0.91 to 1.00, p = 0.05). The association between low income and ED utilization was not significantly different in the USA vs. countries with universal health care (p = 0.51).

Conclusions—Asthma and exposure to environmental tobacco smoke are potentially modifiable risk factors for greater ED use in children with SCD. Low income is associated with greater ED use for SCD pain in countries with and without universal health care.

INTRODUCTION

Sickle cell disease (SCD) is an inherited disorder of hemoglobin that affects approximately 100,000 Americans.[1] In affected individuals, hemoglobin forms rigid polymers in response to tissue hypoxia or stress, which gives erythrocytes a sickle shape. Etiology for vaso-occlusive pain episodes is not completely understood, but evidence suggests inflammation and other rheologic processes (coagulation and platelet activation, endothelial dysfunction) contribute to increased cell adhesion, which leads to vasoocclusion and ultimately, clinical

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Presented at the Society for Academic Emergency Medicine Annual Meeting. Boston MA, June 2011.

Disclosures: The authors have no potential conflicts of interest or other financial disclosures to report.

manifestations of SCD.[2–7] The hallmark of the disease and the most frequent reason for ED visits is the vasoocclusive crisis,[8] marked by paroxysmal attacks of debilitating pain. A leading cause of death is the acute chest syndrome,[9] marked by pulmonary infiltrate, fever, and respiratory distress. Despite being a monogenic disorder, wide clinical variation in the severity of SCD exists, suggesting that non-genetic factors contribute. Individuals with severe disease suffer frequent complications and early mortality, while others can live into their eighth decade. Clinical, environmental, and social factors are now believed to contribute to SCD morbidity, and this has prompted interrogation of modifiable risk factors for increased health care utilization.

In children with SCD, comorbid asthma is associated with higher rates of hospital admissions for pain, acute chest syndrome, and death;[10–12] however, the relationship between comorbid asthma and ED use for SCD has not been adequately explored. The presumed mechanism is that asthma increases complications of SCD via the convergence of the two inflammatory processes.[13,14] Inflammation of the airways (asthma) and inflammation of the endothelium (SCD) are synergistic and thus the balance is tipped toward increased vasoocclusion. Transgenic mice with SCD have increased airway inflammation at baseline,[15] and show greater increases in pulmonary inflammation than wild type mice when experimental models of asthma are induced.[16] Human data support these findings, as individuals with SCD have high rates of airway hyper-reactivity even in the absence of asthma.[17] Demonstration that asthma is associated with increased ED utilization for SCD would provide support for future research to evaluate asthma interventions (both ED- and clinic-based) that could reduce SCD morbidity and ED use.

Poverty has been identified as a significant threat to the health of all Americans (attributed to cause 133,000 deaths in the United States each year),[18] but the data regarding the effects of income on SCD are mixed. Prior studies using Medicaid insurance as a proxy for lower income showed an increase in health care utilization among children with SCD enrolled in Medicaid compared to those with private insurance.[19,20] In contrast, a prospective study of 232 adults with SCD followed for a mean of 4.4 months did not find statistically significant differences in income or education levels between low and high users of ED care.[21] Identification of poverty in this cohort as a risk factor for ED use would suggest that even low-income families with subspecialty follow-up are at increased risk.

The objective of this study was to identify factors associated with increased ED utilization in children with SCD. This study represents an analysis of ED utilization data from a multinational cohort of children participating in a prospective clinical trial. As all children in the study receive high-quality subspecialty care, these data provide information about risk factors for ED utilization and SCD morbidity when issues of access to and quality of care are removed. Our hypotheses are that low income and comorbid asthma are associated with increased ED use. A secondary objective was to explore the association between income and ED utilization in countries with and without universal access to health care. Further understanding of the associations between ED utilization and risk factors such as asthma and income may enable clinicians to better target high-risk groups for intervention.

METHODS

The Silent Cerebral Infarct Transfusion (SIT) Trial

The SIT trial includes 25 active clinical sites located in North America (US and Canada) and Europe (U.K. and France). The primary aim of the trial was to test the hypothesis that prophylactic blood transfusion therapy in children with silent cerebral infarcts (SCI) will result in at least an 86% reduction in the rate of subsequent overt strokes or new or progressive cerebral infarcts as defined by magnetic resonance imaging (MRI) of the brain.

Details of the recruitment were described in the recently published study design manuscript for the SIT Trial (clinicaltrials.gov Identifier: NCT00072761).[22] Between December 2004 and June 2010, baseline demographic, clinical, and laboratory data were collected from children participating in the trial and kept in an SPSS database (IBM SPSS, Armonk, NY). Analysis of these baseline data are the subject of this article. The SIT trial was approved (including a positive pre-study review) by the institutional review boards of all participating sites. Written informed consent was obtained from caretakers and verbal assent from each participant.

Study Design

This study was a post-hoc analysis of potential predictor variables for ED use among subjects enrolled in the SIT trial. The primary outcome of our analysis, incidence rate of ED visits for pain, was determined by chart review of each subject encompassing the three years prior to enrollment in the SIT trial. Baseline demographic (including self-reported income, race, sex, and other socio-demographic variables via cross-sectional survey), clinical (co-morbidities, prior illnesses, medication use, and other clinical variables via cross-sectional survey), and laboratory data were prospectively collected at the time of enrollment. Children were enrolled between December 2004 and June 2010. This secondary analysis was approved by the executive committee of the SIT trial and the data safety monitoring board appointed by the National Institute of Neurological Disorders and Stroke.

Study Setting and Population

Tertiary medical centers with multidisciplinary SCD services at 25 sites in Canada, England, France, and the United States were included. Patients with hemoglobin SS (94%) or Sβ zero (6%), the most severe types of SCD, were recruited between 5 and 14 years of age. Children included did not have any evidence of overt stroke, were not on regular blood transfusion therapy, and were not receiving hydroxyurea therapy. An entry criterion of the study was an ongoing prior relationship with the physicians of the hematology service at participating clinical sites. This criterion was instituted because of the intensity of the clinical trial, requiring patients who were randomized to the treatment arm of the trial to receive blood transfusion therapy for 36 months. Children who did not have an existing relationship with the hematology service (as determined by the site director) were not enrolled in the study.

Study Protocol

Training of Chart Abstractors—Before the chart abstraction was performed, all site coordinators and auditors were trained in the methods of chart abstraction. Definitions for key variables and all data abstraction forms were reviewed. Individual chart abstractors (research nurses) were trained by site coordinators. For each individual in the SIT trial, charts were reviewed for all visits to the medical center for the three years prior to signing consent. Before the start of the study, coordinators at all sites agreed to case definitions for outcome variables, including ED visit, hospital admission, painful episode, and acute chest syndrome. Periodic meetings were held with study coordinators to review coding rules and ensure accurate and uniform chart abstraction procedures. Chart abstractors were blinded to the hypothesis for this study.

The primary outcome for this study was the number of ED visits for painful episodes. An ED visit was defined as any visit to the ED, including patients who were admitted to the hospital and those who were discharged home. A painful episode was defined as an ED visit that required treatment with opiates that could not be attributable to a cause other than SCD. A secondary outcome for this analysis was the number of ED visits for acute chest syndrome, defined as a pulmonary process (abnormal chest radiograph) that required admission to the hospital.[23] Pneumonia was indistinguishable from acute chest syndrome,

and thus considered an episode of acute chest syndrome in this analysis. Visits that met criteria for both painful episode and acute chest syndrome were recorded as acute chest syndrome. For each patient, all acute chest syndrome and pain episodes in the three years prior to signing informed consent were extracted from the medical record at the patient's trial site.

Classification of Income—Participants self-reported their yearly household income in $10,000 increments up to $100,000, with additional categories for $100,000 – $150,000 and greater than $150,000. For trial sites outside the United States, income was converted to U.S. dollars on the day the information was recorded. Participants also indicated the number of people living in their households. The 2010 Health and Human Services poverty guidelines for the 48 contiguous states provide different cut-points for the federal poverty line based on the number of people in a given household (Data Supplement 1).[24] Using the number of people in each individual's household, income was re-coded into a dichotomous variable indicating whether or not the patient lived below the federal poverty line. Per-capita income for each participant's household was calculated by dividing unadjusted household income by the number of people living in that household.

Asthma—Asthma was defined as the parent or guardian answering "yes" to the question: "Did a doctor ever say the patient has asthma?" The use of asthma medication was also recorded. When a diagnosis of asthma was made and no asthma medication was recorded in the SIT Trial database, we confirmed the diagnosis of asthma with a review of the medical records by the site coordinator for any hospital admissions, ED visits, or medications for asthma. Similarly, if the patient was recorded in the medical records as having prescriptions for inhaled corticosteroids, bronchodilators, or a cysteinyl leukotriene receptor antagonist, but the parent did not state that the child had asthma, the site coordinator was required to recheck the medical records for a diagnosis of asthma. An assumption was made that asthma is a chronic condition.[25]

All data were recorded onto the SIT Demographic and Phenotypic form and entered into a SPSS database. Performance of chart abstractors was checked regularly by site coordinators and audited during site visits by the primary investigator. All laboratory values and clinical parameters were checked for outliers and missing data. Specifically, based on the distribution, each value below the 5th percentile and above the 95th percentile was re-confirmed for accuracy at the local site, and when discrepant, was changed accordingly. For all missing key variables, additional contact was made with the local site coordinator to determine if the data were not available or simply not recorded. Interrater reliability of chart abstraction was not assessed. Instead, all values below the 5th percentile and above the 95th percentile were re-confirmed by a second reviewer at the local site.

Data Analysis

All data analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC). Missing values were estimated using a multiple imputation approach,[26,27] in which five data sets were created (data regarding missing variables are listed in Figure 1). T-tests and chi-square tests were used to compare mean differences (of normally distributed variables) and proportions when appropriate. Multivariable negative binomial regression models were used to estimate adjusted rate ratios for ED visits. Separate models were run using ED visits for pain and ED visits for acute chest syndrome as the outcome variable. Alpha was set at 0.05 for the primary and secondary analyses. Variables with biologically plausible, known associations with SCD morbidity were included in the multivariable model. In addition to income and trial site, covariates considered for inclusion included age, sex, sickle cell genotype, asthma diagnosis, steady state hemoglobin, steady state leukocyte count, fetal

hemoglobin percent, and the presence of tobacco smokers living in the home.[28] Because income and insurance status were collinear among participants from U.S. sites, insurance status was not included in the multivariable models. Continuous variables were modeled with linear or quadratic terms when appropriate. According to a pre-specified protocol for regression analyses of SIT trial data, only covariate terms with p values below 0.2 remained in the final regression models. To assess if the effect of family income was significantly different in countries with universal health care vs. the USA, a test for heterogeneity of effect was performed.

RESULTS

Characteristics of Study Subjects

Of 1,003 participants in the SIT trial at the time of analysis, 18 did not have data regarding ED visits for pain, and 12 were missing data regarding ED visits for acute chest syndrome (Figure 1). Thus, the sample included 985 subjects with a total of 2,955 patient-years of data, 2,201 visits for pain (0.74 per patient-year), and 193 visits for acute chest syndrome (0.06 per patient-year). Baseline characteristics of the cohort are listed in Table 1. The mean age was 9 years and the cohort was 52% male. Nearly one-quarter (24.4%) of patients had a diagnosis of asthma. The median yearly household income was $25,000 with a median of four individuals per household. Among U.S. children, more than half (53.7%) of children in the cohort live below the poverty line, 71% were insured by Medicaid, 33% had private insurance, and 1% were uninsured.

Main Results

Asthma and Low Self-Reported Income are Associated with Increased ED Use for Pain—Table 2 lists ED use by income category, and Table 3 shows results of the multivariable models. Asthma was associated with a 28% increase in the frequency of ED visits for pain (RR 1.28, 95% CI = 1.04 to 1.58, p = 0.02). There was an inverse relationship between income and ED use for pain (Figure 2). Each $10,000 increase in income was associated with a 5% reduction in ED visits (RR 0.95, 95% CI = 0.91 to 1.00, p = 0.05 – Table 3). A separate multivariable model showed that income below the federal poverty line was associated with a 31% increase in ED visits for pain (RR 1.31, 95% CI = 1.04 to 1.64, p = 0.02). The relationship between per-capita income and rate of painful crises was not statistically significant (RR 0.87, 95% CI = 0.75 to 1.01, p = 0.07). Other variables significantly associated with ED use for pain were fetal hemoglobin percent and trial site (Table 3).

Environmental Tobacco Smoke and Asthma are Associated with Increased ED Use for ACS—The two variables associated with increased risk of ED utilization for acute chest syndrome were asthma and environmental tobacco smoke exposure. Exposure to environmental tobacco smoke within the home was associated with a 73% increase in the rate of ED utilization for acute chest syndrome (RR 1.73, 85% CI = 1.09 to 2.74, p = 0.02) and a physician diagnosis of asthma was associated with a 60% increase in ED visits for acute chest syndrome (RR 1.60, 95% CI = 1.03 to 2.49, p = 0.04). A diagnosis of HbSβThalassemia^0 was associated with a significantly reduced risk of acute chest syndrome (RR 0.29, 95% CI = 0.09 to 0.93, p = 0.04). Income and other variables thought to be associated with SCD morbidity were not significantly associated with ED utilization for acute chest syndrome (Table 3).

The Effect of Income on ED Use is not Significantly Different in Countries with Universal Health Care—A test for heterogeneity of effect to determine if the effect of income on ED utilization was different in countries with universal health care was not

statistically significant (p = 0.51). Rates of ED use for pain (0.76 vs. 0.68, p = 0.06) and ACS (0.07 vs. 0.06, p = 0.17) were not significantly different between the USA and international trial sites (Table 2).

DISCUSSION

This study represents an analysis of clinical, environmental, and socioeconomic risk factors for ED utilization in a cohort of children who receive high quality subspecialty care as part of a clinical trial. Asthma and low income were associated with higher rates of ED use for pain, and the two greatest risk factors for acute chest syndrome were asthma and exposure to environmental tobacco smoke in the home. These results have import for future research. The magnitude of these associations may be greater in the general population of children with SCD.

Our group has demonstrated that children with SCD who also have asthma have higher hospitalization and mortality rates,[10,11] and that asthma exacerbations may precipitate painful episodes,[12] but ED use had not been specifically studied. As expected, asthma was associated with increased ED utilization for SCD. Asthma was the only variable associated with increased ED utilization for both pain and acute chest syndrome in the SIT cohort. The magnitude of this association may be even greater in children without access to subspecialty follow-up. Future multi-modal interventions may include aggressive management of asthma in the ED, more frequent follow-up visits for children with asthma, and targeted support for children who live in poverty. Until prospective trials are conducted, we recommend that clinicians carefully assess SCD patients for signs and symptoms of asthma, and closely follow recommended guidelines for the management of asthma in the ED.

Statistically significant associations were noted for household income and living below the federal poverty line and the painful episode rate; however, the association between per-capita income and ED utilization for pain was not statistically significant. These results suggest, but do not confirm, that there is a minimum threshold of family income, where regardless of the number of individuals that live in the house, living below the federal poverty line results in an increase in ED utilization. Another possible source for the discrepancy is the methodology used for calculating household per-capita income.

Our analysis was also designed to test the hypothesis that the association between low self-reported income and ED use would not be present in trial sites with universal access to health care. However, we did not find evidence to support this hypothesis. These data suggest that regardless of location and access to health care, children with SCD who live in low-income households have higher rates of ED utilization. This relationship may be mediated directly through deleterious effects of the physical environment and the social environment experienced by members of low-income households at both the individual and community levels.[22–27,29] Another possible mechanistic explanation might involve the association between low income and less formal education; less educated individuals may be less likely to acquire the knowledge and skills required for successful parental/self-management of symptoms.[30,31] Education-related health outcomes often show a threshold pattern similar to the findings in our study.[32] Yet another contributing factor may be the greater prevalence in low-income areas of physician practices with characteristics shown to be related to increased ED utilization (e.g. limited evening/weekend hours, lack of 24-hour phone access, no availability of nebulizer therapy).[33] The association between low income and ED utilization, demonstrated even for children with access to subspecialty care, suggests that parents with low income may need specific support to overcome barriers to using physician services other than the ED.

A new finding is that the presence of tobacco smokers living in the same household as the patient was associated with an increase in acute chest syndrome diagnoses in the ED. The presence of a household tobacco smoker was associated with a 73% increase in acute chest syndrome events when compared to those that did not have household exposure. There is strong data regarding the association between environmental tobacco smoke and increased asthma morbidity,[34–37] and there is emerging data about its association with SCD morbidity.[38,39] These data strengthen the evidence that environmental tobacco smoke is associated with SCD morbidity, particularly lung disease.

LIMITATIONS

There are several important differences between the patients in this study and the general population of children with SCD that affect the generalizability of the results. 1) Participants in this study are receiving SCD care at a tertiary medical center under the direction of a primary hematologist and a multi-disciplinary care team, whereas only 10% of Medicaid-enrolled children with SCD in the United States are under the regular care of a primary hematologist.[40] 2) Participants in this study consent to randomization in a clinical trial, thus they are likely to have greater trust and rapport with their providers than the general population. 3) Subjects in the trial cannot have evidence of overt stroke or be on hydroxyurea, which creates selection bias towards milder cases of SCD. These differences may have influenced some of the results of this study, thus limiting the generalizability of the findings. For example, in the general population, patients with SCD average 1.5 to 2.04 acute-care visits per patient-year,[41] vs. 0.74 in the current study. It is likely that higher quality care and more intensive therapies were provided by the hematologists caring for these children. These differences may have masked differences (i.e. create bias towards the null hypothesis) in ED utilization rates based on health care delivery system that actually exist in the general population.

In this study, family income was a self-reported variable that may not accurately reflect true income. If patients were likely to self-report income higher than their true income, this would bias our results towards the null hypothesis. Additionally, our data cannot necessarily be extrapolated to assume that low socioeconomic status (a more global measure of a person's income, education, occupation, and neighborhood disadvantage) will also be associated with increased ED utilization.

Some of the data were prospectively collected specifically for the SIT study (household income, number of people in household, and other sociodemographic and clinical variables); however, the rate of painful episodes, acute chest syndrome events, and diagnosis of asthma were based on chart review at each subject's participating institution. All retrospectively collected variables were extracted with a rigorous prespecified protocol to minimize overestimation of outcome events. It is possible that ED visits were missed; however, this would tend to create bias towards the null hypothesis. Visits to EDs other than the SIT trial site were only recorded if the team knew about the event; no specific measures were taken to capture visits to other hospitals. We believe that failure to systematically record the ED visits that did not occur at the primary tertiary care center where the patient was followed would not bias the results away from the null hypothesis. Thus, the validity of the results is not significantly weakened.

Data on factors such as family income and environmental tobacco smoke were collected at the time of consent, but ED utilization data (the primary outcome) were collected for the three years prior to consent. The collection of outcome data for periods preceding the collection of exposure data creates the possibility that individuals were not exposed to a given risk factor (e.g. low income or tobacco smoke) for the entire duration of the sampling

period. This does not significantly threaten the validity of the study, since this would tend to bias the results towards the null hypothesis. Individuals who were exposed to second hand smoke or to poverty for only part of the sampling period may have been part of the "exposed" group; the association would likely be stronger if these partial exposures could be accounted for. Additionally, children who had recently moved into the catchment area would not have ED visits recorded prior to their move. The vast majority of patients in the trial had been in the area for over three years because a requirement for entry into the study was an ongoing relationship with the hematology service.

CONCLUSIONS

We report that asthma, low income, and environmental tobacco smoke exposure are associated with higher rates of ED use for vasoocclusive complications of SCD in children enrolled in the SIT trial. These associations are likely to be even greater in the general population of children with SCD. A statistically significant difference was not found in the rates of ED utilization or the effect of income on ED utilization in countries with and without universal access to health care. Clinicians should carefully assess children with SCD for signs and symptoms of asthma and follow national guidelines for the management of asthma exacerbations. Future research is warranted to determine the magnitude of these associations in the general population of children with SCD. Targeted interventions to modify these risk factors should be evaluated in prospective trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Gary Yu, Columbia University, Mailman School of Public Health, for statistical analysis (financial support was given for this contribution); Joanne Brady, Columbia University, Departments of Anesthesiology and Epidemiology, for statistical analysis (no financial support was given for this contribution); Charles DiMaggio, PhD, MPH, Columbia University, Departments of Anesthesiology and Epidemiology, for statistical analysis (no financial support was given for this contribution); and Charles T. Quinn, MD, MS, Cincinnati Children's Hospital Medical Center, Sharada A. Sarnaik, MD, Wayne State University School of Medicine, and David Newman, MD, Mount Sinai School of Medicine, for critical revisions of the manuscript for important intellectual content (no financial support was given for these contributions).

Supported by a grant from the National Institutes of Health (M.R.D., U01-NS42804).

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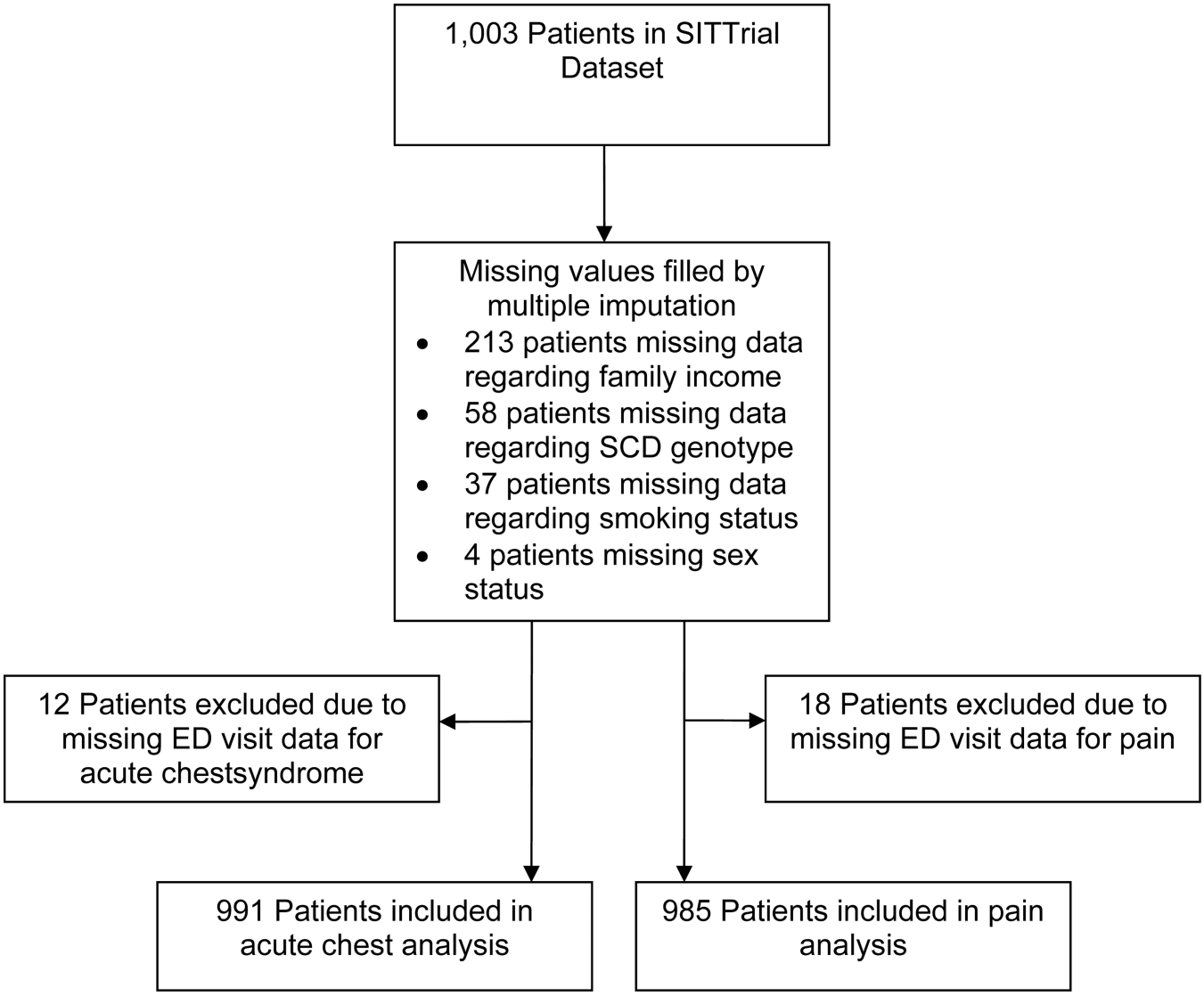

Figure 1.
Patient Selection

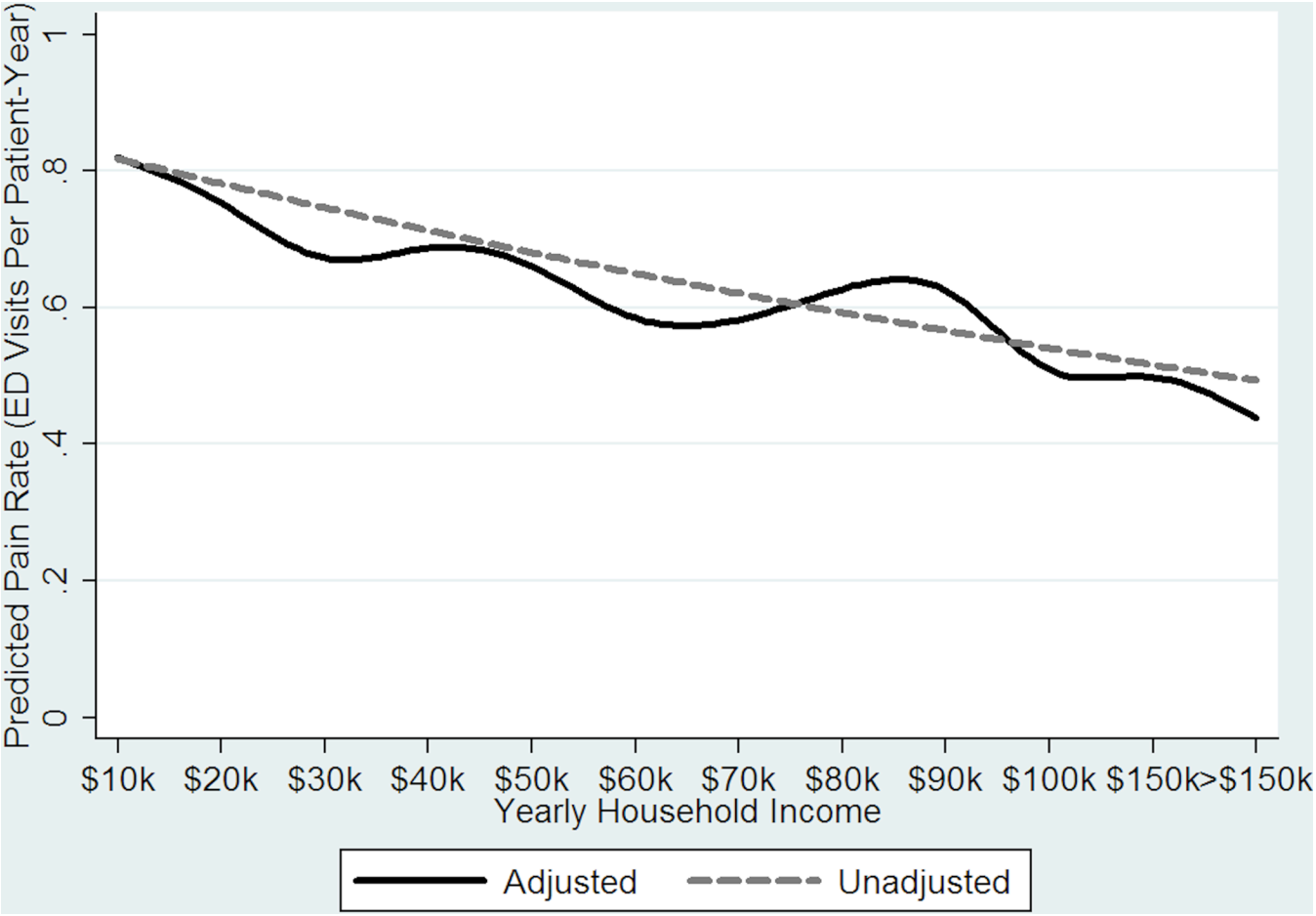

Figure 2.
Association between Categories of Household Income and ED Use for Pain

Table 1

Clinical Characteristics and Demographic Data

Characteristic	USA	International	p-value
N	810	193	
ED visits for pain	1812	156	
Pain visits/pt-year	0.76	0.68	0.41
ED visits for acute chest	389	37	
Acute chest visits/pt-year	0.06	0.06	0.96
Age†‡	8.71 (6.88–10.83)	9.67 (7.59–11.39)	0.01
Sex (% male)	51.4%	53.9%	0.31
Race‡			<0.01
Black or African American	97.8%	79.3%	
Asian	0.1%	1.6%	
Pacific Islander	0.1%	0%	
White	0.4%	0.5%	
Other	1.1%	18.7%	
Type of insurance (USA only)^			
Medicaid	70.5%		
Private insurance	32.7%		
Uninsured	1.2%		
Household income†	$20,000 – $29,000 ($10,000–$59,000)	$20,000 – $29,000 ($10,000–$69,000)	0.09
Asthma‡	26.7%	14.0%	>0.01
People per household†	4 (3–5)	4 (3–5)	0.46
Below poverty line	53.7%	48.3%	0.41
Smoker in household‡	27.4%	15.5%	>0.01
Steady state hemoglobin (g/dL)†‡	8.0 (7.3–8.6)	8.3 (7.6–9.1)	>0.01
Fetal hemoglobin %*†‡	11.0% (6.0–17.0)	9% (5.0–15.0)	>0.01
Steady state WBC (count/microL)†	12,000 (10,000–14,500)	12,000 (9,200–15,000)	0.14

*Fetal hemoglobin level obtained after 3 years of age at local site

^Values do not add up to 100% because patients can answer “yes” to more than one question

†Values are expressed as a median with inter-quartile range in parentheses

‡Difference between groups statistically significant (p<0.05)

Table 2

ED Utilization Rates by Income Category

	USA			International Sites		
	n	Visits Per Pt-year	SD	n	Visits Per Pt-year	SD
ED visits for pain						
< $10k	117	0.75	1.060	13	0.31	0.480
$10–$19K	153	0.93	1.243	22	0.76	0.868
$20–$29k	129	0.72	1.292	26	0.31	0.541
$30–$39k	77	0.70	1.031	19	0.49	0.706
$40–$49k	57	0.67	0.885	7	1.19	0.742
$50–$59k	29	0.47	0.843	5	0.60	1.164
$60–$69k	26	1.06	1.733	7	0.43	0.713
$70–$79k	17	0.96	2.131	5	0.40	0.596
$80–$89k	14	0.24	0.356	1	1.67	NA
$90–$99k	17	0.33	0.425	5	0.80	0.767
$100–$149k	24	0.44	0.679	4	0.33	0.272
$150k+	5	0.40	0.596	2	0.17	0.236
Refused	60	0.73	0.771	19	1.02	2.218
Unknown	69	0.96	1.311	55	0.88	1.216
Total	794	0.76	1.158	190	0.68	1.114
ED visits for acute chest syndrome						
< $10k	118	0.04	0.146	13	0.00	0.000
$10–$19K	154	0.06	0.235	22	0.17	0.337
$20–$29k	130	0.07	0.209	26	0.05	0.155
$30–$39k	77	0.05	0.214	19	0.02	0.076
$40–$49k	57	0.05	0.164	7	0.19	0.325
$50–$59k	29	0.06	0.201	5	0.00	0.000
$60–$69k	26	0.04	0.109	7	0.00	0.000
$70–$79k	17	0.12	0.485	5	0.00	0.000
$80–$89k	14	0.00	0.000	1	0.00	NA
$90–$99k	17	0.08	0.146	5	0.00	0.000

	USA			International Sites		
	n	Visits Per Pt-year	SD	n	Visits Per Pt-year	SD
$100–$149k	24	0.08	0.246	4	0.00	0.000
$150k+	5	0.20	0.298	2	0.00	0.000
Refused	60	0.12	0.367	19	0.14	0.256
Unknown	70	0.07	0.187	57	0.05	0.187
Total	798	0.07	0.223	192	0.06	0.199

Table 3

Negative Binomial Regression Models of ED Visits for Pain and Acute Chest Syndrome

Variable	Rate Ratio	95% CI	p-value
ED visits for pain			
Asthma	1.28	1.04–1.58	0.02
Family income	0.95	0.91–1.00	0.05
Universal health care	0.77	0.22–0.98	0.06
Baseline hemoglobin	1.10	1.00–1.20	0.04
Fetal Hb percent	1.01	0.99–1.01	0.20
Trial site	1.02	1.01–1.04	0.01
ED visits for acute chest syndrome			
Asthma	1.60	1.03–2.49	0.04
Family income	1.06	0.96–1.17	0.22
Universal health care	2.58	0.67–9.95	0.17
Sickle cell genotype (HbSS vs. Hb SβThal^0)	0.29	0.09–0.93	0.04
Sex	0.89	0.59–1.33	0.55
Smoker in household	1.73	1.09–2.74	0.02
Trial site	1.02	0.99–1.05	0.25