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Factors Associated with the Need for Hospitalization, Length of Hospital Stay, and Parental Consent to Participate in Research among Children with Community Acquired Pneumonia

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FACTORS ASSOCIATED WITH THE NEED FOR HOSPITALIZATION, LENGTH OF HOSPITAL STAY, AND PARENTAL CONSENT TO PARTICIPATE IN RESEARCH AMONG CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

by

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DEDICATION

I would like to dedicate this work to my family. To my parents, Louis and Marlene Cohen, who taught me the importance of an education and instilled in me the belief that I could do anything. I miss you both every single day.

To my children, Shira, Beryl, and Dena Grant, who supported and encouraged me, even when it meant that I couldn't be there to support and encourage them. I am so proud of the amazing people that you have become and of all of your accomplishments. I'm certain that each one of you will make the world a better place in your own special way.

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PREFACE

This dissertation is original and unpublished work by the author and has been formatted according to the Journal of the American Medical Association guidelines.

ABSTRACT

Grant, Cori Cohen. Ph.D. The University of Memphis. December, 2017. Factors Associated With the Need for Hospitalization, Length of Hospital Stay, and Parental Consent to Participate in Research Among Children with Community Acquired Pneumonia Major Professor: Fawaz Mzayek, M.D, Ph.D.

Community-acquired pneumonia (CAP) is the third leading cause of hospitalization among children in the U.S. This research project is comprised of three studies of children with CAP. The data were collected for the CDC's Etiology of Pneumonia in the Community (EPIC) study. Study one aimed to examine the association of clinical factors with potentially unnecessary hospitalizations, as defined by a length of stay (LOS) in the hospital ≤ 24 hours. Study two aimed to validate the Canadian Acute Respiratory Illness and Flu Scale (CARIFS) questionnaire among an inpatient pediatric population with CAP. This study also examined the utility of the CARIFS questionnaire in predicting LOS in the hospital. Study three examined factors that could influence parental consent for their child to participate in research. Participants were children, 0-18 years old, classified into five age-categories, who were hospitalized with CAP at one of three sites: Le Bonheur Children's Hospital, Monroe Carell Jr. Children's Hospital at Vanderbilt and Primary Children's Hospital. A short length of stay, ≤ 24 hours, was associated across all ages with higher oxygen saturation level at admission. Study two, the CARIFS survey, had high internal reliability among this population (Cronbach's alpha = 0.89). The 18 CARIFS questions loaded onto four domains (physical function, parental impact, subjective symptoms and objective symptoms). Except for infants, the more severe the symptoms of physical function, the longer the LOS. In study three, households with less education were more likely to give consent for their child to participate than those with a college degree (OR = 4.78, 95% CI = 1.75, 13.05). Desire to learn more about their child's illness (OR = 1.59, 95% CI = 1.06, 2.39) and altruism (OR = 3.64, 95% CI = 2.20, 6.02) was also associated with higher participation, while

concern about the nose and throat swab (OR = 0.48, 95% CI = 0.36, 0.65) was associated with lower participation. These findings show clinical presentation of CAP does not adequately predict LOS, while parent-reported markers of a child's physical function may predict LOS. Detailed explanation of potential benefits and reducing invasive procedures could improve participation in research.

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List of Abbreviations

CARIFS	Canadian Acute Respiratory Illness and Flu Scale
CAP	Community-acquired Pneumonia
ED	Emergency Department
EPIC	Etiology of Pneumonia in the Community
CDC	Centers for Disease Control
PSI	Pneumonia Severity Index
HIV	Human Immunodeficiency Virus
GLM	Generalized Linear Model
LBCH	Le Bonheur Children's Hospital
LOS	Length of Stay
	National Institutes of Health
RSV	Respiratory Syncytial Virus
UTI	Urinary Tract Infection
VIF	Variation Inflation Factors

Chapter 1 Introduction

Community-acquired pneumonia (CAP) is a leading cause of hospitalization among children under 18 years of age in the United States,[1] and ranks third among leading causes of pediatric hospitalization outside the neonatal period.[2] There is evidence of wide-variation in pediatric community acquired pneumonia CAP-related admissions rates as documented in previous studies. One such study, conducted by Gorton in 2006,[2] found high levels of variation among county rates of hospitalization in Pennsylvania. In this study, the annual rates of hospitalization ranged from 18.3 per 100,000 to 350.3 per 100,000.[3] This is also acknowledged in the current clinical guidelines for CAP (referred to as clinical guidelines) published by Bradley in 2011,[4] (Bradley et al "The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Disease Society and the Infectious Disease Society of America"). "The wide variation in CAP-related admission rates between neighboring geographic regions[2] suggests that physicians do not use consistent criteria to make site-of-care decisions."[3] These findings suggest the need for better ways to help physicians make decisions pertaining to the appropriate site-of-care and acknowledge an important gap in the clinical guidelines resulting from the lack of this information.

This research project comprises three discrete, albeit interrelated, studies of children with CAP. The project uses data collected for the Centers for Disease Control and Prevention's (CDC) Etiology of Pneumonia in the Community (EPIC) study. The first study aims to examine factors associated with one type of potentially unnecessary hospitalization, as defined by a length of stay (LOS) in the hospital for ≤ 24 hours for children hospitalized with CAP. The second study aims to validate the Canadian Acute Respiratory Illness and Flu Scale (CARIFS)

questionnaire among an inpatient pediatric population with CAP. Furthermore, this study will examine the utility of the CARIFS instrument in predicting LOS, measured by days in the hospital. The CARIFS data were collected as part of the EPIC study. Finally, a third set of data from the EPIC study will be utilized to examine factors that influence parental consent for their child to participate in epidemiological research. This will be done by comparing parental attitudes toward motivational factors among study participants with those who refused to participate.

The EPIC study

The EPIC study is a prospective, population-based study that was conducted to determine the incidence and etiology of hospitalized CAP in children and adults in the U.S.[5] The study was conducted from January 2010-June 2012 at three pediatric sites: Le Bonheur Children's Hospital in Memphis, the Monroe Carell Jr. Children's Hospital at Vanderbilt in Nashville and the Primary Children's Hospital in Salt Lake City.[5] These analyses only address the pediatric study subjects. Three thousand eight hundred and three children, up to the age of 18, were identified as eligible for the study and 2,638 (69%) were enrolled.[5] As a part of the EPIC study, key clinical, socioeconomic, and demographic information was collected through caregiver interviews and medical record review. Detailed methodology for EPIC is described elsewhere.[5]

In this project, data from the EPIC study will be used to identify factors associated with a mild course of pneumonia among children who were hospitalized, as indicated by discharge from the hospital within ≤ 24 hours.

The CARIFS survey

CARIFS is a caregiver questionnaire that assesses the parent's perceived functional burden of illness related to acute respiratory disease in their child according to three domains of

illness: 1) physical symptoms, 2) the child's function, and 3) impact on the parents' daily routine.[6] The questionnaire was designed through a joint effort between parents and pediatricians to ensure that the questions reflect signs and symptoms that are important to both groups. CARIFS was originally designed to meet the need for an objective outcome measure of disease severity among children with acute respiratory infections. It has been validated for use among children treated in outpatient settings such as physician practices[7] but not, to our knowledge, among children who are hospitalized with pneumonia.

CARIFS may prove to be a valid tool for evaluating disease severity, as measured by LOS, among children hospitalized with CAP. Furthermore, it may provide additional information on determinants of unnecessary hospitalization for children with CAP. The CARIFS survey was completed upon admission into the EPIC study by a parent or caregiver. For this project, data from CARIFS will be used to assess the validity of the CARIFS instrument among inpatient children with CAP, and examine its utility in predicting LOS in this patient population.

The Parental Research Consent Survey

Engagement of all eligible subjects to participate in research studies ensures the benefits of research to all regardless of age, sex, socioeconomic status, race or ethnicity and health status. Additionally, a high participation rate is important to ensure the study sample mirrors the entire patient population and decreases the effects of selection bias on the results. Recent reports suggest that participation rates for epidemiologic studies have been declining over the past 30 years.[8] Patients who participate in research studies must not only meet the inclusion criteria, as defined by the study protocol, but then agree to participate after receiving information about possible risks and potential benefits (informed consent). Subject participation can be enhanced through a focus on factors that influence parents' decisions to allow their child to participate in

research studies. This project is designed to identify those factors using data from the EPIC study. This is important because it can guide the development of targeted communications that facilitate the recruitment of all study participants including those in under-represented demographic populations.

Each of the three studies will be described, in its own chapter, beginning with the study that examined factors associated with potentially unnecessary hospitalizations in Chapter Two.

Chapter 2 Assessing Factors Associated with Potentially Unnecessary Hospitalization of Children with CAP

Background and Significance

Community-acquired pneumonia (CAP) is a leading cause of hospitalization among children under 18 years of age in the United States[1] and results in approximately 375,000 emergency departments (ED) visits and 155,000 hospitalizations each year.[9] CAP ranks third among leading causes of pediatric hospitalization outside the neonatal period.[2] There are differences in hospital utilization by age. One study reported an overall rate of 201.2 CAP-related hospitalizations per 100,000 in 2006.[7] Children less than one year of age had the highest rate, 912.9 per 100,000; those one to five years of age, 390.4 per 100,000; those six to twelve years of age, 84.5 per 100,000, and those 13 to 18 years of age had a rate of 62.8 per 100,000.[1]

Interestingly, there is also wide variation in the proportion of children with CAP who are hospitalized across the US. A study of more than 1,000,000 ED encounters in 35 pediatric hospitals across the US found that admission rates for pneumonia ranged from 17-69 percent.[10] Pneumonia was one of seven common conditions that were studied including: asthma, bronchiolitis or respiratory syncytial virus (RSV), kidney disease and urinary tract infection (UTI), concussion, cellulitis or bacterial skin infections, pneumonia, and seizure; the amount of range in hospitalization for pneumonia was second only to concussion, which had a variance of 5-72 percent.[10] This variation, which was largely independent of population differences or disease severity, is evidence of a lack of sufficient guidelines to help determine who needs to be hospitalized, and indicates a need for better strategies to proactively identify children who need hospitalization.[10]

Typically, the need for hospitalization of patients with CAP is determined by an ED physician based on clinical assessment and guidelines. Clinical guidelines are "systematically developed statements to assist practitioners and patients in making decisions about appropriate health care for specific clinical circumstances."[11] However, guidelines require clinical evidence upon which to make recommendations. In the absence of adequate evidence, expert opinion is used.

Clinical guidelines for pediatric CAP

The current clinical guidelines for pediatric CAP were published by Bradley et al in 2011[4] and provide guidance on when infants and children in the U.S. need to be hospitalized.

According to the guidelines, hospitalization is recommended for the cases of CAP that present in respiratory distress (see Figure 1) that includes the following:

1. Children and infants who have moderate to severe CAP as defined by several factors, including respiratory distress and hypoxemia (sustained SpO_2, <90 % at sea level) . . . should be hospitalized for management including skilled pediatric nursing care. *(strong recommendation; high-quality evidence)*

2. Infants <3–6 months of age with suspected bacterial CAP are likely to benefit from hospitalization. *(strong recommendation; low-quality evidence)*

3. Children and infants with a suspicion or documentation of CAP caused by a pathogen with increased virulence, such as CA-MRSA, should be hospitalized. *(strong recommendation; low-quality evidence)*

4. Children and infants for whom there is concern about careful observation at home or who are unable to comply with therapy or unable to be followed up should be hospitalized. *(strong recommendation; low-quality evidence)*

Signs of Respiratory Distress
1. Tachypnea, respiratory rate, breaths/mina
Age 0–2 months: >60
Age 2–12 months: >50
Age 1–5 Years: >40
Age >5 Years: >20
2. Dyspnea
3. Retractions (suprasternal, intercostals, or subcostal)
4. Grunting
5. Nasal flaring
6. Apnea
7. Altered mental status
8. Pulse oximetry measurement <90% on room air

Figure 1. Criteria for Respiratory Distress in Children with Pneumonia[4]

The clinical guidelines also note young age, dehydration, comorbid conditions, vomiting or inability to take oral medications, and psychosocial concerns as additional considerations for hospitalization. Psychosocial concerns may represent concern for parental noncompliance with therapy or limited access to follow-up care.

> "Furthermore, those with psychosocial concerns, such as noncompliance with therapy or lack of reliable follow-up for any reason, may warrant admission. Studies from both the United States and Canada found that children and infants with pneumonia were more likely to be hospitalized if they were of lower socioeconomic status. This may be attributed, in part, to nonmedical issues, including inaccessibility to adequate outpatient services."[4]

The clinical guidelines also note the need for a scoring system, as is present in the adult realm, to determine whether or not a child with CAP needs to be hospitalized as most of the aforementioned recommendations, while strong, were based on low quality evidence.

> "In the past few decades, many consensus guidelines and clinical decision rules have been proposed for adults with CAP. There are multiple adult studies that describe scoring systems that have been demonstrated to be useful in predicting both which adults should be hospitalized and which adults require intensive care. Unfortunately, these scoring systems have not been validated in children and do not consider pediatric comorbid conditions, developmental stage, or psychosocial factors that influence the treating clinician's decision on the site of treatment for pediatric patients with CAP."[4]

Clinical decision rules for adults with CAP

Clinical decision rules are tools that aid in facilitating patient management decisions based on the patient's level of risk. Among adults, tools like the CURB-65 (confusion, urea, respiratory rate, and blood pressure)[12] and the Pneumonia Severity Index (PSI)[13] were developed for patients with CAP. These tools are currently being used in clinical practice, and several published studies indicate that their use is associated with reduced hospitalization among low risk individuals.[14] The adult models, however, have not been validated in children because they lack factors that are specific to children. The adult models do not consider pediatric comorbid conditions, developmental stage, or psychosocial factors that influence the treating clinician's decision on the site of treatment for pediatric patients with CAP.[4] Additionally, the adult models are based on the patient's risk of death, which is rare in children and not a useful outcome measure for guiding treatment decisions in pediatric patients with CAP.[3]

A clinical decision rule for pediatric CAP, noted as a need in the current clinical guidelines,[4] would assist physicians with determining the need for hospitalization in children with CAP, and could result in the reduction of precautionary hospitalizations. This is important because hospitalization, for children, is intrusive and may have physical and emotional effects that extend beyond their time in the hospital. Keeping children out of the hospital, when

hospitalization isn't necessary, will not only reduce the large financial burden of pediatric CAP, but, more importantly, will protect the children from additional adverse health outcomes such as healthcare-acquired infections and exposure to radiation and families from the stresses of hospitalizations such as missed work and need for child care. A better understanding of factors associated with mild cases of CAP will provide physicians with better information to determine the patients who can be treated safely at home. The abundant information that was collected as part of the EPIC study provides a unique opportunity to assess factors related to decisions of hospitalization.

The purpose of the proposed research is to identify factors associated with a mild course of pneumonia, as indicated by discharge from the hospital ≤ 24 hours, among children who are hospitalized. The factors that we studied are mainly related to factors identified in the clinical guidelines and easily assessed in the ED. A clear understanding of the association of these factors to a mild course of pneumonia, is the first step in designing and implementing effective counter strategies for reducing unnecessary hospitalizations among children with CAP. The ultimate goal is to provide evidence for developing guidelines for managing pediatric pneumonia to reduce the number of unnecessary hospitalizations.

Methods

The EPIC study is a prospective, population-based study that was conducted to determine the incidence and etiology of children with CAP who required hospitalization in the U.S. From January 1, 2010, to June 30, 2012. Children up to the age of 18 years of age, were enrolled in the EPIC study at three large pediatric hospitals across the country: Le Bonheur Children's Hospital (LBCH) in Memphis, TN, Monroe Carell Jr. Children's Hospital at Vanderbilt in Nashville, TN, and Primary Children's Hospital in Salt Lake City, UT.[5] Investigators sought to enroll all eligible

children; therefore, trained staff screened children for enrollment at least 18 hours per day, seven days per week. Written informed consent was obtained from parents or caregivers before enrollment, with children providing assent when age appropriate. The study protocol was approved by the institutional review board at each institution and at the CDC. Weekly study teleconferences, required weekly enrollment reports, data audits, and annual study-site visits were conducted to ensure uniform procedures among the study sites. Study coordinators who collected the study data were trained in a standard fashion and conducted all consent and parent interviews.[5]

Inclusion/Exclusion criteria

Children were included in the study if they were admitted to one of the three study hospitals; resided in one of the counties in the study catchment areas; had evidence of acute infection (defined as reported fever or chills, documented fever or hypothermia, leukocytosis or leukopenia in conjunction with respiratory symptoms); had evidence of an acute respiratory illness (defined as new cough or sputum production, chest pain, dyspnea, tachypnea, abnormal lung examination, or respiratory failure), and had evidence consistent with pneumonia as assessed by means of chest radiography within 72 hours of admission.[5]

Children were excluded if they were not enrolled into the study within 72 hours of admission or declined participation, had been hospitalized recently (<7 days for immunocompetent children and <90 days for immunosuppressed children), had been enrolled in the EPIC study within the previous 28 days, resided in an extended-care facility, or were newborns who never left the hospital. Children were also excluded if they had a tracheostomy tube, if they had cystic fibrosis or cancer with neutropenia, if they had received a solid-organ or hematopoietic stem-cell transplant within the previous 90 days, if they had active graft-versus-

host disease or bronchiolitis obliterans or if they had human immunodeficiency virus (HIV) infection with a CD4 cell count of less than 200 per cubic millimeter (or a percentage of CD4 cells <14%). Children with a clear alternative non-pneumonia diagnosis were also excluded. Final determination of inclusion in the study required independent confirmation by the board-certified pediatric study radiologist at each study hospital; these radiologists (all of whom are co-investigators in the study) were blinded to the patients' demographic and clinical information.[5] Radiographic evidence of pneumonia was defined as the presence of consolidation (a dense or fluffy opacity with or without air bronchograms), other infiltrate (linear and patchy alveolar or interstitial densities), or pleural effusion.[15]

Study sample

Participants included children, up to the age of 18, with respiratory illness who were admitted to LBCH between January 2010 and June 2012 and participated in the EPIC study.[5] Figure 2 shows a flowchart of the EPIC study. There were adequate sample sizes for each of the age groups. Two hundred seventy four patients were included in the youngest age group, zero to five months old; 781 in the six to twenty three month age group; 595 in the two to four year old age group; 422 in the five to nine year old age group and 286 in the ten to eighteen year old age group.

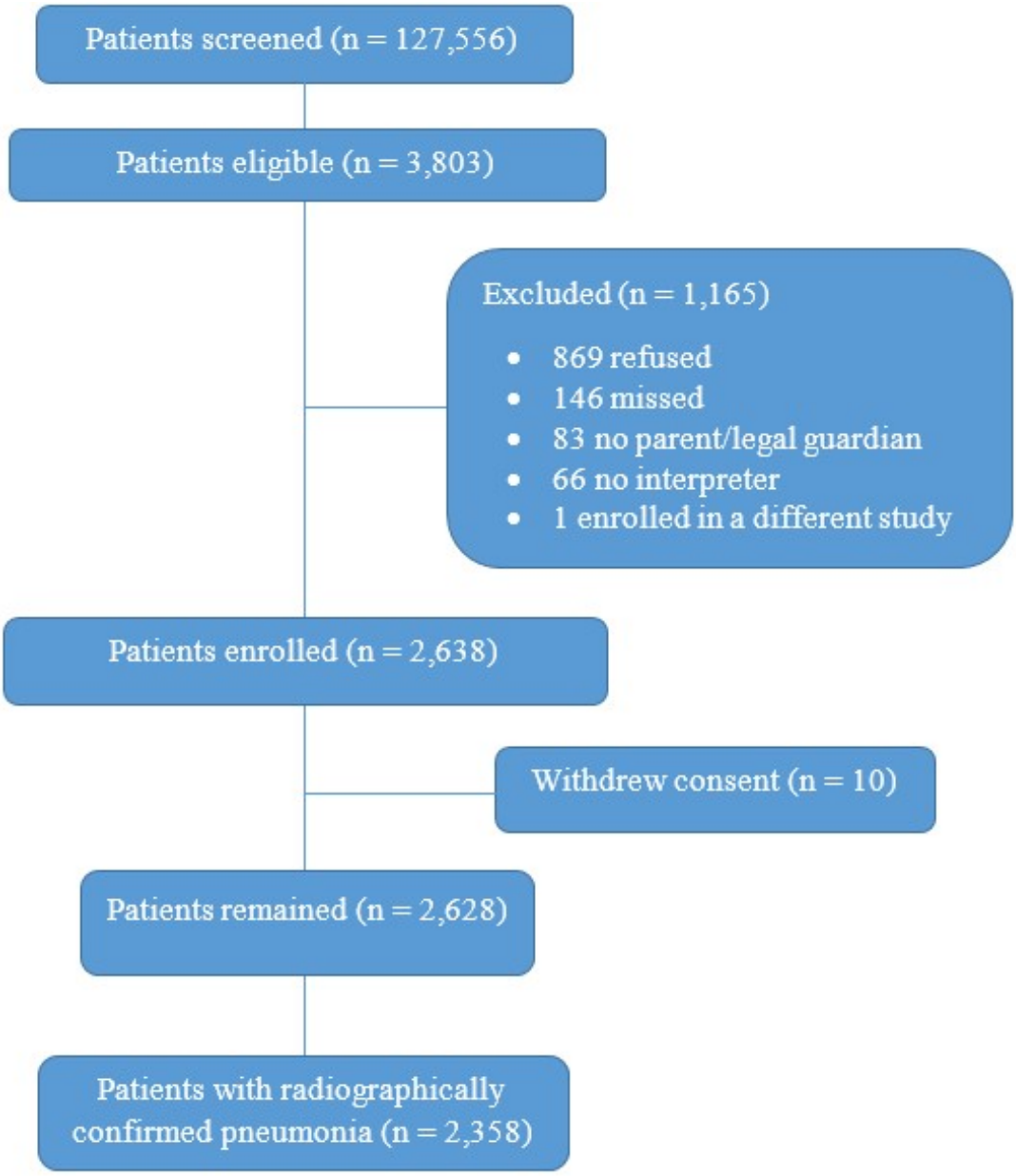

Figure 2. Consort diagram of the EPIC Study.

Study variables

Variables included in this study are typically associated with respiratory illness in children. They are easily assessed in the ED and potentially help in determining the need for hospitalization among children seen in the ED.

Outcome variable. A LOS in the hospital, measured in hours between time of decision to admit and leaving the hospital, dichotomized as ≤24 hours and > 24 hours. For the purpose of this study, a LOS ≤ 24 hours is considered an indicator of unnecessary hospitalization.

Main independent variables. The following clinical factors, which are routinely ascertained in the ED, will be evaluated: tachypnea, respiratory rate, dyspnea (see Figure 1), intercostal retraction, altered mental status, oxygenation, fever, chills hypothermia vomiting/nausea, wheezing, heart rate, age-specific systolic blood pressure, and asymmetric breath sounds.

Covariates. Based on published literature and clinical and epidemiological plausibility, other covariates include: age, gender, race, and health insurance status. Table 1 illustrates the independent variables and covariates that are used in this analysis.

Table 1. Description of study variables

Variable	Description
Fever	History during this illness (Y/N)
Chills	History during this illness (Y/N)
Nausea	History during this illness (Y/N)
Wheezing	Existence of (Y/N)
Confusion	Existence of (Y/N)
Respiratory rate	Breaths per minute (at presentation)
Heart rate	Beats per minute (at presentation)
Systolic blood pressure	mmHg (at presentation)
Oxygen saturation	Percent (at presentation)
Temperature	Degrees Fahrenheit (at presentation)
Intercostal retraction	History during this illness (Y/N)
Decreased breath sounds	Existence of (Y/N)
Age of the child	Months
Child's gender	Male/Female

Table 1 (Continued)

Variable	Description
Child's race	Non-Hispanic black, non-Hispanic white, Hispanic, multiracial, other
Health insurance	Public, private, none

Analysis

Demographic characteristics of participants were summarized by five age groups zero to five months, six to twenty three months, two to four years, five to nine years, and ten to eighteen years. They included gender race and type of insurance (Table 2).

Logistic regression was used to evaluate bi-variable associations between independent clinical and demographic variables and the study outcome variable (LOS ≤ 24 hours and >24 hours). Clinical variables with a significance level of 0.3 and less were included in the multivariable models. The less stringent level of 0.3 was used to ensure the inclusion of all potentially important clinical variables due to the exploratory nature of the study.

Multivariable logistic regression was performed to assess the adjusted associations of demographic and clinical factors with the study outcome. Variables identified from the bi-variable analyses were entered into the model and they were removed, one at a time, based on the largest significance level, using the stepwise backward elimination method. Variables with a significance level of 0.05 were retained in the model. All bi-variable and multivariable analyses were performed within each age category. For the multivariable logistic modelling, collinearity between variables was also assessed. Variation Inflation Factors (VIF) values for a variable over three indicated multicollinearity. All analyses were conducted with SPSS version 24 (IBM).[16] Tests of statistical significance were two sided, with an alpha level of 0.05, and are reported with three significant digits.

Results

Of 3,803 eligible children, 2,638 (69.4%) were enrolled between January 2010 and June 2012; 2,358 (89.4%) are included in this study. Just over half, 54.7% (n=1,291) were boys and 45.3% (n=1,067) were girls. Sixty two percent (n=1,468) had public insurance, 35.8% (n=843) private insurance, and 1.6% (n=38) had no insurance. The racial breakdown was 39.8% (n=939) white, 33.1% (n=781) black, 19.2% (n=452) Hispanic, and 7.5% (n=176) other. The percent of patients with a household education level less than a high school degree was 11.8% (n=278), high school graduate 28.3% (n=667), some college 24.2% (n=571), and a college degree or more 29.1% (n=687). Twenty two percent of the participants (n=515) were hospitalized for 24 hours or less and 78.2% (n=1.843) were hospitalized for more than 24 hours. This was consistent across age groups (Figure 3). The missing data for each of the factors ranged from 0.4% to 6.5%. Table 2 shows the study sample characteristics by age category.

Table 2. Demographic characteristics of the EPIC study population, by age group

Age Group		0-5 months	6-23 months	2-4 years	5-9 years	10-18 years
		N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Race	White	105 (38.3)	239 (30.6)	242 (40.7)	196 (46.4)	157 (54.9)
	Black	76 (27.7)	275 (35.2)	209 (35.1)	138 (32.7)	83 (29.0)
	Hispanic	64 (23.4)	194 (24.8)	99 (16.6)	58 (13.7)	37 (12.9)
	Other	29 (10.6)	70 (9.0)	41 (6.9)	28 (6.6)	8 (2.8)
	Missing	0 (0.0)	3 (0.4)	4 (0.7)	2 (0.5)	1 (0.3)
	Total	274 (100.0)	781 (100.0)	595 (100.0)	422 (100.0)	286 (100.0)
Gender	Male	160 (58.4)	436 (55.8)	301 (50.6)	244 (57.8)	150 (52.4)
	Female	114 (41.6)	345 (44.2)	294 (49.4)	178 (42.2)	136 (47.6)
	Total	274 (100.0)	781 (100.0)	595 (100.0)	422 (100.0)	286 (100.0)
Insurance	Public	199 (72.6)	567 (72.6)	384 (64.5)	210 (49.8)	108 (37.8)
	Private	72 (26.3)	201 (25.7)	198 (33.3)	201 (47.6)	171 (59.8)
	None	3 (1.1)	11 (1.4)	8 (1.3)	9 (2.1)	7 (2.4)

Table 2 (Continued)

Age Group	0-5 months	6-23 months	2-4 years	5-9 years	10-18 years
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Missing	0 (0.0)	2 (0.3)	5 (0.8)	2 (0.5)	0 (0.0)
Total	274 (100.0)	781 (100.0)	595 (100.0)	422 (100.0)	286 (100.0)

Bi-variable Regression

Tables 3-7 show the results of the bi-variable analyses by each age category.

A higher respiratory rate and heart rate were associated with a longer length of stay, and a high oxygen saturation level was associated with a LOS ≤ 24 hours. Increasing age was associated with a LOS of 24 hours or less. History of wheezing, chills and retraction were not associated with LOS. Variables in bold font were included in the multivariable models.

Table 3. Unadjusted odds ratios of the associations of study variables with length of stay (≤24 hours) for age group 0-5 months (n=274)

Variable	**OR**	**95% CI**		**P**
Fever (history)	**2.15**	**0.73**	**6.36**	**0.166**
Confusion	0.63	0.08	5.08	0.665
Wheezing	0.78	0.38	1.56	0.477
Nausea	1.40	0.69	2.85	0.355
Chills	**0.56**	**0.19**	**1.67**	**0.301**
Retraction	1.27	0.63	2.57	0.505
Breathing	0.71	0.26	1.91	0.493
Oxygen Saturation (%)	**1.11**	**1.02**	**1.21**	**0.017**
Heart Rate (beats/min)	**0.97**	**0.95**	**0.98**	**<0.001**
Respiratory Rate (per minute)	**0.98**	**0.96**	**1.00**	**0.060**
Systolic Blood Pressure	1.00	0.97	1.02	0.891
Temperature	0.96	0.79	1.16	0.652
age (months)	**1.47**	**1.16**	**1.87**	**0.001**
Patient Gender (ref is Male)	**0.64**	**0.31**	**1.33**	**0.226**

Table 3 (Continued)

Variable	OR	95% CI		P
Insurance (ref is Public)				
Private	1.61	0.77	3.36	0.207
None	0.00	0.00	0.00	0.999
Race (ref is White)				
Black	0.49	0.19	1.24	0.132
Hispanic	0.90	0.39	2.08	0.797
Other	0.36	0.08	1.64	0.186

Table 4. Unadjusted odds ratios of the associations of study variables with length of stay (≤ 24 hours) for age group 6-23 Months (n=781)

Variable	OR	95% CI		P
Fever	1.14	0.54	2.41	0.732
Confusion	**0.50**	**0.23**	**1.07**	**0.074**
Wheezing	**0.72**	**0.51**	**1.02**	**0.063**
Nausea	**0.80**	**0.56**	**1.12**	**0.190**
Chills	1.12	0.76	1.65	0.563
Retraction	**0.61**	**0.43**	**0.87**	**0.006**
Breathing	0.95	0.65	1.39	0.790
Oxygen Saturation (%)	**1.06**	**1.02**	**1.09**	**0.001**
Heart Rate (beats/min)	1.00	0.99	1.01	0.559
Respiratory Rate (per minute)	**0.983**	**0.97**	**1.00**	**0.004**
Systolic Blood Pressure	0.999	0.99	1.01	0.802
Temperature	0.992	0.92	1.08	0.844
age (months)	**1.032**	**1.00**	**1.07**	**0.073**
Patient Gender (ref is Male)	**1.286**	**0.91**	**1.81**	**0.153**
Insurance				
Private	0.96	0.64	1.42	0.819
None	2.13	0.61	7.39	0.234
Race (ref is White)				
Black	0.49	0.19	1.24	0.132
Hispanic	0.90	0.39	2.08	0.797
Other	0.36	0.08	1.64	0.186

Table 5. Unadjusted odds ratios of the associations of study variables with length of stay (≤ 24 hours) for age group 2-4 Years (n=595)

Variable	OR	95% CI		P
Fever (history)	**0.67**	**0.31**	**1.43**	**0.297**
Confusion	1.00	0.98	1.01	0.705
Wheezing	**0.77**	**0.52**	**1.13**	**0.182**
Nausea	**0.70**	**0.48**	**1.03**	**0.067**
Chills	0.83	0.56	1.24	0.367
Retraction	1.11	0.76	1.63	0.596
Breathing	**0.8**	**0.54**	**1.17**	**0.248**
Oxygen Saturation (%)	**1.06**	**1.02**	**1.10**	**0.004**
Heart Rate (beats/min)	1.00	1.00	1.01	0.424
Respiratory Rate (per minute)	**0.99**	**0.97**	**1.00**	**0.051**
Systolic Blood Pressure	**0.99**	**0.98**	**1.01**	**0.300**
Temperature	0.99	0.90	1.09	0.856
Age	1.01	0.99	1.03	0.583
Patient Gender (ref is Male)	**1.30**	**0.88**	**1.90**	**0.185**
Insurance				
Private	1.19	0.80	1.79	0.393
None	0.52	0.06	4.27	0.541
Race (ref is White)				
Black	1.07	0.69	1.66	0.764
Hispanic	0.92	0.52	1.62	0.760
Other	1.10	0.51	2.38	0.815

Table 6. Unadjusted odds ratios of the associations of study variables with length of stay (≤ 24 hours) for age group 5-9 Years (n=422)

Variable	OR	95% CI		P
Fever (history)	**2.59**	**1.07**	**6.28**	**0.035**
Confusion	**0.26**	**0.03**	**2.00**	**0.194**
Wheezing	**0.77**	**0.49**	**1.20**	**0.245**
Nausea	**1.88**	**1.19**	**2.97**	**0.007**
Chills	1.25	0.81	1.95	0.313
Retraction	1.20	0.77	1.89	0.420
Breathing	**1.39**	**0.88**	**2.21**	**0.163**
Oxygen Saturation (%)	**1.05**	**1.01**	**1.10**	**0.030**

Table 6 (Continued)

Variable	OR	95% CI		P
Heart Rate (beats/min)	**0.99**	**0.98**	**1.00**	**0.086**
Respiratory Rate (per minute)	**0.99**	**0.97**	**1.01**	**0.199**
Systolic Blood Pressure	1.00	0.98	1.02	0.977
Temperature	1.01	0.90	1.14	0.829
Age	1.00	0.99	1.01	0.806
Patient sex	**0.77**	**0.49**	**1.20**	**0.245**
Insurance (ref is Public)				
Private	0.93	0.60	1.46	0.755
None	2.31	0.60	8.92	0.224
Race (ref is White)				
Black	0.99	0.98	1.00	0.086
Hispanic	0.99	0.97	1.01	0.199
Other	1.00	0.98	1.02	0.977

Table 7. Unadjusted odds ratios of the associations of study variables with length of stay (≤ 24 hours) for age group 10-18 Years (n=286)

Variable	OR	95% CI		P
Fever (history)	**2.15**	**0.62**	**7.51**	**0.228**
Confusion	0.78	0.37	1.66	0.521
Wheezing	1.00	0.58	1.71	0.991
Nausea	**0.73**	**0.42**	**1.25**	**0.249**
Chills	**1.22**	**0.69**	**2.14**	**0.49**
Retraction	0.75	0.40	1.42	0.378
Breathing	0.98	0.56	1.70	0.927
Oxygen Saturation (%)	**1.13**	**1.05**	**1.22**	**0.001**
Heart Rate (beats/min)	**0.99**	**0.97**	**1.00**	**0.058**
Respiratory Rate (per minute)	**0.96**	**0.93**	**0.99**	**0.013**
Systolic Blood Pressure	**1.02**	**1.00**	**1.04**	**0.070**
Temperature (Fahrenheit)	**1.13**	**0.97**	**1.31**	**0.117**
Age	1.00	0.99	1.01	0.552
Gender	**1.43**	**0.83**	**2.46**	**0.195**
Insurance (ref is Public)				
Private	0.87	0.50	1.52	0.631

Table 7 (Continued)

Variable	OR	95% CI		P
None	1.14	0.21	6.23	0.877
Race (ref is White)				
Black	0.84	0.44	1.58	0.585
Hispanic	1.28	0.58	2.83	0.541
Other	0.43	0.05	3.62	0.439

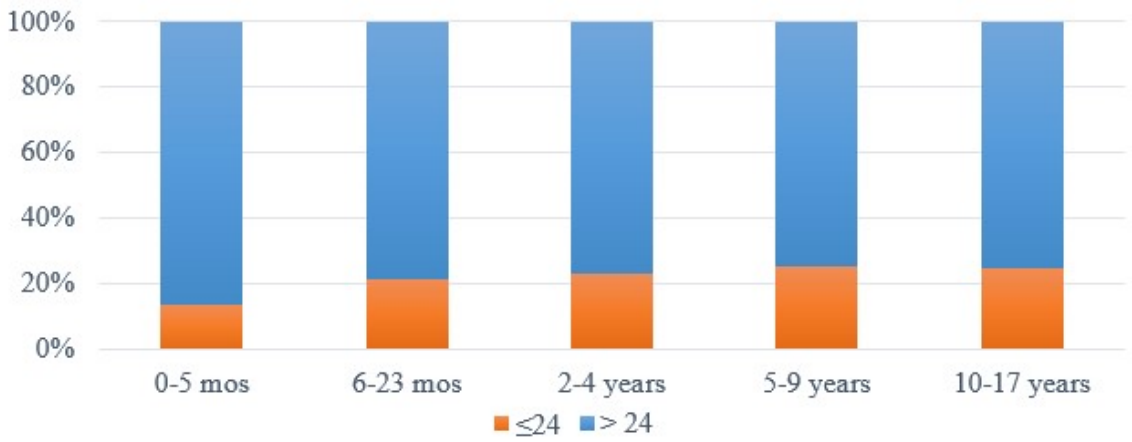

Figure 3. Study length of stay (≤ 24 hours and > 24 hours) for EPIC participants, by age group

Multivariable Regression

Tables 8–12 show factors potentially associated with a LOS ≤ 24 hours. Higher oxygen saturation level at presentation was consistently associated with a LOS of 24 hours or less across all age groups. Among those under six months old, as age increased the chances of having a LOS of 24 hours or less increased indicating residual confounding by age. A history of fever, chills, respiratory rate, patient gender, insurance, and race were not associated with LOS. The VIF did not exceed 3.0 in any analysis indicating the absence of multicollinearity.

Table 8. Adjusted odds ratios of factors associated with length of stay in age group 0-5 months

Variable	OR	95% CI		P
Heart Rate	0.97	0.95	0.99	0.001
Oxygen Saturation (%)	1.12	1.02	1.23	0.022
Age (months)	1.45	1.13	1.87	0.004

Table 9. Adjusted odds ratios of factors associated with length of stay in age group 6-23 months

Variable	OR	95% CI		P
Oxygen Saturation (%)	1.06	1.02	1.09	0.001

Table 10. Adjusted odds ratios of factors associated with length of stay in age group 2-4 years

Variable	OR	95% CI		P
Nausea	0.65	0.45	0.98	0.033
Oxygen Saturation (%)	1.0 6	1.02	1.11	0.003

Table 11. Adjusted odds ratios of factors associated with length of stay in age group 5-9 years

Variable	OR	95% CI		P
Nausea	1.96	1.23	3.12	0.005
Oxygen Saturation (%)	1.05	1.00	1.10	0.050

Table 12. Adjusted odds ratios of factors associated with length of stay in age group 10-18 years

Variable	OR	95% CI		P
Oxygen Saturation (%)	1.13	1.05	1.22	0.001

Discussion

Using data from a large prospective study of pediatric community-acquired pneumonia hospitalizations in the U.S., we examined variables associated with potentially unnecessary hospitalizations among different age groups of children with pneumonia. The ultimate goal,

which wasn't achieved, was to provide evidence for developing guidelines for managing pediatric pneumonia to reduce the number of unnecessary hospitalizations.

LOS, among our study population is consistent with other studies in the literature. In our sample the mean LOS for the entire groups was 3.92 (± 3.77). Our study found that the youngest children had longer hospitalization, 5.49 (±4.66) indicating a greater severity which is consistent with previous studies.[1]

Our finding of the association between a higher oxygen saturation level and LOS ≤ 24 hours is consistent with the clinical guidelines.[3] Oxygen saturation level is the only one high-quality recommendation for hospitalization from the clinical guidelines.

Asthma is potentially an important confounder. Thirty percent of the children in this study had a history of asthma. This is less than the findings of a national study that was conducted among 17,299 pediatric pneumonia cases in 125 hospitals across the U.S. In that study, they found 42% of the children had a history of asthma.[17] The majority of children in our sample, (70%) in each age group, with asthma were hospitalized more than 24 hours. We evaluated the relationship between asthma and LOS and found that it was not associated with a LOS ≤ 24 hours among this population.

A strength of our study is that it was conducted with data from three large children's hospitals in the U.S. While this sample is large, and somewhat diverse, it is limited to children who were seen in children's hospitals in only two states across the country. As a result, these findings may not be consistent among other patient populations across the U.S.

Limitation

A limitation of our study is misclassification of historical subjective clinical factors that were obtained through parental interview. One example is nausea.

Conclusion

Developing guidelines for more consistent management of pediatric CAP may reduce the number of potentially unnecessary hospitalizations and is an important clinical advancement. Our data suggest that the percent of oxygen saturation may be a strong indicator of LOS in all ages and is important to consider for future models.

Further prospective studies are needed, preferably designed specifically for each age-group, to identify the age-specific factors related to potentially unnecessary hospitalizations, including relevant co-morbidities.

Chapter 3 Evaluation of the Canadian Acute Respiratory Illness and Flu Scale (CARIFS) as a Predictor of Length of Stay among Pediatric Inpatients with CAP

Background and significance

Community-acquired pneumonia (CAP), a common and potentially serious infection in childhood, affects approximately three million children and is a leading cause of hospitalization among children under 18 years old in the United States.[1] CAP accounts for >200,000 hospitalizations each year in the United States,[18] with an estimated cost for hospitalizations of approximately three billion dollars in 2009.[2] Despite this large disease burden, critical gaps in our knowledge about the appropriate course of care for children with CAP remain.

These gaps in knowledge are due, in part, to the difficulty measuring the severity of the disease as noted in the current clinical guidelines. These guidelines, referred to as clinical guidelines, (Bradley, 2011 "The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America")[4] express a need for better ways to assess disease severity among children with CAP." A potential tool for measuring disease severity among an inpatient pediatric population with CAP is the Canadian Acute Respiratory Illness and Flu Scale (CARIFS).[6]

The CARIFS survey, comprised of 18 questions, was originally designed to measure disease severity among children with acute respiratory illness, in outpatient areas such as physician practices.[6] CARIFS is completed by the parent of the child and assesses disease severity according to three conceptual domains of illness: clinical symptoms, physical function, and items that impact the parent. It has been used to evaluate the treatment effectiveness of antibiotics and other antimicrobial agents.[6;7]

The three domains are comprised of multiple items or questions. Items in the clinical symptoms domain include: headache, sore throat, muscle aches, fever, cough, nasal congestion and vomiting. The function domain includes: poor appetite, disrupted sleep, irritability, feeling unwell, low energy, not playing well, excessive crying. The parental impact domain includes: the need for extra care, clinginess, not interested in what's going on and unable to get out of bed. Each question in the survey is graded on a four-point scale that measures the level of severity.

CARIFS was evaluated, in a study of 206 children with acute respiratory illness, utilizing data from the outpatient clinics at The University of Toronto. To assess construct validity, the CARIFS scores were compared between the physician, nurse and parental assessment of the of the child's health. Correlations between the parental assessment and the physician assessment and the parental assessment and the nurses assessment were weak, Spearman correlation coefficients were 0.30 and 0.28 respectively.[4]

To our knowledge, the CARIFS scale has not been evaluated in an inpatient setting. The instrument, however, may prove to be a useful tool for evaluating disease severity among pediatric patients hospitalized with CAP. This is important because it may provide additional information to help physicians determine the appropriate LOS in the hospital. This may lead to a reduction of days in the hospital among children with CAP.

The purpose of this study is to assess the validity of the CARIFS instrument among inpatient children with CAP, and examine its utility in predicting LOS in this patient population, using data collected by the CARIFS instrument as a supplemental part of the EPIC study.

Methods

The18 items in the CARIFS instrument are graded on a four-point Likert scale. Response options include: no problem, minor problem, moderate problem, major problem and don't know

or not applicable. The instrument was completed by the parent with the assistance of a trained study assistant.

Study sample

Children under the age of 18 years with respiratory illness who were admitted to LBCH between January 2010 and June 2012 and participated in the EPIC study.

Inclusion/Exclusion criteria

Children were included in the study if they were admitted to Le Bonheur Children's Hospital; resided in one of the counties in the study catchment areas; had evidence of acute infection (defined as reported fever or chills, documented fever or hypothermia, leukocytosis or leukopenia in conjunction with respiratory symptoms); had evidence of an acute respiratory illness (defined as new cough or sputum production, chest pain, dyspnea, tachypnea, abnormal lung examination, or respiratory failure), and had evidence consistent with pneumonia as assessed by means of chest radiography within 72 hours before or after admission. A caregiver had to complete the CARIFS survey upon admission.[5]

Children were excluded if they were not enrolled into the study within 72 hours of admission or declined participation, had been hospitalized recently (<7 days for immunocompetent children and <90 days for immunosuppressed children), had been enrolled in the EPIC study within the previous 28 days, resided in an extended-care facility, or were newborns who never left the hospital. Children were also excluded if they had a tracheostomy tube, if they had cystic fibrosis or cancer with neutropenia, if they had received a solid-organ or hematopoietic stem-cell transplant within the previous 90 days, if they had active graft-versus-host disease or bronchiolitis obliterans or if they had human immunodeficiency virus (HIV) infection with a CD4 cell count of less than 200 per cubic millimeter (or a percentage of CD4

cells <14%). Children with a clear alternative non-pneumonia diagnosis were also excluded. Final determination of inclusion in the study required independent confirmation by the board-certified pediatric study radiologist at each study hospital; these radiologists (all of whom are coauthors of the study) were blinded to the patients' demographic and clinical information.[5] Radiographic evidence of pneumonia was defined as the presence of consolidation (a dense or fluffy opacity with or without air bronchograms), other infiltrate (linear and patchy alveolar or interstitial densities), or pleural effusion.[15] Those who did not complete the CARIFS survey within 48 hours of admission were excluded.

Study variables

The outcome variable is LOS, defined as number of days in the hospital. Main independent variables include factors that were identified through factorial analysis that was conducted with the 18 CARIFS questions. Covariates include age, gender, race, highest level of household education, and type of insurance. Table 13 shows the variables used in the study.

Table 13. Definition of independent variables used in the CARIFS study

Variable name	**Definition**
Demographic Variables	
Age of child	In months
Gender of child	Male/Female
Race of the child	White, Black, Hispanic, and other
Insurance type	Public, private, and none
Physical Function Domain	
Poor appetite	4-point Likert scale; no problem, minor problem, moderate problem, major problem, don't know/not applicable
Not sleeping well	4-point Likert scale
Irritable, cranky, fussy	4-point Likert scale
Feels unwell	4-point Likert scale
Low energy, tired	4-point Likert scale
Not playing well	4-point Likert scale

Table 13 (Continued)

Variable name	Definition
CARIFS Questions	
Excessive crying	4-point Likert scale
Parental Impact Domain	
Needing extra care	4-point Likert scale
Clinginess	4-point Likert scale
No interest in what's going on	4-point Likert scale
Unable to get out of bed	4-point Likert scale
Clinical Symptoms Domain	
Headache	4-point Likert scale
Sore throat	4-point Likert scale
Muscle aches or pains	4-point Likert scale
Fever	4-point Likert scale
Cough	4-point Likert scale
Nasal congestion/runny nose	4-point Likert scale
Vomiting	4-point Likert scale

Analysis

Participants were characterized by gender, age, race, and type of insurance. Analyses were subsequently stratified by age into five age groups: zero to five months, six to twenty three months, two to four years, five to nine years, and ten to eighteen years. The percent of questions not answered for each CARIFS item was evaluated by age group (Table 15). Internal reliability of the CARIFS instrument was evaluated overall and by each age group using Cronbach's Alpha.

To identify the number of domains among the 18 CARIFS survey questions, factor analysis, a statistical method that identifies the subthemes (latent variables) and combines survey questions into subsets based on response patterns, was conducted using principal axis factoring for extraction. Additionally, Varimax rotation was used to rotate the domains making the patterns more pronounced and assisting in determining the domain loadings. Themes were then identified for each domain.

Multivariable associations of independent variables with the LOS were assessed using generalized linear (GLM) regression models with a gamma distribution. A Gamma distribution was used since LOS exhibited extreme values. To evaluate the effect of the demographic factors on the CARIFS survey, we analyzed five models, one for each age group. Each model included all demographic variables and all of the factors created through the factorial analysis.

Insurance was included in two categories, private and public; due to small numbers in each of the groups, Hispanic and other race was combined into other. The four domains created by the factor analysis were included as independent variables in the model.

All analyses were conducted with IBM SPSS version 24 (IBM).[16] Tests of statistical significance were two sided, with an alpha level of 0.05, and are reported with three significant digits.

Results

Subject Characteristics

Nine hundred sixty-eight children, under the age of 18 years, were enrolled into the EPIC study at the LBCH site. Among these, 951 (98%) completed a CARIFS survey upon admission. Table 14 shows the demographic description of the study sample, by age group.

Table 14. Demographic characteristics of the CARIFS study population, by age group, between January 2010 and June 2012

Variable	0-5 months	6-23 months	2-4 years	5-9 years	10-18 years
	N (%)	N (%)	N (%)	N (%)	N (%)
Child's Gender					
Male	74 (60.2)	198 (58.4)	132 (55.5)	98 (58.3)	58 (53.2)
Female	49 (39.8)	141 (41.6)	106 (44.5)	70 (41.7)	51 (46.8)
Child's Race					
White	33 (26.8)	41 (12.1)	39 (16.4)	32 (19.0)	31 (28.4)

Table 14 (Continued)

Variable	0-5 months	6-23 months	2-4 years	5-9 years	10-18 years
	N (%)	N (%)	N (%)	N (%)	N (%)
Black	73 (59.3)	247 (72.9)	178 (74.8)	115 (68.5)	70 (64.2)
Hispanic	15 (12.2)	37 (10.9)	9 (3.8)	12 (7.1)	7 (6.4)
Other	2 (1.6)	13 (3.8)	12 (5.0)	9 (5.4)	1 (0.9)
Insurance					
Public	101 (82.1)	296 (87.3)	194 (81.5)	103 (61.3)	57 (52.3)
Private	21 (17.1)	37 (10.9)	42 (17.6)	59 (35.1)	46 (42.2)
None	1 (0.8)	3 (0.9)	1 (0.4)	4 (2.4)	6 (5.5)
Both	0 (0.0)	2 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)

Table 15. Frequency of unanswered questions for each CARIFS question, LBCH EPIC study population, by age group, between January 2010 and June 2012

Age Group	**0-5 mos (N=123)**	**6-23 mos (N=339)**	**2-4 yrs (N=238)**	**5-9 yrs (N=168)**	**10-18 yrs (N=109)**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Poor appetite	7 (5.8)	13 (3.9)	10 (4.2)	4 (2.4)	10 (9.3)
Not sleeping well	6 (5.0)	7 (2.1)	6 (2.5)	3 (1.8)	5 (4.6)
Irritable, cranky	6 (5.0)	9 (2.7)	4 (1.7)	1 (0.6)	5 (4.6)
Feels unwell	10 (8.3)	12 (3.6)	4 (1.7)	2 (1.2)	5 (4.6)
Low energy, tired	9 (7.5)	13 (3.9)	4 (1.7)	2 (1.2)	7 (6.5)
Not playing well	22 (18.3)	14 (4.2)	6 (2.5)	4 (2.4)	11 (10.2)
Crying more	5 (4.2)	8 (2.4)	5 (2.1)	3 (1.8)	11 (10.2)
Needing extra care	4 (3.3)	11 (3.3)	6 (2.5)	4 (2.4)	6 (5.6)
Clinginess	10 (8.3)	15 (4.5)	7 (3.0)	3 (1.8)	10 (9.3)
Headache	85 (70.8)	207 (61.6)	77 (32.5)	12 (7.2)	12 (11.1)
Sore throat	77 (64.2)	173 (51.5)	65 (27.4)	5 (3.0)	14 (13.0)
Muscle aches	76 (63.3)	182 (54.2)	66 (27.8)	8 (4.8)	12 (11.1)
Fever	5 (4.2)	8 (2.4)	6 (2.5)	2 (1.2)	6 (5.6)
Cough	5 (4.2)	11 (3.3)	7 (3.0)	2 (1.2)	5 (4.6)
Nasal congestion	3 (2.5)	10 (3.0)	3 (1.3)	1 (0.6)	6 (5.6)
Vomiting	8 (6.7)	11 (3.3)	6 (2.5)	3 (1.8)	7 (6.5)
No interest	26 (21.7)	22 (6.5)	8 (3.4)	2 (1.2)	9 (8.3)
Assistance w/bed	80 (66.7)	59 (17.6)	13 (5.5)	7 (4.2)	12 (11.1)

Validation and evaluation of the CARIFS instrument

Among the youngest age group, assistance with bed was not relevant and, as a result, nearly 70 percent of parents did not provide a response to this question. Furthermore, headaches, sore throat, and muscle aches are difficult to assess among children under two years old and, as a result, between 52 and 70 percent of parents did not provide responses to these questions, resulting in high percentages of missing data among 6-23 months and 2-4 years.

Seventeen of the CARIFS items loaded on four domains. Domain one, represents physical function and includes: poor appetite, feels unwell, low energy/tired, not playing well, and assistance with bed. Domain two represents parental impact and includes: not sleeping well, irritable or cranky, more frequent crying, needing extra care, and clinginess. Domain three represents clinical variables that are not observable and domain four represent clinical symptoms that are observable. The assignment of each question to a domain was based on a level of association that was at least a 0.300. The question "No interest in what is going on" is not reported in Table 16 because it was less than 0.300.

Table 16. The latent variables (domains) identified within the CARIFS questionnaire and the strength of association of each question to the domain among the LBCH EPIC population, January 2010 and June 2012

Question	**Identified Domains**			
	One	**Two**	**Three**	**Four**
Poor appetite	0.506			
Feels unwell	0.626			
Low energy, tired	0.829			
Not playing well	0.799			
Unable to get out of bed	0.328			
Not sleeping well		0.370		
Irritable, cranky, fussy		0.673		
Excessive crying		0.699		

Table 16 (Continued)

Question	Identified Domains			
	One	Two	Three	Four
Needing extra care		0.624		
Clinginess		0.597		
Headache			0.637	
Sore throat			0.611	
Muscle aches or pains			0.682	
Fever				0.370
Cough				0.551
Nasal congestion/runny nose				0.643
Vomiting				0.347

The internal consistency of the instrument in this study population was high among all age groups and ranged from 0.84 to 0.90 as shown in Table 17.

Table 17. Internal reliability of CARIFS questions, by age group, among the LBCH EPIC population, January 2010 and June 2012

Age Group	Cronbach's Alpha	Mean Score	SD
0-5 months	0.84	38.81	9.65
6-23 months	0.89	40.24	12.14
2-4 years	0.90	41.23	12.81
5-9 years	0.88	36.29	11.58
10-18 years	0.89	40.93	12.14

Assessing factors associated with length of stay

Multivariable analyses. Tables 18-22 show the results of the multivariable analyses. Domain one, (poor appetite, feels unwell, low energy/tired, not playing well, and assistance with bed) has a positive association with LOS in all age groups except for the youngest ages (zero to five months). Domain four (fever, cough, nasal congestion, and vomiting) is inversely associated

with LOS among those 2-4 years of age. Private insurance is inversely associated with LOS among children 6-23 months of age. Age is associated with LOS among those six months to four years of age. These results vary some among the different age groups indicating that the CARIFS survey is less effective among the youngest age group. Domain two, domain three, race and gender were not associated with LOS in any age group.

Table 18. Multivariable logistic regression, in age group 0-5 months (n=49), LBCH EPIC population, between January 2010 and June 2012

Variable	B	Std. Error	95% CI		P
Factor One	0.027	0.1604	-0.287	0.342	0.865
Factor Two	-0.120	0.1611	-0.435	0.196	0.457
Factor Three	0.086	0.1355	-0.179	0.352	0.524
Factor Four	0.187	0.1624	-0.132	0.505	0.250
Race (ref is white)					
Black	0.492	0.3290	-0.152	1.137	0.135
Other Race	-0.314	0.4020	-1.102	0.474	0.434
Female child	0.152	0.2097	-0.259	0.563	0.468
Private insurance (ref is public)	-0.239	0.3920	-1.008	0.529	0.542
Age of the child	-0.057	0.0663	-0.187	0.073	0.393

Table 19. Multivariable logistic regression, in age group 6-23 months (n=180), LBCH EPIC population, between January 2010 and June 2012

Variable	B	Std. Error	95% CI		P
Factor One	**0.180**	**0.0803**	**0.023**	**0.338**	**0.025**
Factor Two	-0.004	0.0776	-0.156	0.148	0.955
Factor Three	-0.024	0.0543	-0.130	0.083	0.662
Factor Four	-0.040	0.0752	-0.187	0.108	0.598
Race (ref is white)					
Black	-0.094	0.1823	-0.451	0.263	0.606
Other	-0.198	0.2065	-0.603	0.206	0.337
Female child	0.043	0.1039	-0.160	0.247	0.676

Table 19 (Continued)

Variable	B	Std. Error	95% CI	P	Variable
Private insurance (ref is public)	**0.430**	**0.1958**	**0.047**	**0.814**	**0.028**
Age of the child	**-0.047**	**0.0096**	**-0.065**	**-0.028**	**<0.001**

Table 20. Multivariable logistic regression, in age group 2-4 years (n=184), LBCH EPIC population, between January 2010 and June 2012

Variable	**B**	**Std. Error**	**95% CI**		**P**
Domain One	**0.336**	**0.0618**	**0.215**	**0.457**	**<0.001**
Domain Two	-0.062	0.0742	-0.207	0.083	0.403
Domain Three	0.045	0.0730	-0.098	0.188	0.536
Domain Four	**-0.250**	**0.0698**	**-0.387**	**-0.113**	**<0.001**
Race (ref is white)					
Black	0.020	0.1625	-0.299	0.338	0.903
Other	0.016	0.2377	-0.450	0.482	0.946
Female child	0.146	0.0974	-0.045	0.337	0.133
Private insurance (ref is public)	0.018	0.1485	-0.273	0.309	0.902
Age of the child	**-0.009**	**0.0048**	**-0.019**	**0.000**	**0.047**

Table 21. Multivariable logistic regression, in age group 5-9 years (n=156), LBCH EPIC population, between January 2010 and June 2012

Variable	**B**	**Std. Error**	**95% CI**		**Wald Chi-square**	**P**
Domain One	**0.237**	**0.0789**	**0.082**	**0.391**	**8.989**	**0.003**
Domain Two	-0.125	0.0771	-0.276	0.026	2.626	0.105
Domain Three	0.030	0.0790	-0.125	0.185	0.144	0.704
Domain Four	-0.046	0.0983	-0.239	0.146	0.221	0.638
Race (ref is white)						
Black	0.076	0.1521	-0.222	0.374	0.252	0.616
Other	-0.107	0.2165	-0.532	0.317	0.246	0.620
Female child	-0.157	0.1125	-0.377	0.064	1.941	0.164
Private insurance (ref is public)	0.224	0.1249	-0.020	0.469	3.225	0.073
Age of the child	0.000	0.0033	-0.007	0.006	0.007	0.933

Table 22. Multivariable logistic regression, in age group 10-18 years (n=92), LBCH EPIC population, between January 2010 and June 2012

Variable	B	Std. Error	95% CI		Wald Chi-square	P
Domain One	**0.366**	**0.1153**	**0.140**	**0.592**	**10.098**	**0.001**
Domain Two	-0.095	0.1275	-0.345	0.154	0.560	0.454
Domain Three	-0.046	0.1042	-0.246	0.163	0.160	0.689
Domain Four	-0.070	0.1268	-0.338	0.159	0.495	0.482
Race (ref is white)						
Black	0.232	0.1665	-0.122	0.530	1.503	0.220
Other	0.301	0.2880	-0.258	0.871	1.133	0.287
Female child	0.093	0.1508	-0.222	0.369	0.236	0.627
Private insurance (ref is public)	-0.105	0.1570	-0.492	0.123	1.380	0.240
Age of the child	0.002	0.0027	-0.004	0.007	0.270	0.603

Discussion

This study was among the first to evaluate the usefulness of the CARIFS survey in assessing disease severity, as defined by LOS, among children with CAP in a hospital setting.

Questions in the physical function domain represent the symptoms of toxicity which are consistent with someone who is really sick and not easily treatable. As a result, our finding that these factors, which represent poor appetite and feeling unwell or tired, are most associated with a longer LOS is logical. Among those who scored all of these questions with the highest degree of severity, the LOS in the hospital was nearly a full day longer compared to those with less severity.

For the most part, this study validated the original domains, from the outpatient setting, among this group of hospitalized patients. The original study categorized the CARIFS questions into three domains: physical function, parental impact, and clinical symptoms. Our study found the first two original domains were similar to the original study and that domain three was split

into two separate domains. In our study, domain one represents symptoms of not feeling well (constitutional symptoms); domain two represents parental impact factors; domain three subjective clinical symptoms of disease; and domain four represents observable or objective clinical symptoms of the disease that are objective. With the exception of domain three, headache, muscle ache and sore throat, the domains identified in the factor analysis are consistent with the original domains. The question related to inability to get out of bed moved from the parental impact domain in the original study to the physical function domain in this hospitalized population. Additionally, the disrupted sleet and irritability questions moved from the physical function domain to the parental impact domain.

Our study found that the CARIFS scale had high internal consistency, or reliability, in this inpatient population among children over the age of six months old. The highest reliability was among the oldest age group, 10-18 years old. This finding is consistent with previous findings in the outpatient setting.[6] Furthermore, consistent with our findings, the authors of the CARIFS questionnaire found a high proportion of unanswered questions among respondents with children under the age of five for the subjective questions pertaining to headache, sore throat, and muscle aches.[6] The original study (EPIC) included these questions among the younger age groups so we included them in the analysis. Our findings, however, support the need to remove these questions when administering the survey to parents evaluating children under the age of four years old.

A limitation of our study is that our data reflect the pediatric experience in one large children's hospital in Memphis, TN. As a result, our findings may not be consistent among other patient populations and in other care settings across the U.S. Additional research is needed to determine whether or not our findings can be generalized to other demographic populations.

While the utility of the CARIFS questionnaire is limited among younger ages, we did find the CARIFS questionnaire has good internal reliability among older children. Additionally, we found an association between the domain that represents physical function and LOS. Future studies should evaluate the individual items in the CARIFS questionnaire.

Conclusion

While the utility of the CARIFS questionnaire is limited among younger ages, we did find that it has some promise, based on good internal reliability, among older children. Additionally, we found an association with LOS. Because CARIFS consistently predicted LOS, this study may provide further information on important factors that may guide the formulation of a predictive model.

Chapter 4 Identification of Factors that Influence Parental Consent for Participation in Hospital-based Pediatric Epidemiologic Research

Background and significance

Clinical research is important because it leads to the generation of scientific evidence and the adoption of evidence-based practices by healthcare providers, which are more likely to improve health outcomes. The best evidence is that which results from well-designed research studies that minimize the chances of selection bias. Self-selection bias results when there are differences between those who choose to participate in a study and those who do not.[19] The resulting differences may lead to false conclusions, threatening the validity of a study's findings. Studies with higher participation rates are less vulnerable to this bias than those with lower rates, thus minimizing the risk of invalid results.[20] As a result, successful recruitment is key; however, according to Denhoff[21], it is also very challenging.

> "One of the most challenging aspects of conducting clinical research is the ability to successfully recruit participants. The inability to recruit the target sample size has been estimated to occur in approximately 80% of clinical trials. The impact of low recruitment to a study can be serious, leading to early termination with insufficient sample size and subsequent losses in statistical power and limited generalizability. In addition, slower than anticipated recruitment may increase the duration of the study, delaying the reporting of results and causing unanticipated stress on the budget and resources."[19]

To participate in research studies, patients must not only fulfill the inclusion criteria, as defined by the study protocol, but also agree to participate in the study after receiving detailed information about risks, benefits, and requirements of participation (informed consent).

Morton, et al. conducted a retrospective review of studies published in the literature from January through April 2003.[22] "Journals that published peer-reviewed, original research articles in English and were listed in the 2003 Science Edition of Journal Citation Reports (The Thompson Corporation, Philadelphia, Pennsylvania) were eligible for inclusion." Their intent was to survey the practice of the reporting of participation rates in epidemiologic studies, assess

changes in participation over time, and evaluate the impact of increased biologic specimen collection on participation. Among the 355 original research studies they identified, a small percentage, ranging from 4-32 percent by study type, reported adequate information to evaluate the participation rate. Among these, there was a decline in participation over time. Thirty eight percent (n=134) of the studies included the collection of biologic specimens to measure exposure or disease and the proportion of studies that collected biological specimens increased over time.[22] Twenty seven percent of the studies (n=36) that collected biologic specimens reported a separate response rate for the biologic specimen component.[22] Among these, there was a high proportion of participation among the case-control and cohort studies (86 and 99.5 percent respectively), which is likely due, to the participation in the biologic specimen component being mandatory.[22]

Parental consent for their child to participate in research is important because it is necessary to obtain or maintain funding for clinical studies that ensure research is representative of children. Prioritization of the inclusion of children in research is becoming increasingly more important to agencies like the National Institutes of Health (NIH). This is evidenced by the need to justify the exclusion of children in research protocols.[23] Gaining informed consent from the parents, who are often the proxy decision-makers for their child's participation in research, has unique challenges.

Despite its importance, there are only a handful of studies in the literature on factors that influence parental consent. The current state was summarized by Hoberman[24]:

> "Research to date of factors influencing a parent's decision to provide consent for his or her child to participate in clinical research has been limited to cancer studies and less-than-minimal risk studies. Further, most investigators have collected data only from parents who consented to their child's involvement; very few have examined the motives of parents who declined consent. The aggregate of reported findings suggests that the health of the child, positive perceptions of the research team and consent process, and altruistic motives play a significant role in the decision-making process."

Rothmier[25] found that the most important motive for parents when enrolling their child in biomedical research is learning more about their child's illness, followed by the motivation of helping medical knowledge. Hoberman[24] found that parents who declined participation had more anxiety about their decision and found it harder to make a decision, when compared with consenting parents, who had higher levels of trust and altruism, stronger expectations for enhanced care, and lower levels of decisional uncertainty.[24] Parents report that giving consent for their child to participate in research is more difficult than giving consent for themselves due to the added sense of responsibility, a fear of regretting their decision, and a need to protect their child that outweighs their sense of altruism.[26] In hospital-based studies, additional motives include: not wanting the child to undergo further investigations, research delaying discharge, and anxiety regarding written consent and length of information sheets.[27]

The role of education status on consent in the literature is mixed. In one study, education-level of the parent was not shown to influence the consent decision.[28] Hoberman,[24] however, found that parents were more likely to decline consent if they had a college degree, compared to less educated parents.

There are limitations to the studies in the literature. Several of these studies collected data only from parents who consented to their child's involvement[25;29]; and few have examined the motives of parents who declined consent.[30-32] Additionally, there is a paucity of information on the effect of the inclusion of biological specimens on parental consent.

The purpose of this study is to examine potential factors associated with parents' decisions to participate in pediatric epidemiologic research. Understanding these factors is important to addressing possible barriers for participation

Methods

All English-speaking parents of children who qualified for the EPIC study[5] at Le Bonheur Children's Hospital (LBCH) site were approached to participate in this ancillary study during the last four months of the study. Participants were asked to complete a 17-item questionnaire that included demographic questions and items representing eight potential motivating factors. Parents were asked to voluntarily complete the questionnaire after the consent discussion and before they signed the study consent.

The study questionnaire collected information related to: 1) Parent/caregiver demographics (e.g., age, race, sex); 2) patient's health status (e.g., severity of illness; 3) parent/caregiver believes and attitude on health research (e.g., altruism, trust in the medical system; 4) perceived benefit (e.g., child's illness and payment); 5) concerns about clinical procedures (e.g., blood draws, nose and throat swabs), and 6) study-related communication (e.g., clarity of purpose of the study). Figure 1 illustrates the data collection instrument.

Inclusion and Exclusion criteria

Inclusion criteria are consistent with the criteria for inclusion in the CDC Etiology of Pneumonia in the Community (EPIC) study as follows. Children were included in the study if they were admitted to LBCH; resided in one of the counties in the study catchment areas; had evidence of acute infection, defined as reported fever or chills, documented fever or hypothermia, leukocytosis or leukopenia; had evidence of an acute respiratory illness, defined as new cough or sputum production, chest pain, dyspnea, tachypnea, abnormal lung examination, or respiratory failure, and had evidence consistent with pneumonia as assessed by means of chest radiography within 72 hours before or after admission.[5]

Children were excluded if they were not enrolled into the study within 72 hours of admission or declined participation, had been hospitalized recently (<7 days for immunocompetent children and <90 days for immunosuppressed children), had been enrolled in the EPIC study within the previous 28 days, resided in an extended-care facility, had an alternative diagnosis of a respiratory disorder or were newborns who never left the hospital. Children were also excluded if they had a tracheostomy tube, if they had cystic fibrosis or cancer with neutropenia, if they had received a solid-organ or hematopoietic stem-cell transplant within the previous 90 days, if they had active graft-versus-host disease or bronchiolitis obliterans or if they had human immunodeficiency virus infection with a CD4 cell count of less than 200 per cubic millimeter (or a percentage of CD4 cells <14%). Children with a clear alternative non-pneumonia diagnosis were also excluded.[5]

Study sample

English-speaking parents of children with respiratory illness who were admitted to LBCH between January and June 2012, and found eligible to participate in EPIC study, were approached to complete the survey. Survey completion took place after the consenting discussion but before the parent consented to the study.

Study variables

Outcome. Parental consent for child to participate in the EPIC study, as a binomial response (yes/no).

Main independent variables. Survey responses to the following questionnaire items: 1) my child's illness is an important factor; 2) this study is an important part of improving medical care; 3) purpose of the study was clearly explained; 4) my information will be kept private; 5)

concern about blood collection; 6) concern about nose/throat swab; 7) concern over the follow-up visit, and 8) payment is an important factor.

Covariates. Demographic variables including: age, race, employment status and sex of the parent; household education; insurance status; frequency of hospitalization and severity of the child's illness. Table 23 provides a description of the independent variables.

Table 23. Description of the data collection instrument used in the motivational factors study

Variable	Description
Demographic Factors	
Age of the parent/caregiver	Years
Gender of the parent/caregiver	Male/Female
Race of the parent	Non-Hispanic black, non-Hispanic white, Hispanic, other
Highest household educational status	<high school, high school graduate, some college, college graduate/advanced degree
Employment status	Employed, not employed, student, homemaker, disabled
Marital status	Married/non-married couple, never married, divorced, separated, widowed
Frequency of child's hospitalization	Number of time, past 5 years
Insurance type	Public, private, both or self-pay
Number of children	Living in the household (continuous)
Motivational Factors	
My child's illness in an important factor	5-point Likert scale; strongly disagree, disagree, neutral, agree and strongly agree
I feel that this study is an important part of improving medical care	5-point Likert scale
The purpose of the study was clearly explained to me	5-point Likert scale
I feel my information will be kept private	5-point Likert scale
I am concerned about the blood collection	5-point Likert scale
I am concerned about the nose and throat swab	5-point Likert scale
I am concerned about the follow-up visit	5-point Likert scale
Payment is an important factor	5-point Likert scale

Analysis

Summary descriptive statistics were calculated using frequency distributions and means as appropriate (Table 24 and Table 25). Logistic regression was used to estimate the crude association of each demographic and motivational variable with consenting to participate. Odds rations and p values were generated. Adjusted odds rations and their 95% confidence intervals were calculated using a fixed-effects logistic regression model. Variables associated with outcomes on bi-variable analyses as defined by a significance of 0.3 or less were included in the multivariable model. Stepwise backward elimination method with an elimination cut off threshold of $p<0.05$ was used to arrive at the final model. Because of the exploratory nature of the study, a less stringent level of 0.3 was used to ensure all potentially important variables were included in the multivariable model.

Marital status was categorized into married and not married. The non-married category combined divorced, separated, and single. Employment status was categorized into employed (self-employed and employed by others), not employed, and other (student/retired/disabled). The responses for the motivational factors were included as a continuous variable with a scale coded from one to five strongly disagree to strongly agree.

Collinearity between variables was assessed using Variation Inflation Factors (VIF) values. A VIF value over three for any variable was considered indicative of multicollinearity. Tests of statistical significance were two sided, with an alpha level of 0.05, and are reported with three significant digits. All analyses were conducted with SPSS version 24 (IBM).[16]

Results

Two hundred sixty two out of the 388 eligible parents (67.5%) completed the survey. Among those who completed a survey, 181(69%) consented to participate in the EPIC study. Figure 4 displays a flowchart of the study.

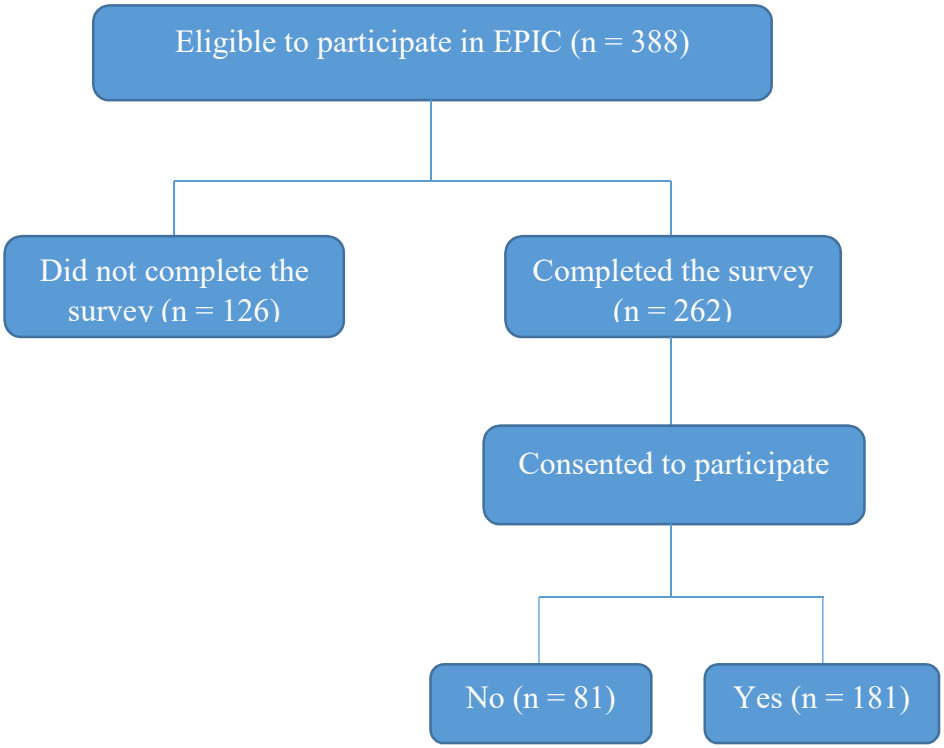

Figure 4. Consort diagram of respondents who completed a survey of motivating factors for research as part of the EPIC study at LBCH

Mean age (SD) of the respondents was 30 years (7.97). Two hundred and sixteen (82.4%) of the participants were female, 167 (63.7%) were African American, and 70 (26.7%) had at least a college degree. One hundred fifty (56%) had public health insurance. Among those who completed the survey, 181(69.1%) consented to participate in the EPIC study.

Table 24. Demographic characteristics of LBCH EPIC study participants, between January and June 2012

Characteristic	N (n=262)	%
Gender		
Male	39	14.9
Female	216	82.4
Missing	7	2.7
Age		
15–24	79	30.0
25–34	109	42.0
35+	61	23.0
Missing	13	5.0
Race		
Caucasian	77	29.4
African American	167	63.7
Hispanic	10	3.8
Other	8	3.1
Education		
< High School Grad	57	21.8
High School Grad	58	22.1
Some College	76	29.0
College Graduate	53	20.2
Advanced Degree	17	6.5
Missing	1	0.4
Employment		
Employed	156	59.5
Not Employed	64	24.4
Other (ret/stud/DA)	39	14.9
Missing	3	1.1
Insurance		
Public	150	57.3
Private	82	31.3
None	24	9.2
Missing	6	2.3
Marital status		
Married/Couple	120	45.8
Never married	112	42.7

Table 24 (Continued)

Characteristic	N (n=262)	%
Divorced	10	3.8
Separated	9	3.4
Widowed	4	1.5
Missing	7	2.7
Children in household		
None	2	0.8
One	68	26.0
Two	80	30.5
Three	62	23.7
≥Four	49	18.7
Missing	1	0.4
Severity of child's illness		
Not sick	15	5.7
Somewhat sick	29	11.1
Moderately sick	103	39.3
Very sick	113	43.1
Missing	2	0.8
Hospitalizations of child during past 5 years		
0	93	35.5
1	53	20.2
2	55	21.0
3+	60	22.9
Total	262	100.0

Table 25. Positive and negative responses for each motivational factor, LBCH EPIC study participants, between January and June 2012

Motivational Factor	Total	Agree*		Disagree*	
	N	N	%	N	%
The purpose of the study was clearly explained to	260	256	97.7	2	0.8
I feel my information will be kept private	261	243	92.7	3	1.1
I feel that this study is an important part of improving medical care	259	226	86.3	7	2.7
My child's illness in an important factor	253	217	82.8	11	4.2
I am concerned about the blood collection	259	109	41.6	90	34.4

Table 25 (Continued)

Motivational Factor	Total	Agree*		Disagree*	
	N	N	%	N	%
I am concerned about the nose/throat swab	258	102	38.9	101	38.5
I am concerned about the follow-up visit	258	97	37.0	110	42.0
Payment is an important factor	250	39	14.9	161	61.5

*Agree includes agree and strongly agree, disagree included disagree and strongly disagree, neutral responses not displayed.

Bi-variable analyses

Mothers were more likely to consent (OR = 1.88, 95% CI = 0.93, 3.77). Greater severity of illness was also associated with increased parental consent (OR = 1.29, 95% CI = 0.96, 1.75). Parents with a college degree were two times less likely to give consent compared to no college degree. Single parents were more likely to give consent than those who were married (OR = 1.59, 95% CI = 0.94, 2.71). As severity of illness and the number of children in the household increased, parental participation increased. Parental consent did not differ by race, employment status, or number of prior hospitalizations (Table 26). Younger parents, those who were single, and those with lower household education levels were more likely to participate.

Parents who agreed that the study is an important part of improving medical care were approximately three times more likely to participate than those who did not agree or were neutral; those who agree that their child's illness will be improved through the research were two times more likely to participate; those who believe the information will be kept private were nearly three times more likely to participate. Parents who had concerns about blood collection and nose and throat swabs were approximately 40% less likely to participate than those parents who did not have concerns (OR = 0.62, 95% CI = 0.50, 0.78 and OR = 0.60, 95% CI = 0.48, 0.75 respectively).

Table 26. Unadjusted odds ratios of study variables with study participation, LBCH EPIC study participants, between January and June 2012

Demographic Variables	**OR**	**95% CI**		***P***
Age (ref is 15-24)				
25-34	0.55	0.29	1.06	0.076
35+	0.65	0.31	1.39	0.267
Gender (ref is male)	1.88	0.93	3.77	0.077
Education (ref is ≥ college graduate)				
Some high school	2.04	0.97	4.29	0.062
High school graduate	2.75	1.27	5.98	0.011
Some college	2.08	1.05	4.15	0.037
Employment (ref is employed)				
Unemployed	0.91	0.49	1.70	0.767
Other	0.84	0.37	1.95	0.692
Insurance (ref is public)				
Private	0.54	0.31	0.96	0.034
Self-pay	0.88	0.34	2.29	0.798
Marital Status (ref is married/couple)	1.59	0.94	2.71	0.087
Race (ref is Caucasian)				
African American	1.03	0.57	1.85	0.921
Hispanic/Other	0.91	0.30	2.70	0.859
Number of Children	1.23	0.96	1.57	0.108
Hospitalizations of child during past 5 years	0.93	0.76	1.15	0.511
Severity of Child's Illness	1.29	0.96	1.75	0.093
Motivating Factors				
My child's illness is an important factor in my decision to participate	2.01	1.47	2.75	<0.001
I feel that this study is an important part of improving medical care	3.30	2.24	4.88	<0.001
I feel my information will be kept private	2.85	1.86	4.38	<0.001
The purpose of this study was clearly explained to me	1.78	1.11	2.87	0.018
I am concerned about the blood collection	0.62	0.50	0.78	<0.001
I am concerned about the nose and throat swab	0.60	0.48	0.75	<0.001
I am concerned about the follow-up visit	0.83	0.68	1.01	0.063
Payment is an important factor in my decision to participate	0.94	0.76	1.17	0.601

Multivariable analyses

Table 27 shows the adjusted associations with parental study participation. Household education level and several motivational factors including: the ability to learn more about their child's illness, altruism, clear understanding of the study purpose and concerns about the collection of biological specimens are all important factors for parental consent or participation. There was an inverse association between participation and education. Parents with the lowest levels of education were the most likely to give consent for their child to participate; furthermore, as education level increased, the likelihood of consent declined. Those who agreed with the statement that represented altruism, "I feel that this study is an important part of improving medical care" were three and a half times more likely to participate than those who did not (OR = 3.64, 95% CI = 2.20, 6.02).

Parents who agreed that their child's illness is an important factor in their decision to participate were one and a half times more likely to participate (OR = 1.59, 95% CI = 1.06, 2.39) than those who disagreed. Parents with concerns about the nose and throat swab were half as likely to give consent for their child to participate in the study compared to those who did not have concerns (OR = 0.48, 95% CI = 0.36, 0.65). Counter to the unadjusted finding, in the adjusted model, those who agreed that the study was clearly explained to them were less likely to participate.

Table 27. Adjusted odds ratios of factors associated with study participation, LBCH EPIC study participants, between January and June 2012

Variable	**OR**	**95% CI**		**P**
Education – reference is ≥ college graduate				
Some high school	4.78	1.75	13.05	0.002
High school degree	3.51	1.34	9.18	0.011

Table 27 (Continued)

Variable	OR	95% CI		P
Some college	2.91	1.21	6.98	0.017
My child's illness is an important factor in my decision to participate	1.59	1.06	2.39	0.025
I feel that this study is an important part of improving medical care	3.64	2.20	6.02	<0.001
The purpose of this study was clearly explained to me	0.45	0.22	0.93	0.032
I am concerned about the nose and throat swab	0.48	0.36	0.65	<0.001

The VIF did not exceed three for any of the variables in the multi-variable model indicating that there was no multicollinearity between the variables in the model.

Discussion

As study participation rates decline over time, it is important to understand the factors that are associated with parental consent to increase participation rates and decrease the chance of bias. Furthermore, as the collection of biologic specimens increases, it is important to understand the effect that this has on parental consent for participation, yet there are few if any published studies on this topic. As a result, this study evaluated attitudes toward predefined motivational factors that may be associated with parental consent to participate in pediatric research.

In our study, we found that parents who consented to research had lower levels of household education, were interested in learning more about their child's illness and were interested in improving medical care. They were less likely to consent if they had concerns about the nose and throat swab. More research is necessary to understand the nuances of clear explanation of the purpose of the study.

Our findings are consistent with the literature regarding the positive association of altruism and improving care for others to parents' decision to allow their child to participate in research. Additionally, we found that parents were more likely to consent if they believed that the study would allow them to learn more about their child's illness. While findings in the literature are mixed, our findings were consistent with Hoberman, et al.[22], regarding the increased likelihood of parents to consent to participation if their household education level was below a college degree. Parental consent did not differ by age, race, employment status, or number of prior hospitalizations.

A limitation of our study is that there may be other factors that are associated with parental consent but were not included in this study. Examples from the literature include respondents' perception of the research team, anxiety level and decisional uncertainty.

A second limitation is the small sample size which prevented us from evaluating the interaction between education level and each of the motivational factors. Additionally, generalizability is a limitation. Because our data reflect the parental attitudes from one large children's hospitals in Memphis, TN, our findings may not be consistent among other patient populations across the U.S. Additional research is needed to determine whether or not our findings can be generalized to other demographic populations.

Conclusion

Overcoming barriers to parental consent in pediatric research is important because it may reduce selection bias resulting from low participation rates which can affect study findings. To our knowledge, this is one of the first to assess important associations like the effect of the collection of biological specimens on parental consent.

We found parents who cared about improving medical care and who had a desire to learn more about their child's condition gave consent more frequently than those who did not; while concerns over the collection of biological specimens, like a nose and throat swab, may result in lower participation. Finding ways to mitigate concerns of parents about the biological specimen collection, for example, less invasive means for collecting specimens, may increase participation by as much as 60 percent.

Chapter 5 Summary

The EPIC study provided robust and unique datasets that were used to investigate the aims of these three studies and to begin to address important questions in the literature.

With these data, we assessed predictive factors associated with potentially unnecessary hospitalizations among different age groups of children with pneumonia. The ultimate goal was to provide evidence for developing a decision support rule that could be used to better manage pediatric pneumonia and reduce the number of unnecessary hospitalizations. Our findings, however, were not enough to achieve this goal.

While the utility of the CARIFS questionnaire is limited among younger ages, our study was the first to find that it had high internal consistency among an inpatient population of children with pneumonia. Furthermore, our findings suggest that the CARIFS survey may provide a means for predicting LOS in the hospital upon admission among older children.

Our findings suggest that motivational factors play an important role in the decision of parents to give consent for their children to participate in research. We found that parents who believe their child's participation in research will lead to an increase in their knowledge about their child's illness or contribute to the wellbeing of other children (altruism) are more motivated to participate in research. Furthermore, finding ways to mitigate the concerns parents have about the collection of biological specimens may also increase participation.

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Appendix Institutional Review Board Approval

Institutional Review Board
Office of Sponsored Programs
University of Memphis
315 Admin Bldg
Memphis, TN 38152-3370

May 26, 2017

PI Name: Cori Grant

Co-Investigators: Vikki Nolan, Cyril Chang

Advisor and/or Co-PI: Fawaz Mzayek

Submission Type: Initial

Title: Predicting length of illness and need for hospitalization among children with CAP

IRB ID: #PRO-FY2017-525

Level of Review: Facilitated Review

Expedited Approval: Apr 25, 2017

Expiration: May 16, 2018

Approval of this project is given with the following obligations:

1. This IRB approval has an expiration date, an approved renewal must be in effect to continue the project prior to that date. If approval is not obtained, the human consent form(s) and recruiting material(s) are no longer valid and any research activities involving human subjects must stop.

2. When the project is finished or terminated, a completion form must be submitted.

3. No change may be made in the approved protocol without prior board approval.

Thank you,

James P. Whelan, Ph.D.
Institutional Review Board Chair
The University of Memphis.