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Title: Risk factors for hospitalization among pediatric intestinal failure patients

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ABSTRACT COVER PAGE

Risk factors for hospitalization among pediatric intestinal failure patients

By

Tatyana Hofmekler
M.D., Morehouse School of Medicine, 2009

Advisor: Andi L. Shane, MD, MPH, MSc

An abstract of

A thesis submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory University in partial fulfillment of the requirements for the degree of

Master of Science

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Abstract

Risk factors for hospitalization among pediatric intestinal failure patients

By Tatyana Hofmekler

Children with intestinal failure are dependent on parenteral nutrition received through a central venous catheter. Complications due to underlying disease, parenteral nutrition, complications associated with central venous access such as vascular catheter associated infections (VCAIs), predispose patients to hospitalizations. Hospitalizations are poor prognostic indicators and contribute to high costs. Our aim was to identify demographic, social, and medical factors that contribute to hospitalization of children who received their medical care in a multidisciplinary intestinal rehabilitation clinic (IROC), with the long-term goal of focusing resource allocation on identified modifiable risk factors. We conducted a retrospective single center cohort study of children enrolled in IROC clinic. The primary outcome was total number of hospitalizations during follow-up time. Secondary outcomes included length of stay and risk of first hospitalization. As bloodstream infections lead to hospitalizations, we also studied the relationship of VCAIs and the number of hospitalizations. Forty-seven patients had 310 hospitalizations with a median duration of 4 days (1-84) per hospitalization. Results from unadjusted negative binomial models suggest that number of VCAIs (IRR 1.22 (1.06-1.42)) and therapy for small bowel bacterial overgrowth (IRR 1.92 (1.00-3.67)) were significant individual risk factors for number of hospitalizations. Social and demographic factors such as race (IRR 1.03 (0.53-1.99)), age at referral (1.00 (0.99-1.01)), and maternal age at delivery (0.96 (0.90-1.02)) were not risk factors for predicting number of hospitalizations. Survival analysis showed that presence of a colon, an ileocecal valve and short bowel syndrome diagnosis were individually protective against the risk of first hospitalization. Twenty-one (45%) children did not have a recognized VCAI during the study period, although VCAI rate and number of hospitalizations were positively correlated (Pearson correlation coefficient=0.54) among children who had a VCAI. In our single-center cohort of children enrolled in a subspecialty clinic, social and demographic factors were not found to be risk factors for hospitalization while anatomical factors were found to be protective against hospitalization frequency. Receipt of care in a multidisciplinary clinic likely reduced the impact of traditional social and demographic risk factors associated with hospitalization and VCAI, justifying resource allocation to a multidisciplinary subspecialty care clinic environment.

COVER PAGE

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To the families and patients living with intestinal failure who balance the complexities of medical management with their daily lives and inspire us to continue to search for answers.

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INTRODUCTION

Pediatric intestinal failure is a complex and debilitating disorder that has significant morbidity and mortality affecting a small portion of the population. The exact number of pediatric patients with intestinal failure is unknown. However, an estimate of 3 to 5 per 100,000 US births per year will suffer from short bowel syndrome [1]. In the UK, an estimate of 60-100 new pediatric patients per year will need parenteral nutrition [2]. Home parenteral nutrition administered through indwelling central venous catheters does improve life expectancy and growth for patients with intestinal failure, but at the cost of catheter associated infections, dependence on central venous access, liver disease, and social stressors [3, 4]. The direct cost of providing one year of parenteral nutrition has been estimated to range from $100,000 to $250,000, without including the cost of hospitalization or supply costs [5]. Hospitalizations increase the yearly cost by an additional $10,000 to $196,000 yearly [5]. There are high indirect costs such as the nonpaid cost for family members to manage home care of chronically ill persons that has been estimated to be $375 billion annually [6] and management of depression, a common diagnosis in families of patients receiving parenteral nutrition, that is estimated to be $80 billion in health services and loss of earnings [7, 8]. Children with intestinal failure are subject to multiple re-hospitalizations, primarily for medical management of mechanical failures and infectious complications of central venous catheters. Hospitalizations are disruptive to family dynamics, inhibit normal child development, and are a huge socioeconomic burden [9]. Causes for hospitalization have been investigated in an attempt to develop interventions, but these investigations have centered on medical causes for hospitalization. Because vascular catheter associated infections (VCAI) require intravenous antibiotics and thus a hospitalization, there has been particular emphasis on understanding and preventing vascular catheter infections. Central venous line infections and subsequent hospitalization have been shown to occur within 30 days of discharge [10] and in socially disadvantaged families [11]. Efforts to decrease hospitalization has been through interventions including ethanol lock therapy for central lines, small bowel bacterial overgrowth therapy, and the provision of care through multispecialty teams that can provide education and social support [12-14]. Despite these efforts, the burden of complications and hospitalizations remain significant and no study has looked at demographic, social and medical factors simultaneously.

To understand the risk factors that contribute to hospitalization of children with intestinal failure, we conducted a retrospective study of pediatric intestinal failure patients followed in a multidisciplinary clinic that specializes in intestinal failure. We utilized electronic medical records to assess the demographic, social and medical risk factors. We hypothesized that there are social and demographic factors associated with increased inpatient hospitalization days. The primary aim was to measure increased hospitalization through total hospitalization count. The secondary aim was to measure total length of stay days and risk to first hospitalization. Because VCAIs require intravenous antibiotics in a hospitalized setting, we studied the relationship of vascular catheter associated bloodstream infections and hospitalization. The information gained from this study is important for future resource allocation in an area that is very expensive and with significant associated morbidity and mortality.

BACKGROUND

Long-term parenteral nutrition is a relatively new phenomenon that started in the 1960's. The first pediatric patient was described in 1968 and sustained for only 44 days [15]. Initial patients requiring long-term parenteral nutrition were all maintained inpatient. However, with improved understanding of the properties of parenteral nutrition, more durable central lines, and increasing number of intestinal failure multidisciplinary teams, physicians strive to keep patients out of the hospitals [16].

Previously, patients requiring long-term parenteral nutrition would have high probability to develop complications such as Intestinal Failure Associated Liver Disease (IFALD) and require a multivisceral transplant [1, 16]. Multivisceral transplants are complicated procedures with five year survival rates of about 50 percent [16]. With better understanding of how to keep patients healthy and safe on parenteral nutrition, we are able to avoid or minimize IFALD in many patients. In 2012, fourteen pediatric intestinal failure centers described the state of intestinal failure through the Pediatric Intestinal Failure Consortium (PIFCON)[1]. This was the first and last large multicenter description of pediatric intestinal failure patients. At that time, roughly one half of patients (n = 272) developed intestinal adaptation allowing them to come off parenteral nutrition, one quarter went on to have a small bowel transplant and another quarter died [1]. Since the publication of PIFCON, the rates of intestinal transplantation have further decreased due to continued improvement in the management of patients. Thus, patients are now living with parenteral nutrition for longer periods of time and it is imperative to keep intestinal failure patients healthy, happy, and out of the hospital[17-19].

One of the most common indications for hospitalization of patients with intestinal failure is a vascular catheter associate infection (VCAI) requiring intravenous antibiotics. Other indications can include central line malfunctions, dehydration, complications associated with IFALD, and feeding intolerance problems. Because VCAIs are a primary cause of hospitalization, effort has been devoted toward augmenting the rate of VCAIs. Ethanol lock protocols involving the home instillation of ethanol into the "dead space" of central lines several times a week are an accepted way to decrease VCAI rates [20-22]. Small bowel bacterial overgrowth is diagnosed clinically by a medical team and treatment is aimed to alleviate symptoms and prevent bacterial translocation from intestine to the central line via the bloodstream. Small bowel bacterial overgrowth protocols involve the administration of enteral antibiotics routinely to prevent VCAI [13]. Additionally, protocols exist to teach families optimal care for their central lines. Adherence to these guidelines is intensive and requires detailed medical oversight. Intestinal rehabilitation programs have gained acceptance in the United States and participation in a multidisciplinary intestinal rehabilitation program optimizes patient success [18, 23].

Goals for patient care include appropriate growth and development, minimization of liver disease, while maximizing quality of life. These factors are directly attributed to hospitalization days because patients with hospitalizations are more likely to have decreased quality of life, more complications with their liver, and interference with normal growth and development [24].

Prior research of patient outcomes has centered on addressing medical factors. As an example, from the same cohort of patients that participated in PIFCON, a retrospective analysis showed that having necrotizing enterocolitis, versus other causes of intestinal failure, was associated with better outcomes such as survival and ability to wean off parenteral nutrition [25]. Alternative studies have supported this as well [26, 27]. Necrotizing enterocolitis is the leading cause of short gut syndrome. Short gut syndrome, gastrointestinal motility disturbances, and gastrointestinal mucosal diseases are the common etiologies leading to intestinal failure. Other research endeavors have focused on intestinal rehab programs [18, 23]. However, demographic and social factors as risk factors for hospitalizations in this complex patient population have not been evaluated.

METHODS

Specific Aim

The aim of the study was to identify the social, demographic and medical risk factors associated with hospitalization among children with intestinal failure and having a central venous access. The study was reviewed and approved by Children's Healthcare of Atlanta Institutional Review Board.

Study Design

Retrospective single center cohort study of children with intestinal failure and central venous access who received care in the multidisciplinary Intestinal Rehab of Children's Healthcare of Atlanta (IROC) clinic from July 1, 2010-February 1, 2016.

Study Population

Inclusion criteria included subjects aged up to 21 years of age, documented encounters for a minimum of six months after the date of enrollment, with IROC medical team oversight of home parenteral nutrition and central venous catheter management during the study period.

Measures and definitions

The follow-up time differed among the identified patients who were cared for by the IROC medical team. Measured follow-up time was defined as the number of days the patient had a central line in place over the course of the study, July 1st, 2010 through March 1st, 2016. The differing follow times of each patient was adjusted for in the analysis.

The primary outcome was number of hospitalizations or hospitalization count. Secondary outcomes included length of hospitalization in days and time to first hospitalization. The various potential risk factors were categorized as social, demographic or medical factors. All source of data were electronic medical records. Social, demographic, and medical factors were assessed on the date of IROC enrollment, unless otherwise specified. Most of the social and demographic variables were self-reported by family members. Medical factors were defined by the medical team. As an example, caregivers reported the gender, race, ethnicity, maternal age, distance to the clinic, number of children living at home, relationship of the primary caregiver at enrollment, language used at home, household income, insurance type, and if the family was intact. The family was determined to be intact if both parents lived together with the patient on the date of enrollment. Length of follow-up was defined as the number of days patients had a central line during the course of the study. "No show" rate to clinic was defined by the number of missed appointments divided by the number of scheduled appointments multiplied by 100.

Small bowel bacterial overgrowth therapy was prescribed by the medical team based on symptoms such as bloating, feeding intolerance, diarrhea in the setting of abnormal bowel anatomy such as missing an ileocecal valve. Set enteral antibiotic protocols exist within the IROC team that start patients on alternating antibiotics that continue on a monthly basis indefinitely unless stopped by the medical team. The receipt of small bowel overgrowth therapy was assessed 3 months following the date of IROC enrollment, which is the optimal time period over which a child with intestinal failure can be observed and assessed for the benefit of small bowel overgrowth therapy.

Vascular catheter associated infection (VCAI) rate, calculated as number of infections per 1,000 line days, were defined as growth of an organism that was clinically considered significant and not related to another source from a blood culture obtained from a central venous catheter. Two VCAIs were determined to be separate in an individual if spaced by negative blood culture and the patient having completed the prescribed antibiotic therapy for the initial blood culture. Of note, within the IROC clinic, all caregivers of patients with a fever are taught to present to the emergency department for an admission because a fever can be a sign of sepsis. For all patients that are enrolled in the multidisciplinary specialized intestinal failure team, standardized teaching of central line care was done with a minimum of two caregivers by specially trained nurses and nurse practitioners from the multidisciplinary team clinic. Home central venous catheter care was done by individual home health care companies or caregivers that had received the standardized teaching.

Statistical analysis

All statistical analyses were conducted using SAS 9.4 (Carey, NC). The analysis plan is depicted in Figure 1. Descriptive analysis of social, demographic and medical factors was conducted for subjects with any hospitalization versus no hospitalization using Wilcoxon rank sum tests for continuous non-normal variables and Chi-squared tests of proportions or Fisher's Exact tests for categorical variables.

Due to over-dispersion in the distributions of the outcomes of interest, total hospitalization count and length of hospitalization, negative binomial models were used to model the expected total hospitalization count and hospitalization length per patient follow up time (incident rate ratio). An offset term (log of total follow-up time) was used in the models to account for the different follow-up times per patient. This allowed us to model *rates* of expected hospitalizations per follow up time (years) rather than just expected counts of hospitalizations or length of hospitalization. We calculated unadjusted incident rate ratios for each studied risk factor. To develop an adjusted model of incident rate ratios, backward and forward selection methods were run at 0.05 significance level, testing groups of risk factors (e.g. social, demographic, medical). This was repeated with a 0.10 significance level, a less conservative approach, although this allowed us to decrease the probability of a type II error with the study's smaller sample size.

Survival analysis was conducted to assess the risk of being admitted or the time to the first hospitalization. Kaplan-Meier survival curves were plotted to show the estimated trajectory of risk changing over follow-up time for each risk factor of interest, and to also assess the proportional hazards assumption. Cox proportion hazard models (PH) were used to model the risk of being admitted at any time during the follow-up; right censoring was used for participants that were no hospitalized during follow-up time. Using Cox PH models allowed us to include all patients in the analysis, including those without hospitalizations during the study period (censored observations) and model their cumulative survival probability. The PH assumption was checked before including risk factors in the Cox models.

Scatterplots of VCAIs versus total hospitalizations and hospitalization days were inspected to assess a possible relationship in our population. These relationships were estimated with Pearson correlation coefficients. Additionally, descriptive analysis comparing patients without hospitalization against those with any hospitalization demonstrated the VCAI instances in both groups.

Missing data

There was no missing data for the primary or secondary measured outcomes. Six potential risk factor variables had missing values ranging from 1 to 9 values. There was a maximum of 20% of data missing for given risk factor variables, therefore imputation methods were not used. By default, for negative binomial and Cox PH models, SAS performs list wise deletion of any case with a missing value, essentially ignoring-observations with missing values. All models were checked for convergence and assessed for good fit (deviance, residuals).

RESULTS

Baseline characteristics

Forty-seven children met the study inclusion criteria; median (25^{th}-75^{th}) follow up time was 759 days (423-836) for all subjects; 8 (21%) did not have a hospitalization during the study period; all had a vascular access catheter in place as was defined in the inclusion criteria. Subjects had a median gestational age of 34 weeks (27.0-38.0), 22 (47%) were female, 27(58%) were African American (Table 1). Mothers were the most common primary care giver at enrollment (N=43, 92%). There were no fathers listed as a primary care giver. Short gut syndrome was the most common diagnosis (N=39, 83%).

Comparing the eight subjects without a hospitalization during the study period with the 39 (83%) who had one or more hospitalizations, noted a similar median maternal age at delivery, 24 years (21-28), (p=0.80). The ileocecal valve and full colon were more frequently present among those without a hospitalization (88% vs. 47%, p = 0.05, 50% vs. 13% p=0.05, respectively). Subjects without a hospitalization were followed for 885 days compared to those with one or more hospitalization 753 days, (p = 0.13).

Unadjusted negative binomial model of all risk factors among the hospitalized subjects (n=39)

The hospitalization frequency and lengths of hospitalization were widely distributed (Figure 2). Median hospitalization count was five, ranging from 0-25 per subject and the variance was 40.33. Median length of hospitalization was 42 days, ranging from 0 to 336 days, with a variance of 5028.88, indicating a much larger over-dispersion (variability) in hospitalization count distribution compared to length of hospitalization distribution. There were no significant findings for length of hospitalization (results not shown). A single demographic or social risk factor was not identified as a significant risk factor for the predicted number of hospitalizations over the follow-up time (incidence rate). However, among the medical risk factors, receiving small bowel bacterial overgrowth therapy or having a VCAI increased the incidence rate for having higher number of hospitalization counts (IRR 1.92 (1.00-3.67), p=0.05; IRR 1.22 (1.06-1.42), p=0.01, respectively); in other words, the rates at which hospitalizations occur are greater when SBBO therapy or VCAIs are present.

Adjusted negative binomial model

Having a short gut diagnosis and having an ileocecal valve was associated with lower rates of hospitalization count, although the model only neared significance at α=0.10 level (IRR 0.47 (0.20-1.12), p=0.09; IRR 0.56 (0.29-1.05), p-0.07, respectively) (Figure 3a). In addition, small bowel bacterial overgrowth therapy had an increased incidence rate (IRR 4.48 (1.84-10.90)) of VCAI count, while female gender was protective (lower incidence rate of VCAI) (IRR 0.36 (0.16-0.81)) (Figure 3b).

Risk to first hospitalization with Kaplan Meier survival curves and Cox proportion hazard model (n=47)

Kaplan Meier Survival curves show that small bowel bacterial overgrowth therapy treatment is associated with an increased risk (lower survival probability) of having a first hospitalization (Figure 4a). Having any length of colon present, short gut diagnosis, or ileocecal valve being present appear to have a lower risk for first hospitalization (higher survival probability) (Figure 4b-d).

The adjusted risk to first hospitalization was not shown to be significant (α=0.10) when backward selection was applied for factors such as small bowel bacterial overgrowth therapy, small bowel length, present ileocecal valve, short gut diagnosis, and present colon (Table 3). However, the receipt of small bowel bacterial overgrowth therapy trended to significance for risk of first hospitalization. Having an ileocecal valve and having any colon were protective against first hospitalization (Hazard Ratio <1.0) and trended towards significance.

Vascular Catheter Associated Infections (VCAIs)

There were 79 discrete VCAI events among the 26 patients followed for a total of 18,355 line days. Almost half (21) subjects (45%) did not experience a VCAI during the study period. An additional 21 subjects (45%) experienced 1 to 3 VCAIs. The remaining five subjects (11%) had 4 or more VCAIs each during the study period (Table 4). The median VCAI rate was 3.5 (0.0-69.4) per 1000 line days. Scatter plots of VCAI rate and hospitalizations among all forty-seven subjects showed a stronger correlation between VCAI rate and length of hospitalization (0.68, p<0.0001, Figure 5b) then between VCAI rate and hospitalization count (0.54, p=0.0003, Figure 5a).

DISCUSSION/CONCLUSION

Management of pediatric patients with intestinal failure is a complex process that requires significant resources due to the complexity of their needs. Hospitalizations incur high costs and provide additional stress to the caregivers and patients [8]. Identifying social, demographic and/or medical factors that are associated with hospitalizations allows for proper resource utilization to help future patients.

Our study found that medical factors were associated with hospitalization count or duration while social and demographic factors were not associated with hospitalization count or duration in this cohort of children receiving care in a multispecialty clinic devoted to intestinal rehabilitation. The receipt of small bowel bacterial overgrowth therapy and VCAIs were associated with higher hospitalization frequency. Kaplan Meier Survival Plots and descriptive analysis showed that having a colon, having an ileocecal valve and having a short gut diagnoses are all individually protective against having a hospitalization. The association of VCAI and hospitalization count was expected as a child with a presumptive or confirmed VCAI would be hospitalized. Small bowel bacterial overgrowth therapy has historically been used to suppress symptoms of bacterial overgrowth, common in children with intestinal failure, resulting in abdominal distention, feeding intolerance, and translocation of bowel bacteria to the bloodstream VCAI[13]. In our clinical setting, as in that of others, the majority of bacterial overgrowth was diagnosed clinically based on symptoms, signs, and risk given their gastrointestinal anatomy. Furthermore, treatment for bacterial overgrowth is variable with multiple regimens used in our clinical setting. Small bowel bacterial overgrowth therapy appeared to increase the risk for higher hospitalization count because small bowel bacterial overgrowth therapy is more likely to be prescribed for patients with more severe intestinal failure. Therefore, the statistical association that we observed may have been due to more severely affected intestinal rehabilitation subjects were more likely to have bacterial overgrowth and clinicians were more likely to initiate medical interventions for such patients.

Prior studies have shown that having a colon, having an ileocecal valve and having a short gut diagnoses are all individually associated with better patient outcomes, including time to transition to enteral nutrition [1, 26, 27]. The subjects in our cohort were less likely to have an initial hospitalization if they had a colon, an ileocecal valve or a had short gut as a primary diagnosis.

We sought to explore the relationship of VCAI and hospitalizations. In our study of 47 patients, the VCAI rate was 3.53 per 1000 vascular catheter days or a total of 79 VCAI events over the course of 18,355 line days. This is in contrast to a previously completed study of a comparable intestinal failure cohort assessed from 2005 to 2008, prior to the formation of IROC. In this study, VCAI were tracked in 44 patients over the first 6 months after initial discharge from the hospital when parenteral nutrition was initiated. There were 72 incidences of VCAI in just the first month after initial discharge. There were a total of 178 VCAI events over the course of the 6 months of follow up[10]. Since these cohorts are comparable in terms of geography, intestinal failure manifestations, and need for central vascular access, the notable decrease in VCAI incidence that we observed among our cohort who were enrolled in IROC compared with the historical cohort supports the effectiveness of a multidisciplinary subspecialty clinic on decrease VCAI rates, which correspond to decreased hospitalization rates. The impact of IROC may be attributed to the standardized central venous access teaching and protocols provided to caregivers as well as centralization of care, both of which were added with IROC. In 2015, Ardura et al. described rates of 3.83 per 1000 catheter days, similar to ours, when utilizing central line care protocols that are similar to ones utilized in IROC [20].

Looking at the relationship of VCAI rate to hospitalization days and hospitalization counts among all the patients in the study, the scatter plots showed a relationship with a Pearson correlation index of only 0.68 (95% CI: 0.45-0.82) and 0.54 (0.26-0.73) respectively. It is important to note that for sake of simplicity, we assumed linear relationship and independence among infection events. In actuality, the relationship from an initial infection to subsequent infection is likely not linear nor independent of one another. Additionally, almost half of the patients in our study did not have a VCAI (Table 4). Despite of these limitations, our data suggests that a large subset of our patients did not get admitted due to VCAI, something that is traditionally thought of as a common cause of hospitalization. This may be a reflection of the implemented protocols in place for vascular catheter care through multidisciplinary efforts of IROC as detailed above. Alternatively, this also suggests that underlying medical factors that are less likely to be changeable by the medical team such as bowel anatomy and primary diagnoses for intestinal failure play a substantial risk for hospitalization. These findings are important for counseling families with patient with intestinal failure.

An association between small bowel bacterial overgrowth therapy and VCAI may be explained by the criteria used for the initiation of small bowel overgrowth therapy in children with more complicated anatomy and more severe manifestations of intestinal failure. Due to their greater severity of illness, these children may have been predisposed to having more VCAIs. Therefore, the association that was observed between small bowel bacterial overgrowth therapy and VCAIs could represent an association between severity of illness and VCAIs.

Female gender appeared to be protective against VCAI in one analysis, although this protective relationship was not observed with hospitalization frequency or length of stay. The protective association seen between female gender and VCAIs may have been the consequence of a small sample size, and needs further assessment to understand completely.

Although our findings may be limited by the retrospective design, misclassification biases, and small sample size, due to the highly-specialized field, these limitations are inherent to studies of pediatric intestinal failure. Despite our small sample size we have a large median follow-up time of 759 (423-836) days per person. The majority of the data was initially collected by family report, predisposing to recall bias. In addition, the variations in underlying diagnoses and underlying gastrointestinal anatomy for many of the intestinal failure patients may lead to misclassification. Although most patients had short gut syndrome, they had related diagnoses that may not have been captured. We attempted to develop a compliance score, but we were unable to develop a satisfactory measure that we could use to reliably reflect patient compliance. IROC no-show rate was an attempt to reflect compliance. However, once patients were hospitalized, their outpatient clinics were canceled and so they had fewer opportunities to miss a clinic appointment making the no-show rate less reliable. In future studies, we hope to develop a reliable score that could be used to reflect compliance with scheduled appointments.

A prospective evaluation would reduce many of the challenges related to a retrospective study and would facilitate a more comprehensive assessment of some of the aspects that appeared to be protective against and those that appeared to predispose to hospitalization. Family detailed interviews would be helpful to understand further social and demographic aspects that were not captured with retrospective data.

Overall, we did not find social or demographic factors to be associated with hospitalization. Alternatively, medical factors, and particularly bowel anatomy were associated with hospitalization. The benefit of a subspecialty clinic in preventing VCAIs is apparent as a notable number of hospitalizations in this cohort were not associated with a VCAI. This allows focus on other factors that we hope to elucidate and address with future studies.

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TABLES/FIGURES

Figure 1. Overall analytic plan

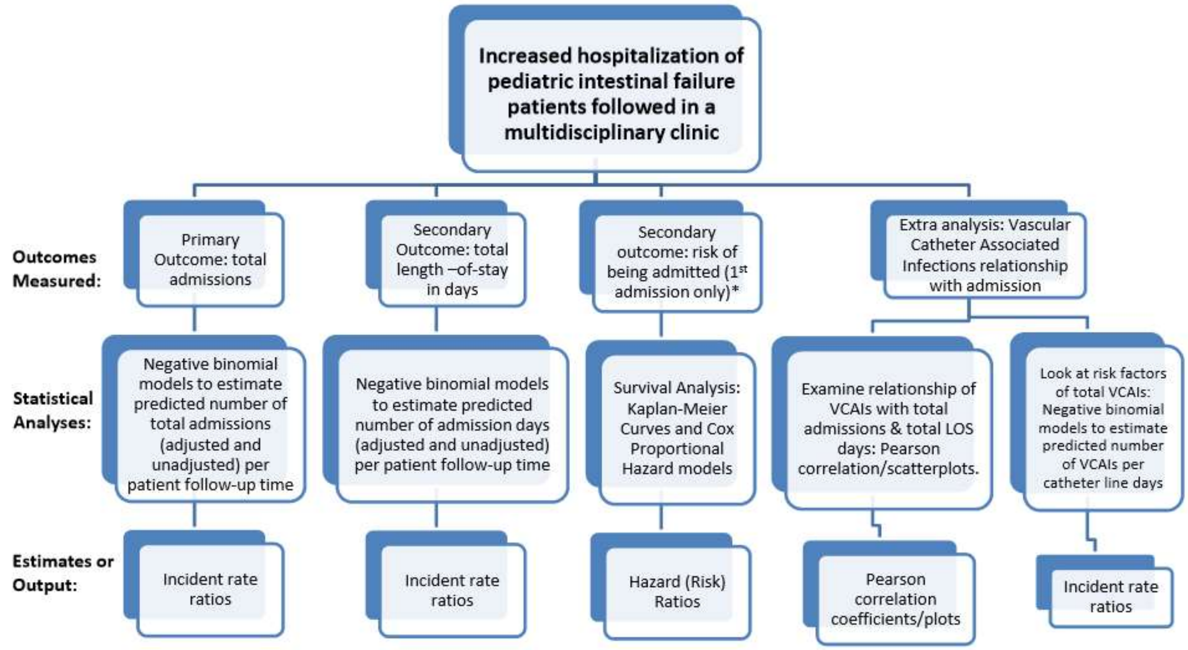

Table 1: Patient baseline characteristics of pediatric patients with intestinal failure enrolled in the intestinal rehab of Children's Healthcare of Atlanta clinic from July 1st 2010 through February 1st 2016.				
N (%) or Median (25th-75th)	**All (N=47)**	**No Hospitalization (N=8)**	**Any Hospitalization (N=39)**	**P-value***
Demographic Factors				
Gestational Age (weeks)	34 (27-38)	33 (26-37)	34 (27-38)	0.82
Female gender	22 (47%)	4 (50%)	21 (54%)	1.00
Race				0.62
African-American	27 (58%)	6 (75%)	21 (54%)	
White	18 (38%)	2 (25%)	16 (41%)	
Other	2 (4%)	0	2 (5%)1	
Race – White (vs. NW)	18 (38%)	2 (25%)	16 (41%)	0.69
Ethnicity				1.00
Hispanic	1 (2%)	0	1 (3%)	
Non-Hispanic	46 (98%)	8 (100%)	38 (97%)	
Social Factors				
Distance from patient residence to clinic (miles)**	31 (12-68)	22 (10-73)	35 (16-68)	0.72
Age of referral to multidisciplinary clinic (months)	16 (6-57)	46 (12-71)	13 (6-43)	0.14
Total Follow-up time (days) (1st IROC*** to Feb 1. 2016)	759 (423-836)	885 (546-1637)	753 (417-836)	0.13
Insurance type				0.70
Private/Commercial/Military	14 (30 %)	2 (25%)	14 (36%)	
State program (Medicaid/Medicare)	31 (66%)	6 (75%)	25 (64%)	
Number children living at home at enrollment				1.00
1	20 (43%)	3 (38%)	17 (44%)	
2	16 (34%)	3 (38%)	13 (33%)	
3	6 (13%)	1 (13%)	5 (13%)	
4	5 (11%)	1 (13%)	4 (11%)	
Relationship of primary caregiver at enrollment				
Mother	43 (92%)	8 (100%)	35 (90%)	1.00
Father	0	0	0	
Other family member	4 (8%)	0	4 (10%)	
Outside of family	0	0	0	
Maternal age at delivery (years)	24 (21-28)	25 (21-26)	23 (21-30)	0.80
Average Percent No-Show appointments	0 (0-25)	0 (0-0.5)	0.1 (0-0.3)	0.19
Primary language used a home				1.00
English	45 (96%)	8 (100%)	37 (95%)	
Spanish	2 (4%)	0	2 (5%)	
Intact family at enrollment	26 (55%)	3 (38%)	23 (59%)	0.44
Household income				0.77
Expenses exceed income	20 (43%)	3 (38%)	17 (44%)	
Income exceeds expenses	8 (17%)	2 (25%)	6 (15%)	

Income meets expenses	19 (40%)	3 (38%)	16 (41%)	
Medical Factors				
Primary diagnosis (*not mutually exclusive)*				
Short gut	39 (83%)	7 (88%)	32 (82%)	1.00
Gastroschisis	8 (17%)	1 (13%)	7 (18%)	1.00
Intestinal atresia	5 (11%)	0	5 (13%)	0.57
Remaining Small Bowe length (cm)****	35.0 (20-50)	42.5 (30-56)	35 (20-50)	0.15
Ileocecal Valve present[1]	25 (54%)	7 (88%)	18 (47%)	**0.05**
Colon present[2]				**0.05**
Full	9 (19%)	4 (50%)	5 (13%)	
Partial	11 (23%)	1 (13%)	10 (26%)	
None	27 (58%)	3 (38%)	24 (62%)	
Colon – Full/Partial (any) vs. None	20 (43%)	5 (63%)	15 (39%)	0.26
Small Bowel Bacterial Overgrowth therapy	27 (58%)	3 (38%)	24 (62%)	0.26

* P-value achieved with Wilcoxon rank-sum tests for continuous variables and Chi-square/Fisher's Exact tests for categorical variables.
**Distance from patient residence to clinic location was calculated using address zip codes in SAS and is the straight-line distance.
***IROC, Intestinal Rehab of Children's
****Five had 'full' SB length and 1 had 'transplant'. Set to missing when computing median.
[1] One observation had 'transplant'. Set to missing when computing median.
[2]Based on whether the ascending, transverse, descending, sigmoid, and rectum part of colon present; if all five present then 'full'; if some present, then 'partial'; if none, then 'none'.

Figure 2: Distribution of hospitalization count and hospitalization days for pediatric patients with intestinal failure enrolled in the intestinal rehab of Children's Healthcare of Atlanta clinic from July 1st 2010 through February 1st 2016 (N=47).

Figure 2a: Distribution of total number of hospitalization counts for all pediatric patients with intestinal failure.

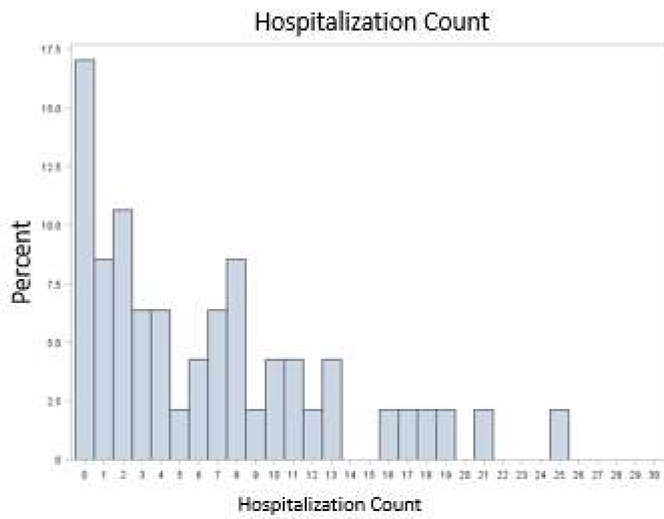

Figure 2b: Distribution of total hospitalization days for all pediatric patients with intestinal failure.

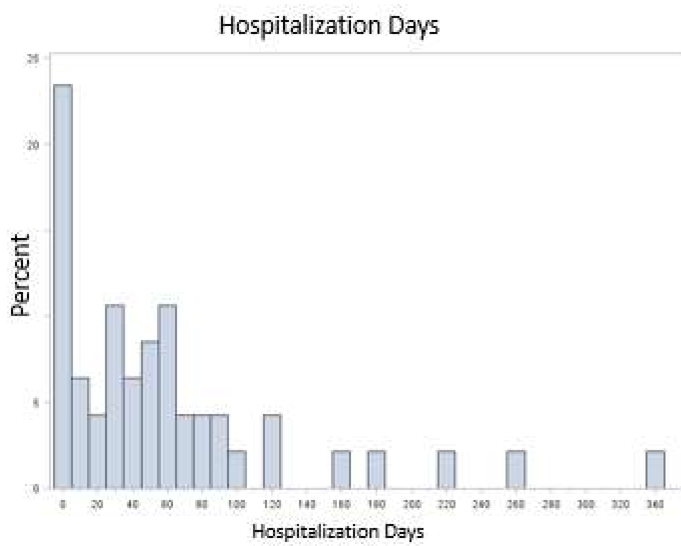

Table 2: Hospitalization incident rate ratios of demographic, social and medical characteristics of pediatric patients with intestinal failure enrolled in the intestinal rehab of Children's Healthcare of Atlanta clinic from July 1st 2010 through February 1st 2016.

N (%) or Median (25th-75th)	Incident rate ratio (N=47)	Wald 95% confidence limit (lower)	Wald 95% confidence limit (upper)	P-value
Demographic Factors				
Gestational Age (weeks)	1.01	0.96	1.07	0.62
Female gender (vs. male)	0.82	0.43	1.59	0.58
Race				
African-American vs. White and other	1.03	0.53	1.99	0.94
Ethnicity				
Hispanic vs. Non-Hispanic	2.66	0.31	21.0	0.38
Social Factors				
Distance from patient residence to clinic (miles)**	1.00	0.99	1.01	0.94
Age of referral to multidisciplinary clinic (months)	1.00	0.99	1.01	0.81
Insurance type (State vs Private (commercial/military))	1.47	0.73	2.95	0.29
Number children living at home at enrollment				
1 vs. all other number	1.17	0.61	2.24	0.65
Relationship of primary caregiver at enrollment				
Mother vs. other	0.91	0.27	3.07	0.88
Maternal age at delivery (years)	0.96	0.90	1.02	0.17
Primary language used a home				
English vs. Spanish	1.72	0.33	8.94	0.54
Intact family at enrollment (Yes vs. No)	1.00	0.52	1.92	0.99
Household income				
Expenses exceed income (vs income exceeds/meets expenses)	0.82	0.42	1.56	0.54
Medical Factors				
Primary diagnosis				
Short gut vs other diagnoses	0.64	0.27	1.49	0.30
Remaining Small Bowel length (cm)***	1.00	0.98	1.01	0.66
Ileocecal Valve present[1]	0.64	0.34	1.23	0.18
Colon present[2]				
Any vs. None	0.84	0.43	1.63	0.61
Small Bowel Bacterial Overgrowth therapy at 3 months	1.92	1.00	3.67	**0.05**
Total Number Vascular Catheter Associated Infections	1.22	1.06	1.42	**0.01**

**Distance from patient residence to clinic location was calculated using address zip codes in SAS and is the straight-line distance.
***Five had 'full' SB length and 1 had 'transplant'. Set to missing when computing median.
[1] One observation had 'transplant'. Set to missing when computing median.
[2]Based on whether the ascending, transverse, descending, sigmoid, and rectum part of colon present; if all 5 present then 'full'; if some present, then 'partial'; if none, then 'none'.

Figure 3: Multivariate model of risk factors on incident rate ratio for hospitalization count and vascular catheter associated infections among all pediatric intestinal failure patients enrolled in Intestinal rehab of Children's from July 1st 2010 through February 1st 2016.

Figure 3a: Multivariate model of risk factors on incident rate ratio for hospitalization count among pediatric intestinal failure patients.

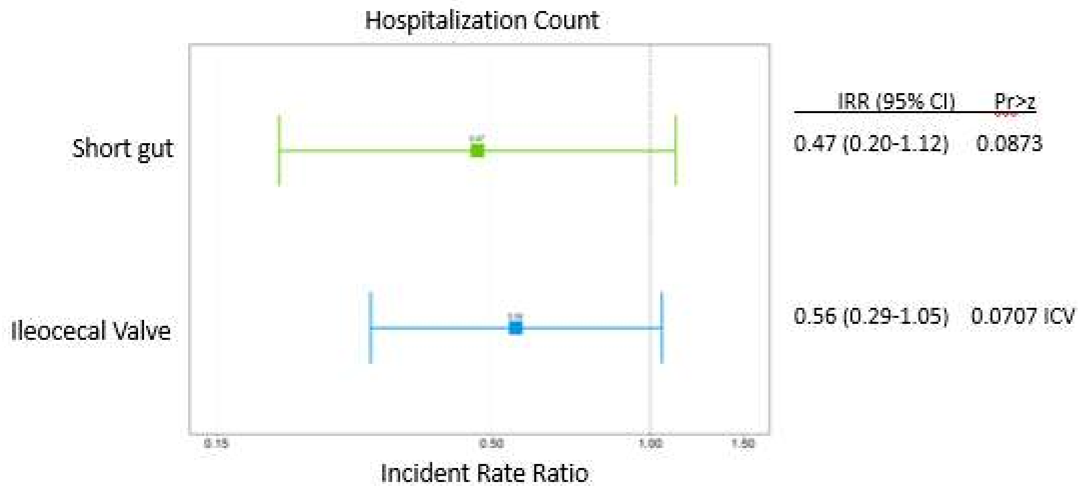

Figure 3b: Multivariate model of risk factors on incident rate ratio for vascular catheter associated infections among all pediatric intestinal failure patients enrolled in Intestinal rehab of Children's from July 1st 2010 through February 1st 2016.

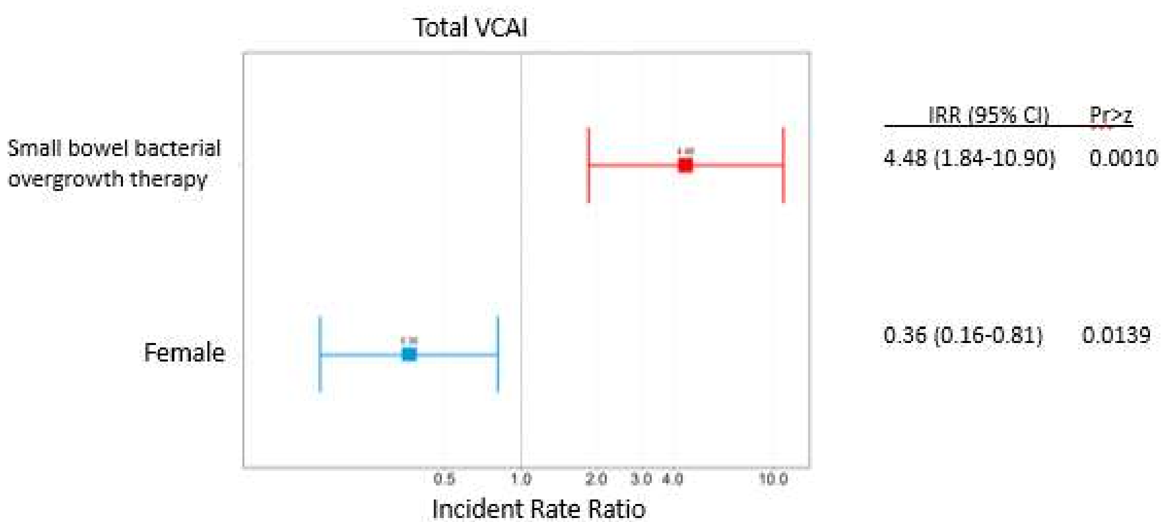

Figure 4: Survival plots of small bowel bacterial overgrowth therapy, colon presence, short gut diagnosis, and ileocecal valve presence to the first hospitalization among all pediatric patients with intestinal failure.

Figure 4a: Survival plot of small bowel bacterial overgrowth therapy among all patients to time of first hospitalization.

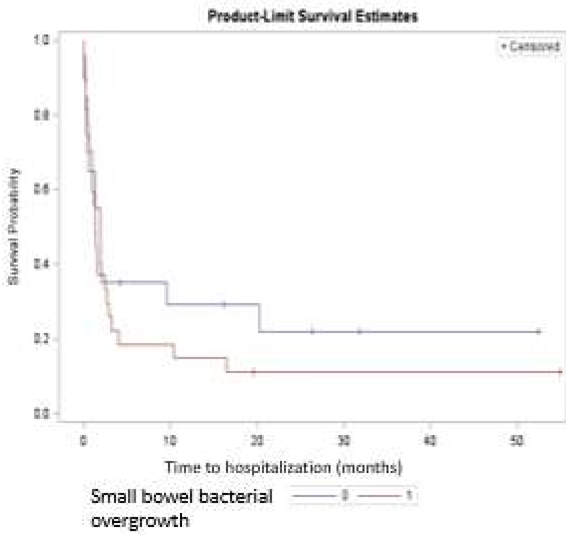

Figure 4b: Survival plot of having any colon among all patients to time of first hospitalization.

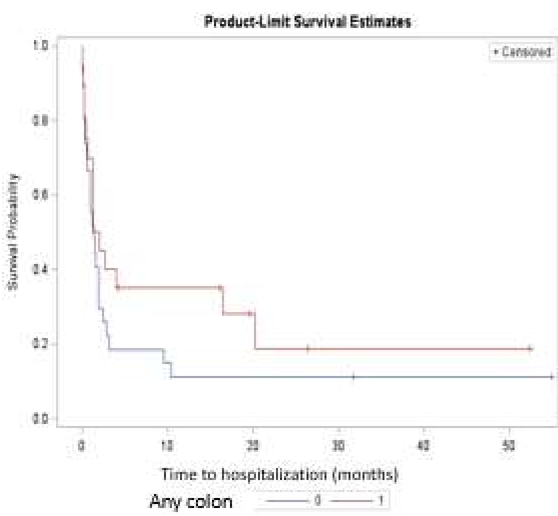

Figure 4c: Survival plot of having short gut diagnosis among all patients to time of first hospitalization.

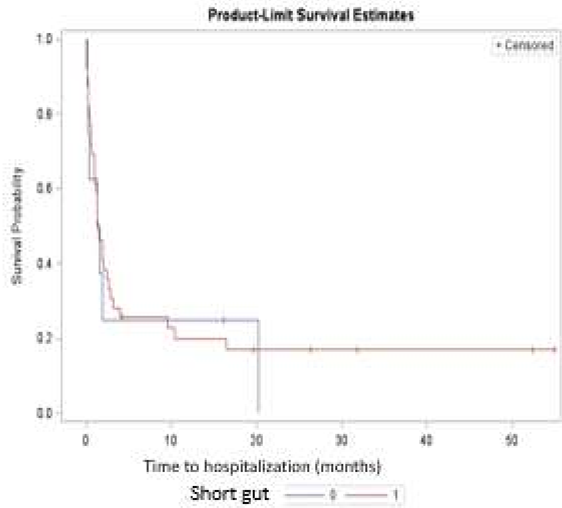

Figure 4d: Survival plot of having an ileocecal valve among all patients to time of first hospitalization.

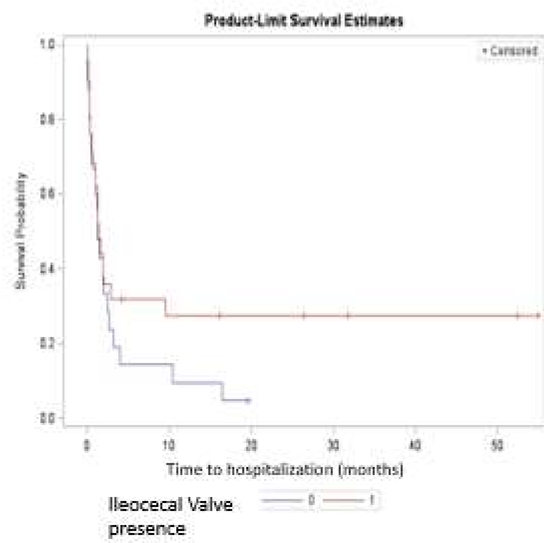

Table 3: Cox proportion hazard model of risk to first hospitalization for small bowel bacterial overgrowth therapy, small bowel length, ileocecal valve presence, short gut diagnosis, or having any colon among all intestinal failure patients followed at the Intestinal Rehab of Children's clinic. (N=47)

Parameter	**95% CI**	**Hazard Ratio**	**Pr > ChiSq**
Small bowel bacterial overgrowth therapy (vs none)	0.50 – 3.28	1.28	0.60
Small bowel length (cm)	0.97 – 1.00	0.99	0.12
Ileocecal valve (vs none)	0.23 – 1.22	0.53	0.14
Short-gut syndrome (vs none)	0.11 – 6.71	0.85	0.87
Colon (any vs. none)	0.23 – 1.11	0.51	0.09

Table 4: Vascular catheter associated infection count and rate for all pediatric intestinal failure patients followed in the Intestinal Rehab of Children's clinic from July 1st 2010 through February 1st 2016. (N=47)

Vascular Catheter Associated Infection count	**N (percent of patients)**
0 infections	21 (44.7%)
1-3 infections	21 (44.7%)
≥4 infections	5 (10.6%)

Median Vascular Catheter Associated Infection rate (per 1,000 line days)	3.53 (0.0-6.94)
Total study vascular catheter line days	18,355

Note: Only those that were admitted had any CLABSI infection. Furthermore, when we compared those who were admitted ≤ 3 days vs. > 3 days, only those with >3 days had any CLABSI infection.

Figure 5: Correlation of vascular catheter associated infections to hospitalizations in pediatric intestinal failure patients followed at the intestinal rehab of Children's clinic.

Figure 5a: Correlation of vascular catheter associated infection rates to hospitalization count in pediatric patients with intestinal failure enrolled in the intestinal rehab of Children's Healthcare of Atlanta clinic from July 1st 2010 through February 1st 2016.

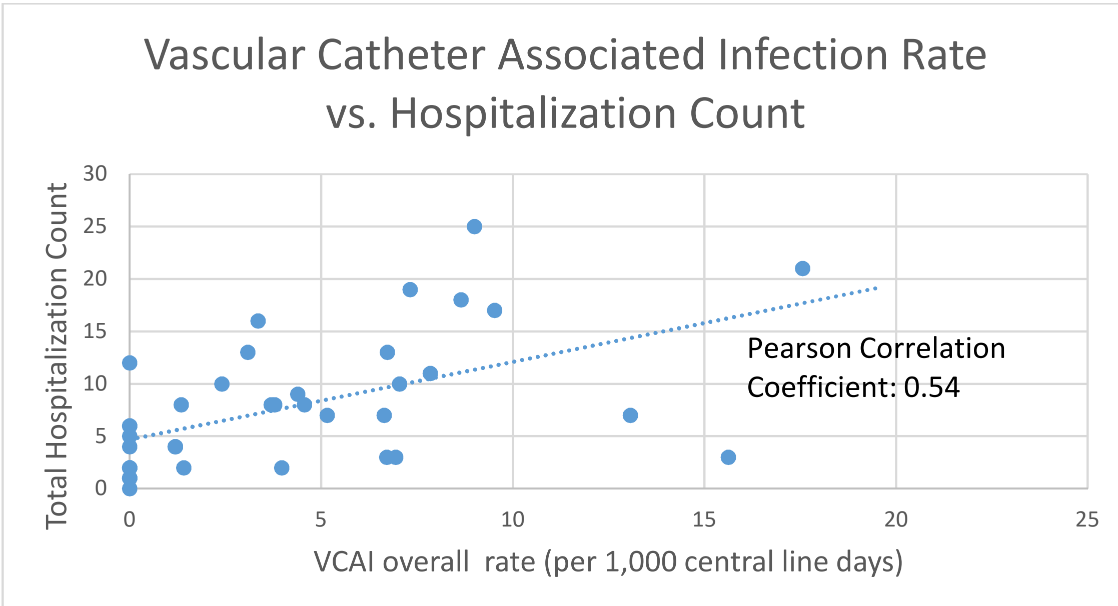

Figure 5b: Correlation of vascular catheter associated infection rates to hospitalization days in pediatric patients with intestinal failure enrolled in the intestinal rehab of Children's Healthcare of Atlanta clinic from July 1st 2010 through February 1st 2016.