Improving management of hospitalized adults with uncomplicated cellulitis or cutaneous abscess

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ABSTRACT

The goal of this study was to determine if implementation of a clinical practice guideline for the management of hospitalized adults with uncomplicated skin and soft tissue infection (SSTI) could improve patient care by decreasing unnecessary broad-spectrum antibiotics, duration of intravenous therapy, duration of total therapy, and length of stay (LOS). Uncomplicated SSTIs are a common reason for hospitalization and can be due to cutaneous abscess or non-purulent cellulitis. Uncomplicated cutaneous abscesses are often caused by *Staphylococcus aureus* (SA), including methicillin-resistant *Staphylococcus aureus* (MRSA) and the mainstay of treatment is drainage; antibiotics should be used (with MRSA coverage initially) only if significant surrounding cellulitis. Uncomplicated non-purulent cellulitis is more likely caused by β-hemolytic Strep (BHS), and does not require vancomycin or broad-spectrum antibiotics for treatment. However, due to concern for MRSA and other organisms, many patients with uncomplicated SSTI are given vancomycin and other broad-spectrum antibiotics. Our Antimicrobial Stewardship Program created and disseminated a guideline for the treatment of uncomplicated SSTI at our large academic tertiary care hospital. The study was an observational study of patients with uncomplicated SSTI during one year periods before and after implementation of the guideline. The primary endpoint was the proportion of uncomplicated SSTIs treated with at least one dose of vancomycin. A total of 259 patients were included in the pre-intervention cohort and 223 patients post-intervention. For non-purulent cellulitis, treatment with vancomycin decreased significantly and the use of broad-spectrum antibiotics decreased significantly for both cutaneous abscess and non-purulent cellulitis, with no increase in clinical failure.

PURPOSE

The objective of this study is to determine if the implementation of the Baystate Medical Center (BMC) Clinical Practice Guideline for the Management of Hospitalized Adults with Cellulitis or Cutaneous Abscess is effective at improving patient care by decreasing unnecessary broad-spectrum antibiotics, duration of intravenous therapy, duration of total therapy, and LOS in the targeted population. The study will also determine if the guideline successfully decreased the incidence of antimicrobial therapy-related complications for patients with uncomplicated cellulitis or cutaneous abscess.

SCOPE

Background

In 2009, SSTIs accounted for almost 630,000 hospitalizations in the United States[1], with an average LOS of 4.4 days, an increase from 590,000 hospitalizations in 2006 and almost double the incidence 10 years prior.[2-3] The rise in the number of community-acquired MRSA infections requiring hospitalization accounts for much of the elevated incidence. Mera et al demonstrated the proportion of abscesses caused by MRSA increased from 26% in 1998 to 70.4% in 2007.[4]

However, Jeng et al recently assessed the treatment of uncomplicated cellulitis without abscess and demonstrated that 96% of the patients treated with a beta-lactam antibiotic alone responded clinically and did not require coverage for MRSA[5]. This work suggests it is often not necessary to treat empirically for MRSA infection in individuals who have uncomplicated cellulitis without a cutaneous abscess.

The 2005 Infectious Diseases Society of America (IDSA) Guidelines for The Diagnosis and Management of Skin and Soft-tissue Infections [6] state cutaneous abscess may be treated with incision and drainage (I and D) alone as long as it is not associated with surrounding cellulitis or fever. If surrounding cellulitis or fever is present, it is recommended to treat with agents effective against MRSA (such as vancomycin, linezolid, clindamycin, daptomycin, doxycycline or trimethoprim/sulfamethoxazole). Regarding typical erysipelas or cellulitis, the 2005 IDSA Guidelines recommend treatment with an antibiotic that covers streptococci, such as β-lactam antibiotics or clindamycin. However, the guidelines concede "many clinicians choose an agent that is also effective against SA, although this organism rarely causes cellulitis unless associated with an underlying abscess or penetrating trauma."

In 2014, an update to this 2005 Guideline was published[7]. Little change was made in the 2014 update regarding cutaneous abscess; I and D is still recommended as primary therapy for mild cases. For moderate cases, I and D and empiric oral anti-MRSA antibiotics (such as doxycycline or trimethoprim/sulfamethoxazole) are recommended. For severe cases with systemic symptoms or if patient has failed I and D with oral antibiotics, other empiric anti-MRSA-antibiotics (such as vancomycin, daptomycin, linezolid, televancin, ceftaroline) are recommended. The 2014 update makes a more clear distinction between purulent and non-purulent cellulitis, recommending oral β-lactam (or clindamycin) therapy for mild nonpurulent cellulitis, and IV β-lactam (or clindamycin) therapy for moderate nonpurulent cellulitis. Perhaps this new IDSA Guideline will change prescribing habits, but often, in clinical practice, due to concern for MRSA and other less common pathogens, even in cases of uncomplicated cellulitis without abscess, many individuals admitted to the hospital for cellulitis treatment are given vancomycin and other broad-spectrum antibiotics.

Vancomycin use comes with well-defined risks, including phlebitis and nephrotoxicity. At BMC 11.9% of patients treated with vancomycin develop nephrotoxicity, increasing the LOS by 4.4 days.[8] This is consistent with a study conducted by Chertow et al.[9] that found that acute kidney injury (AKI), defined as an increase of 0.5 mg/dL in serum creatinine, increased LOS by 3.5 days and increased total cost by almost $7,500 in 2005. Broad-spectrum antibiotics also have their own host of issues including difficult to treat infections and pharmacy costs. Decreases in the rates of broad-spectrum antimicrobials have demonstrated decreases in the rates of infections caused by *Clostridium difficile* infections and drug resistant organisms. [10]

Prior studies have shown improved appropriate antimicrobial choices for SSTI with the implementation of a guideline and educational efforts. Jenkins and colleagues implemented an institutional guideline to standardize the treatment of inpatient cellulitis and abscess which led to shorter durations of more targeted therapy without adverse effects on clinical outcomes.[11]

Setting

Baystate Medical Center (BMC), a 716-bed hospital, serves as the flagship hospital of a three hospital health system known as Baystate Health. It is an academic, tertiary care facility and serves as the only level 1 trauma center in western Massachusetts. Baystate Medical Practices, also a part of Baystate Health, offer many outpatient primary care and specialty services. Inpatient and outpatient facilities are linked by a computerized health information system.

METHODS

Intervention

This is an observational study following the education/implementation of a Guideline for the Management of Hospitalized Adults with Cellulitis or Cutaneous Abscess to compare the treatment of patients with uncomplicated cellulitis or cutaneous abscess. The guideline was reviewed by and approved by the members of the Infectious Diseases Division. It includes recommendations from the IDSA guidelines for both the treatment of MRSA infections and the treatment of SSTIs. It prompts the clinician to differentiate between cutaneous abscess and uncomplicated cellulitis since these two distinct clinical entities usually have different causative organisms and treatment choices. Cutaneous abscesses are more likely to be caused by SA (either MSSA or MRSA) which could be initially treated with either vancomycin or trimethoprim/sulfamethoxazole. Furthermore, a cutaneous abscess that is drained and does not have surrounding cellulitis may not require antibiotic therapy. Uncomplicated cellulitis is most likely caused by *Streptococcus* species and could be treated initially with penicillin, cefazolin or clindamycin.

The guideline was the focus of Antimicrobial Stewardship Education for the appropriate groups. The guideline was disseminated during the lecture series and posted on the institution's intranet. Additionally, computerized order entry care sets were implemented for the Emergency Medicine Department.

Study Design

Patients aged 18 years of age and older were identified if they were discharged from our institution during one year periods before and after implementation and education. The groups include patients between January 1 and December 31, 2011(pre-implementation) or April 1, 2013 and March 31, 2014 (post-implementation) with a principal diagnosis of cellulitis or cutaneous abscess using *International Classification of Diseases, 9th Revision* (*ICD-9*), coding data. ICD-9 codes included in the study were cellulitis and cutaneous abscess of finger and toe (681.x), other cellulitis and abscess (682.x), other infections of skin and subcutaneous tissue (686.x) and erysipelas (035). For patients with multiple hospitalizations for cellulitis or cutaneous abscess during the study period, only the initial admission was considered.

Patients were excluded if they were transferred from an outside hospital, left against medical advice or were identified as having complicated cellulitis. Complicated cellulitis included infection of diabetic or chronic ulcer, surgical site infection, periorbital or orbital cellulitis, perirectal abscess or cellulitis, sepsis, bacteremia, human or animal

bites, burns or severe immunosuppression. For the purposes of this study, severe immunosuppression was defined as an absolute neutrophil count < 500, a CD4+ count < 200, a history of organ transplantation and high dose corticosteroids (20 mg/day of prednisone or equivalent for 2 or more weeks).

Selected demographics and principal diagnosis code were extracted electronically from the hospital billing systems. Manual review of the electronic medical record was used to verify discharge diagnosis and to obtain information about patient presentation at time of admission, drainage procedures, inpatient management of cellulitis, discharge antibiotic therapy and subsequent encounters within the Baystate Health System in the first 30 days following discharge. All data was collected and stored in a REDCap database[12]. The protocol was approved by the BMC institutional review board prior to data collection.

Study Endpoints

The primary endpoint was the proportion of uncomplicated cellulitis treated with at least one dose of vancomycin. The secondary endpoints included all inpatient antibiotics received, LOS, duration of IV antibiotic treatment, duration of all antibiotic treatment and clinical failure. Clinical failure included treatment failure, recurrence and 30 day rehospitalization. Treatment failure was defined as the need to change antibiotics or redrain an abscess 7 days after therapy initiation. Recurrence was defined as the need to reinitiated antibiotics within 30 days of completing an initial treatment course. Safety endpoints were also evaluated and included nephrotoxicity, infusion related reactions and phlebitis. Nephrotoxicity was defined as at least a 50% increase in serum creatinine or at least a 50% decrease in creatinine clearance calculated using the Cockroft-Gault equation. Study endpoints were reported for three distinct groups: non-purulent cellulitis, purulent cellulitis and all cellulitis.

Statistical Analysis

Assuming a vancomycin use baseline use of 75% and a 20% decrease, 98 subjects per group are needed to meet 80% power with a two-sided alpha of 0.05. Statistical analysis for our primary measures included Fisher exact test for categorical data and Wilcoxon Rank Sum for ordinal data.

Limitations

The limitations of this study include its retrospective design and the use of ICD-9 codes to identify patients. This may have resulted in missing patients that actually met the inclusion criteria due to miscoding. Also, all data collected was dependent on what was recorded in the chart. Second, the only post discharge data available for review within our electronic medical record is from Baystate associated practices. Follow-up visits to other hospitals or providers outside of the Baystate system would have been missed. Finally, being a single center study the generalizability of the data is limited, though this method of treatment of cellulitis is not likely unique to our institution.

RESULTS

Study Population

A total of 815 patients met the inclusion criteria for this study. At least one exclusion criteria was met for 333 patients. A total of 259 patients were included in the pre-intervention cohort with 154 non-purulent and 105 purulent. A total of 223 patients were included in the post-intervention cohort with 136 non-purulent and 87 purulent (figure1).

The non-purulent cellulitis patient population was predominantly white (77%) males (51%) with a median age of 61 years. The average duration of symptoms was 4 day prior to presentation. The purulent cellulitis population was also predominantly white (59%) males (57%) with a median age of 39 years. The average duration of symptoms was 4 days prior to presentation. In each group approximately 40% of patients received antibiotics as an outpatient prior to presenting to the hospital (table 1).

Primary and Secondary Endpoints

For uncomplicated cellulitis, treatment with vancomycin decreased significantly, from 92.9% [95%CI 88.8-96.9] in the pre-intervention group to 80.1% [95%CI 73.4-86.9] in the post intervention group. For patients with abscess, vancomycin use did not change (86.7% [95%CI 80.2-93.2] v 87.4% [95%CI 80.4-94.3]) (table 2).

For both uncomplicated cellulitis and abscess, treatment with broad spectrum antibiotics decreased significantly. In the cellulitis group, the use decreased from 43.5% [95%CI 35.7-51.3] in the pre-intervention group to 25.7% [95%CI 18.4-33.1] in the post intervention group. In the group of patients with abscess, the use decreased from 46.7% [95%CI 37.1-56.2] to 25.3 [95%CI 16.2-34.4] (table 2).

Safety Endpoints

There were no differences in clinical failure, which consisted of 30-day rehospitalization, treatment failure and recurrence. Rates of nephrotoxicity, infusion related reaction and phlebitis remained low in all groups (table 2).

Impact

Following provider education and implementation of a guideline for the treatment of uncomplicated non-purulent cellulitis and cutaneous abscess, we were able to show a significant decrease in 1) vancomycin use for non-purulent cellulitis and 2) broad-spectrum antibiotic use for both non-purulent cellulitis and cutaneous abscess. Despite less use of these broad-spectrum antibiotics, there were not increases in recurrence, readmissions or adverse effects. This is important to patient care because it exposes fewer patients to unnecessary broad-spectrum antibiotics and the potential risks associated with these: nephrotoxicity, phlebitis, *C.difficile* infection and increased antibiotic resistance.

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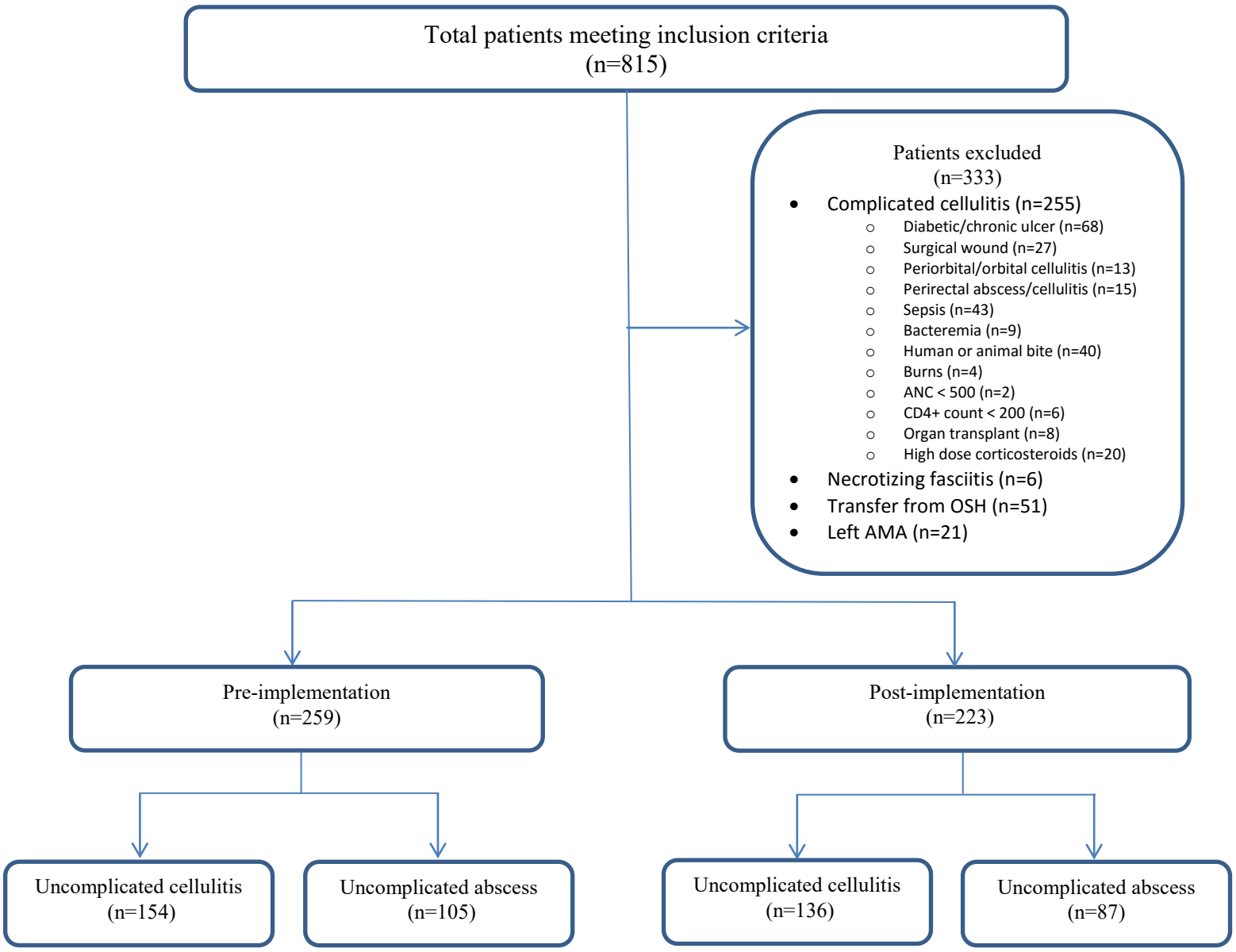

Figure 1. Patient Flow Diagram. Once patient met one exclusion criteria they were not evaluated for fulfillment of additional exclusion criteria.

	Overall n=482	Pre n=259; 53.7%	Post n=223; 46.3%	No Abscess n=290; 60.2%	Abscess n=192; 39.8%
Age					
Mean(sd)	53.9 (20.9)	53.2 (19.1)	54.7 (20.9)	62.0 (17.9)	41.6 (16.2)
Median (range)	53 (18-98)	53 (18-94)	55 (18-98)	61 (18-98)	38.5 (18-91)
Race					
White	336 (69.7)	175 (67.6)	161 (72.2)	223 (76.9)	113 (58.9)
Hispanic	104 (21.6)	58 (22.4)	46 (20.6)	47 (16.2)	57 (29.7)
Black	34 (7.1)	20 (7.7)	14 (6.3)	17 (5.9)	17 (8.9)
Unknown	8 (1.7)	6 (2.3)	2 (0.9)	3 (1.0)	5 (2.6)
Female	223 (46.3)	118 (45.6)	105 (47.1)	141 (48.6)	82 (42.7)
Comorbidities					
BMI >=30	249 (51.7)	141 (54.4)	108 (48.4)	168 (57.9)	81 (42.2)
Cirrhosis	13 (2.7)	8 (3.1)	5 (2.2)	10 (3.5)	3 (1.6)
Diabetes Mellitus	151 (31.3)	83 (32.0)	68 (30.5)	103 (35.5)	48 (25.0)
Hemodialysis	5 (1.0)	1 (0.4)	4 (1.8)	5 (1.7)	0
HIV	6 (1.2)	4 (1.5)	2 (0.9)	1 (0.3)	5 (2.6)
IV Drug Use	48 (10.0)	19 (7.3)	29 (13.0)	6 (2.1)	42 (21.9)
MRSA	43 (8.9)	23 (8.9)	20 (9.0)	20 (6.9)	23 (12.0)
Prior SSTI	134 (27.8)	72 (27.8)	62 (27.8)	91 (31.4)	43 (22.4)
Primary Diagnosis					
Finger and Toe (681.x)	24 (5.0)	12 (4.6)	12 (5.4)	4 (1.4)	20 (10.4)
Other (682.x)	457 (94.8)	247 (95.4)	210 (94.2)	286 (98.6)	171 (89.1)
Erysipelas (0.35)	1 (0.2)	0	1 (0.5)	0	1 (0.5)
Primary Location					
Upper Extremity	109 (22.6)	59 (22.8)	50 (22.4)	28 (9.7)	81 (42.2)
Lower Extremity	297 (61.6)	155 (59.9)	142 (63.7)	238 (82.1)	59 (30.7)
Trunk	24 (5.0)	13 (5.0)	11 (4.9)	8 (2.8)	16 (8.3)
Groin/Buttock	11 (2.3)	8 (3.1)	3 (1.4)	3 (1.0)	8 (4.2)
Face, Head, Neck	30 (6.2)	17 (6.6)	13 (5.8)	10 (3.5)	20 (10.4)
Multiple	11 (2.3)	7 (2.7)	4 (1.8)	3 (1.0)	8 (4.2)
Duration of Symptoms prior to presentation (days)					
Mean(sd)	5.7 (5.8)	5.9 (6.3)	5.5 (5.1)	5.9 (6.0)	5.4 (5.4)
Median (range)	4 (0-50)	4 (0-50)	4 (0-30)	4 (0-45)	4 (0-50)
Prior Outpatient Therapy	200 (41.5)	117 (45.2)	83 (37.2)	121 (41.7)	79 (41.2)
Duration of Prior Outpatient Therapy (days)					
Mean(sd)	4.5 (4.0)	4.8 (4.5)	4.0 (3.1)	5.0 (4.5)	3.7 (2.8)
Median (range)	3 (1-33)	3 (1-33)	3 (1-14)	3.5 (1-33)	3 (1-14)
Fever at Presentation	40 (8.3)	18 (7.0)	22 (9.9)	28 (9.7)	12 (6.3)
Leukocytosis at Presentation	213 (44.2)	116 (44.8)	97 (43.5)	107 (36.9)	106 (55.2)

Table 2. Baseline characteristics.

		Pre (n=259; 53.7%)		Post (n=223; 46.3%)		p-value
	Overall	No Abscess	Abscess	No Abscess	Abscess	
Vancomycin Use: (%)	419 (86.9)	92.9 (88.8 – 96.9)	86.7 (80.2-93.2)	80.1 (73.4-86.9)	87.4 (80.4-94.3)	0.032*
Broad Spectrum Antibiotic Use: (%)	173 (86.9)	43.5 (35.7-51.3)	46.7 (37.1-56.2)	25.7 (18.4-33.1)	25.3 (16.2-34.4)	0.709*
Incision and Drainage: n(%)* **	161 (33.4)	0	89 (84.8)	2 (1.5)	70 (80.5)	0.709*
Adverse Events: (%)	42 (8.7)	n=12 7.8 (3.6-12.0)	n=7 6.7 (1.9-11.4)	n=10 7.4 (3.0-11.7)	n=13 14.9 (7.5-22.4)	0.148*
Nephrotoxicity* **	13 (2.7)	2 (1.3)	4 (3.8)	4 (3.0)	3 (3.5)	--
Infusion Related Reactions* **	25 (5.2)	7 (4.6)	3 (2.9)	5 (3.7)	10 (11.5)	--
Phlebitis* **	8 (1.7)	3 (2.0)	1 (1.0)	4 (3.0)	0	--
Clinical Failure: n(%)* **	8 (1.7)	2 (1.3)	1 (1.0)	4 (3.0)	1 (1.2)	0.700*
Recurrence: n(%)* **	28 (5.8)	12 (7.8)	3 (2.9)	12 (8.8)	1 (1.2)	0.391*
30 Day Re-hospitalization* **	39 (8.1)	16 (10.4)	1 (1.0)	19 (14.2)	3 (3.5)	0.432*
Duration from D/C to Readmission (n=39)* ** **Mean(sd)** **Median (range)**	14.0 (8.7) 10.9 (2.1-28.4)	17.0 (9.0) 21.2 (3.1-27.7)	13.1 (-) -	12.1 (8.4) 10.1 (2.1-28.4)	6.0 - 10.5 -	-
Duration of IV Therapy **Mean(sd)** **Median (range)**	3.1 (2.0) 2.6 (0-16.7)	3.2 (2.9-3.5)	3.0 (2.6-3.4)	3.1 (2.7-3.4)	2.8 (2.4-3.2)	0.809**
Duration of Antimicrobial Therapy **Mean(sd)** **Median (range)**	10.0 (3.1) 10 (0-20.4)	9.9 (9.4-10.3)	10.8 (10.3-11.4)	9.3 (8.8-9.8)	10.5 (9.9-11.2)	0.636**
Length of Stay (days) **Mean(sd)** **Median (range)**	3.7 (2.1) 3.2 (0.5-16.6)	3.9 (3.6-4.3)	3.5 (3.1-3.9)	3.9 (3.5-4.2)	3.3 (2.8-3.7)	0.737**

Table 2. Outcomes (95% CI) over time
**Interaction term from logistic regression model*
***Interaction term from linear regression model*
**** Zero cell and/or limited events, therefore numbers and percentages are presented*

	Pre-Post Change			
	No Abscess	p-value	Abscess	p-value
Vancomycin Use: (%)	-12.7 (-21.7 to -3.7)	0.002	0.7 (-10.2 to 11.6)	0.887
Broad Spectrum Antibiotic Use: (%)	-17.8 (-30.1 to -5.5)	0.001	-21.4 (-36.5 to -6.3)	0.002
Adverse Events: (%)	-0.4 (-7.4 to 6.5)	0.887	8.3 (-1.9 to 18.4)	0.068
Mean Duration of IV Therapy (Days):	-0.12 (-0.64 to 0.40)	0.596	-0.21 (-0.85 to 0.43)	0.458
Mean Duration of Antimicrobial Therapy (Days):	-0.59 (-1.40 to 0.22)	0.102	-0.32 (-1.31 to 0.68)	0.471
Mean Length of Stay (Days)	-0.05 (-0.61 to 0.50)	0.831	-0.18 (-0.87 to 0.50)	0.545

Table 3. Differences (95% CI) over time