

**UNDERSTANDING RISK FACTORS FOR *CLOSTRIDIUM DIFFICILE* INFECTION ACROSS A FIVE
HOSPITAL HEALTH SYSTEM IN THE BALTIMORE/WASHINGTON DC AREA**

by

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ABSTRACT

Statement of Problem – The objective of this study is to understand conditional risk factors for *Clostridium difficile* infection (CDI) over time and between hospitals

Methods – Retrospective cohort of patients admitted to five adult hospitals in the Baltimore/Washington DC area in calendar year 2016 and 2017. International Statistical Classification of Diseases and Related Health Problems (ICD) 10 codes, the Premier’s CareScience™ Mortality Risk Score, room and clinical data were obtained through Premier CareScience reports and EPIC electronic medical record reports. Days of therapy (DOT) for antibiotics, probiotic supplementation and proton pump inhibitor use (PPI) were cumulative through each day of hospitalization. Colonization pressure was calculated as days of exposure multiplied by the number of patients with CDI in a unit that month. A multivariable logistic regression was performed for each day of admission separately and for each hospital.

Results – There were 1922 (1.0%) cases of CDI among 192,522 patients. The Premier’s CareScience™ Mortality Risk Score expected mortality score was the greatest contributor to risk of CDI particularly in the first 5 days of hospitalization. Probiotic supplementation exposure was a significant risk factor in the first (OR 2.67) and third day (OR 1.46) of the hospital course. ICU exposure was protective with 37-33% lower odds of CDI on day 1 and 2 but by day 8 and 11 became a significant risk factor for CDI (OR 1.15, OR 1.12). Colonization pressure risk decreased over time, but remained significant for the first 8 days of admission (OR 1.19-OR 1.03). Carbapenem, penicillin, cephalosporin, quinolone and other antibiotic use was a risk factor for CDI however the conditional risk decreased over time. Clindamycin was protective in our cohort.

The Premier’s CareScience™ Mortality Risk Score was the greatest predictor for CDI in 4/5 hospitals (OR 6-30). Colonization pressure was a significant risk factor for CDI in three hospitals. Carbapenem use was a risk factor in two hospitals and cephalosporin use was only a risk factor in one hospital.

Conclusions – Risk factors for CDI vary over time and by hospital and interventions to prevent CDI need to be tailored by hospital and time to be effective.

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BACKGROUND/INTRODUCTION

***Clostridium difficile* epidemiology and burden of disease**

Clostridium difficile is the most common healthcare-associated infection complicating 1% of all hospital admissions and accounting for 30,000 deaths in the US annually ^{1 2 3}. *Clostridium difficile* infection (CDI) occurs through a complex pathophysiology which includes environmental exposure and microbiome disruption through antibiotic use ^{4 5}. Host factors such as comorbid conditions and advanced age, also play a role in the risk for infection ^{4 5}. Up to 80% of these infections may be preventable, however our understanding of the relative importance of various risk factors over time in the development of infection is limited ⁶.

Risk factors

Antibiotic exposures

Antibiotic exposure is a known risk factor for CDI.

Different classes of antibiotic have different risks of colonization and infection with *Clostridium difficile*. The most strongly associated classes of antibiotics include second, third and fourth generation cephalosporins, clindamycin, carbapenems, trimethoprim/sulphamethoxazole, fluoroquinolones and penicillin combinations ⁷. Unfortunately, most of these data are limited in that only two studies attempted to match or adjust for patient severity of illness, and only a few matched for time at risk and there was considerable heterogeneity in the patient populations studied ^{7 8}. None of the studies adequately address time varying exposures ⁷. In evaluating only randomized controlled trials, where confounding by patient severity would be minimized, carbapenem use was associated with a higher rate of CDI compared to fluoroquinolone use and cephalosporin use was associated with a higher rate of CDI than penicillin and fluoroquinolone use. Clindamycin use was associated with a higher rate of CDI compared to cephalosporin and penicillin use primarily in outpatients ⁹. Some antibiotics may be more associated with colonization. Tigecycline and doxycycline appear to be protective for CDI and colonization with *Clostridium difficile* ¹⁰. One study compared patients who received carbapenem vs tigecycline in which every case of hospital onset diarrhea was evaluated for *clostridium difficile* and weekly rectal swabs were performed for carbapenem-resistant Enterobacteriaceae (CRE) and found that patients who received tigecycline were less likely to be colonized with *Clostridium difficile* but equally likely to be colonized with CRE as compared to patients who received

meropenem¹¹. Decreasing antibiotic usage in hospital settings through antimicrobial stewardship should reduce rates of CDI. A recent meta-analysis reviewing studies of antimicrobial stewardship on CDI rates found that there was a 32% reduction in CDI cases with the implementation of an antibiotic stewardship program¹². These results can be variable as several recent single center studies have shown that reducing antibiotic usage did not decrease the rate of hospital onset CDI^{13 14}.

Confounding is a significant concern in studies looking at the association between antibiotics and CDI. Many factors have been associated with CDI including specific antidepressants and histamine antagonists^{15 16}. While some of these medications may have biologic plausibility by causing microbiome disruption, some may simply be confounded correlations,

Environmental exposure and colonization pressure

Colonization with *Clostridium difficile* is necessary for infection to occur.

Four to 15 percent of patients that are admitted to the hospital are already colonized with *Clostridium difficile* and colonized patients have a 6 fold increased risk of developing infection^{17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32}. Since only 0.5% of the community is colonized with *Clostridium difficile* and history of recent hospitalization is more strongly associated with *Clostridium difficile* colonization compared to even previous antibiotic use acquisition most likely occurs in hospital settings^{33 18}. Ten to twenty percent of hospitalized patients become colonized during their hospitalization^{23 19 32,34}

Hospital environments are often colonized with *Clostridium difficile* spores. One gram of stool in a patient with CDI has 100 million spores and patients with active CDI contaminate 20-51% of surfaces in their rooms^{35 36 37 38 39 40 41 42 43,44 45 46 47 19 48}. Most worrisome is that even asymptomatic patients colonize 7-33% of environmental surfaces in their room. There is clinical evidence of transmission in that roommates and previous room occupants who have CDI or have been exposed to antibiotics have been associated with higher rates of CDI^{49 50 51 52 27}. Interestingly, ward level antibiotic prescribing is a risk factor for CDI independent of patient characteristics and individual antibiotic prescriptions⁵³. In studies looking at various risk factors for CDI, exposure to the hospital environment and colonization pressure seem to be the factors with the greatest effect size^{54 13 55}.

Genotype testing with multilocus variable number of tandem repeats analysis (MLVA) and whole genomic sequencing have shown that 6-30% of cases of CDI are associated with asymptomatic carriers ²⁷.

Hospital variation

It is likely that different hospitals have varying risk factors for CDI due to the different populations they serve and facility design and subsequent transmission risk. One study using whole genomic sequencing of *Clostridium difficile* infection found that the percentage of cases that can be attributed to transmission varies between hospitals ⁵⁶

Epidemiologic methods

The majority of studies investigating risk factors for CDI assess overall risk factors for hospitalization and do not incorporate time-varying exposures which are critical in understanding acute exposures and short durations of risk ⁵⁷. Conditional risk refers to the subsequent risk of acquiring an event if you have survived a certain duration without the event. An example of the importance of differentiating overall risk from conditional risk can be seen by comparing overall relapse rates among patients with testicular cancer vs the conditional relapse rate among patients who survived the first two years without a relapse ⁵⁸. This is important for healthcare-associated infections like CDI where one event influences the next event. This type of analysis also allows us to un-confound length of stay with risk for infection.

Objectives

We sought to understand the conditional risk of CDI over time across a health system and to account for clustering through a colonization pressure metric.

APPROACH/METHODS

Population

The population consists of adult patients admitted to one of 5 acute care hospitals within a health system in Maryland and/or Washington DC between January 1, 2016 and December 31, 2017. The hospitals included one quaternary care hospital (1,100 beds), one tertiary care hospital (426 beds) and three community hospitals (220-320 beds). All five hospitals have medicine and surgical beds and the two academic hospitals have specialty units including neurocritical care, oncology, burn intensive care units and transplant units.

Study design

We performed a retrospective cohort study of all adult inpatients admitted in five hospitals within a health system

Clinical care

The clinical care of patients are similar among all five hospitals. All five hospitals have the same antibiotic formulary and all have antibiotic stewardship teams to minimize unnecessary antibiotic usage. Probiotic prescriptions were left to the discretion of the clinician until 2017, when it was no longer prescribed by the health system. One hospital used a protocol to prescribe probiotics on all patients receiving antibiotics for one year of the study period.

Definitions

Antibiotic days, proton pump inhibitor (PPI) days and probiotic days were measured as days of therapy (DOT). For antibiotics, the DOT was calculated for each class of antibiotic separately, thus a patient receiving two different antibiotic classes would be counted separately for each class. Premier's CareScience™ Mortality Risk Score, a proprietary calculated risk adjustment score ranging from 0-1 was obtained through Premier (Premier Healthcare Solutions, Inc, Charlotte, NC) ⁵⁹. Patients were identified as having CDI based on a positive *Clostridium difficile* nucleic acid amplification test (NAAT) documented in the electronic medical record (EMR). Patients were followed until they (a) had a positive *Clostridium difficile* NAAT test, (b) were discharged or (c) were administratively censored at 30 days after the date of admission. Only the first episode of CDI was included. Those who did not experience CDI by the end of follow-up were considered non-cases. Colonization pressure was calculated as number of cases of CDI cases in a particular patient care unit in a month times the number of days the patient spent in that unit. Units were categorized as intensive care units (ICU) or non ICU. These data sets were combined using the hospital admission record number.

Statistical Analysis:

Patient demographics and clinical parameters were compared among those with CDI and those who did not develop CDI during their hospitalization using Chi-square or two-sample t test as appropriate. We reported means with standard deviation for continuous variables and frequencies for categorical variables. We performed an overall multivariable logistic regression using variables known to be risks for CDI. In order to better understand the conditional risk of infection, we analyzed risk factors for CDI by day of admission separately for each day, 1-14, of

hospitalizations. Days of therapy (DOT) for antibiotics, probiotics and PPI were cumulative up until each day of hospitalization. Patients who developed CDI, died or were discharged prior to the day of analysis were excluded from the risk set for the following day. Additionally a separate multivariable logistic regression was performed for each hospital separately.

We report adjusted odds ratio with p values. The analysis was conducted using Stata Version 15.0 (StataCorp, College Station, Texas) statistical software.

RESULTS:

There were 192,522 patients included in the analysis with 1922 (1.0%) cases of CDI. The characteristics of patients with and without CDI are summarized in Table 1. The non-cumulative incidence of infection by day varied from 12/10,000 patients to 27/10,000 patients (Graph 1). Patient age, female sex, Premier CareScience™ Expected Mortality score, probiotic use, ICU stay and carbapenem, cephalosporin, penicillin and other antimicrobial use were higher among patients with CDI. Clindamycin use was lower among patients with CDI.

In the overall multivariable logistic regression, age (OR 1.015 $p<0.0001$), Premier CareScience™ Expected Mortality score (OR 7.158 (OR 1.015 $p<0.0001$), colonization pressure per one person/day unit of exposure (OR 1.010, $p<0.0001$), ICU exposure by day (OR 1.026, $p<0.0001$) and carbapenem use (OR 1.035 $p=0.017$), were associated with increased odds of CDI. Proton pump inhibitor use (0.950, $p<0.0001$), clindamycin use (OR 0.781 $p<0.0001$) and treating facility other than the reference facility was associated with lower odds of CDI (Table 2). The AUR for the overall model was 0.77.

In assessing conditional risk factors over time, the expected mortality score, a surrogate marker for patient's baseline comorbidities and illness, was the greatest contributor to risk of CDI particularly in the first 5 days of hospitalization (Table 3, Graph 2). Probiotic exposure was a significant risk factor in the first (OR 2.67) and third day (OR 1.46) of the hospital course (Table 3, Graph 3). ICU exposure was initially protective with 37-33% lower odds of CDI on day 1 and 2 but by day 8 and 11 became a significant risk factor for CDI (OR 1.15, OR 1.12). Colonization pressure per 1 person/day of exposure decreased over time, but remained a significant risk factor over the first 8 days of admission (OR 1.19-OR 1.03) (Table 3, Graph 4). Carbapenem, penicillin, cephalosporin, quinolone and other antibiotic use was a risk factor for CDI. Interestingly, for these antibiotic classes, the conditional risk decreased over

time (Table 3, Graph 5). Surprisingly, clindamycin, an antibiotic known to increase risk of CDI, was protective in our cohort. Hospital facility was also independently associated with risk of CDI. Hospital 3, a community hospital, was associated with an increased risk of CDI on the first day of admission and then subsequently was associated with a reduced risk for CDI.

Risk factors for hospital onset CDI (CDI diagnosed on or after day 4 or admission) by facility varied by facility. For 4/5 hospitals, the Premier's CareScience™ Mortality Risk Score was the greatest predictor for CDI with an odds ratio between 6 and 29. Colonization pressure was a significant risk factor for CDI in two hospitals. Carbapenem use, a very broad-spectrum class of antibiotic, was only a risk factor in two hospitals and cephalosporin use was only a risk factor in one hospital (Table 4).

Discussion

Our study demonstrates that many of the known risk factors for CDI vary in their relative importance over time and that factors that are important early in hospital stay are not as important later in the hospital course. This was most notable for antibiotic exposure. The impact of carbapenem exposure and quinolone antibiotic exposure as a risk factor for CDI decreased over the first few days of hospitalization, suggesting that not starting antibiotic treatment may be more important than shortening treatment for these antibiotics. Our data is consistent with data from Barnes-Jewish hospital where cephalosporin, quinolone or intravenous vancomycin for less than 7 days was not associated with CDI risk ⁵⁵ Interestingly, clindamycin was protective for CDI in our cohort, which is different from other studies which focused mostly on community-onset CDI ^{60 61 9 62}. In hospitalized patients, clindamycin exposure has been variably associated with development of CDI ^{63 7 64 65}.

Probiotic exposure was a risk factor for CDI early in the hospital course. Proton pump inhibitor (PPI) exposure has been associated with CDI risk in some studies and not associated with CDI in other studies ⁵. In our study PPI exposure was not associated with an increased risk for CDI, except for hospital day 10.

Understanding time-varying exposures and conditional risk is important for focusing interventions where they will have the greatest impact. This is seen in device-associated infections, where the risk of central-line associated bloodstream infections increase over time. While this makes intuitive sense for device-associated infections, where there is an incremental risk of infection based on duration of line placement, this is less well understood for CDI ^{66 67}

^{68 69 70 71}. Most of the previous studies assessing risk factors for CDI look only at the overall composite risk which does not allow for time-varying risks which we have now shown to be important.

Limitations

The limitations of our study are the relatively low number of cases of CDI over time which reduces the power to detect risk factors that may be important later in the hospital course. While we attempted to include a variety of practice settings, there may be regional differences that limit generalizability. We used the Premier CareScience™ Expected Mortality score to adjust for differences in baseline health, however we are not able to adjust for severity of illness during hospitalization.

Public health significance

CDI causes 30,000 deaths annually in the US and hospital-onset CDI increases cost of care by \$1.5 billion dollars a year ⁵. Hospital onset *Clostridium difficile* infection can be prevented in up to 80% of cases according to modeling studies ⁶. Understanding specific risk factors over time in hospitalized patients will enable interventions to reduce the incidence of these infections.

Recommendations/Next steps

Our study highlights the importance of understanding risk factors for CDI over time and between hospitals. Several interesting findings deserve further evaluation. The association of probiotics with CDI particularly early in the hospital course was an unexpected finding. Next steps would be to review a random sample of charts of patients on probiotics to see if these patients had a previous history of CDI that was not captured by testing at JHHS as this may have confounded the association.

While our models had good predictive ability, they were incomplete. The next steps would be to use machine learning methods such as random forest on additional data from the EMR to detect patterns that may better predict CDI, and then include those variables in a deterministic model to develop actionable predictive tools.

Table 1 Characteristics of Patients by *Clostridium difficile* infection

| Factor | CDI = 0 | CDI = 1 | p-value |
|--|----------------|----------------|----------------|
| Total number of patients | 191887 | 1917 | |
| Age, mean (SD) | 53.5 (23.3) | 61.8 (19.5) | <0.001 |
| Gender | | | |
| Male | 82906 (43.2%) | 891 (46.5%) | 0.016 |
| Female | 108980 (56.8%) | 1026 (53.5%) | |
| Mortality | | | |
| Alive | 185213 (98.0%) | 1757 (93.2%) | <0.001 |
| Died | 3771 (2.0%) | 129 (6.8%) | |
| Facility | | | |
| Hospital 1 | 34744 (18.1%) | 166 (8.7%) | <0.001 |
| Hospital 2 | 33862 (17.6%) | 369 (19.2%) | |
| Hospital 3 | 20346 (10.6%) | 134 (7.0%) | |
| Hospital 4 | 24397 (12.7%) | 358 (18.7%) | |
| Hospital 5 | 78538 (40.9%) | 890 (46.4%) | |
| Premier predicted mortality score (0-1) | 0.0 (0.1) | 0.1 (0.2) | <0.001 |
| PPI mean DOT (SD) | 1.7 (3.6) | 1.6 (3.4) | 0.41 |
| Probiotic, mean DOT (SD) | 0.1 (0.9) | 0.1 (0.9) | 0.007 |
| Colonization pressure mean (SD) | 2.1 (6.8) | 3.6 (8.4) | <0.001 |
| ICU stay, mean days (SD) | 0.5 (2.1) | 1.0 (2.8) | <0.001 |
| Antibiotic class DOT | | | |
| Aminoglycoside, mean DOT (SD) | 0.1 (0.6) | 0.1 (0.5) | 0.21 |
| Carbapenem, mean DOT (SD) | 0.2 (1.1) | 0.3 (1.3) | <0.001 |
| Cephalosporin, mean DOT (SD) | 1.1 (2.3) | 1.3 (2.4) | 0.012 |
| Clindamycin, mean DOT (SD) | 0.1 (0.8) | 0.1 (0.4) | <0.001 |
| PCN, mean DOT (SD) | 0.7 (2.3) | 1.1 (2.3) | <0.001 |
| Quinolone, mean DOT (SD) | 0.3 (1.3) | 0.3 (1.1) | 0.21 |
| Other antimicrobials, mean DOT (SD) | 1.6 (4.7) | 2.3 (4.0) | <0.001 |

Graph 1 – Incidence of CDI by Day of Admission

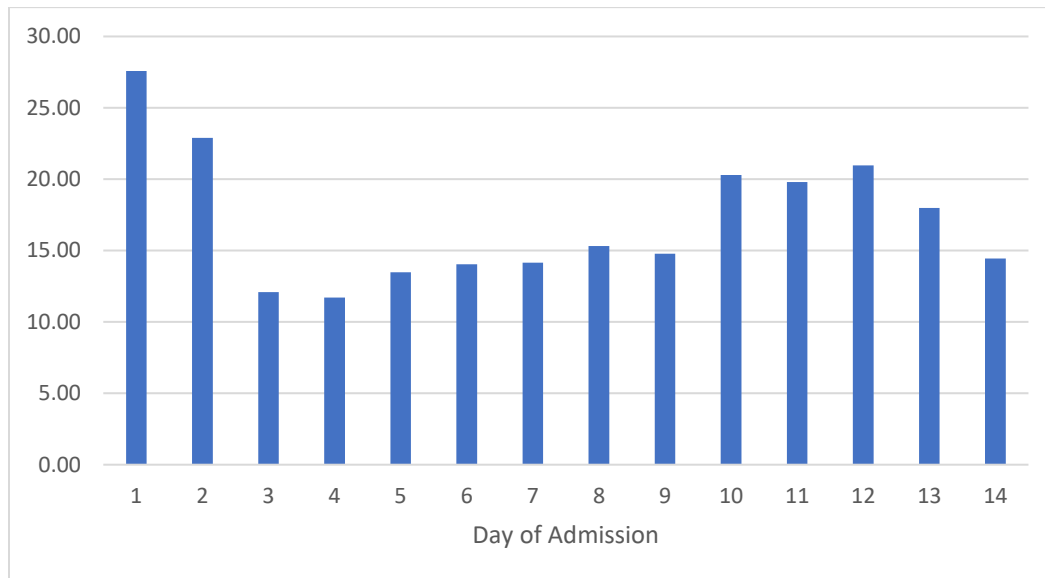


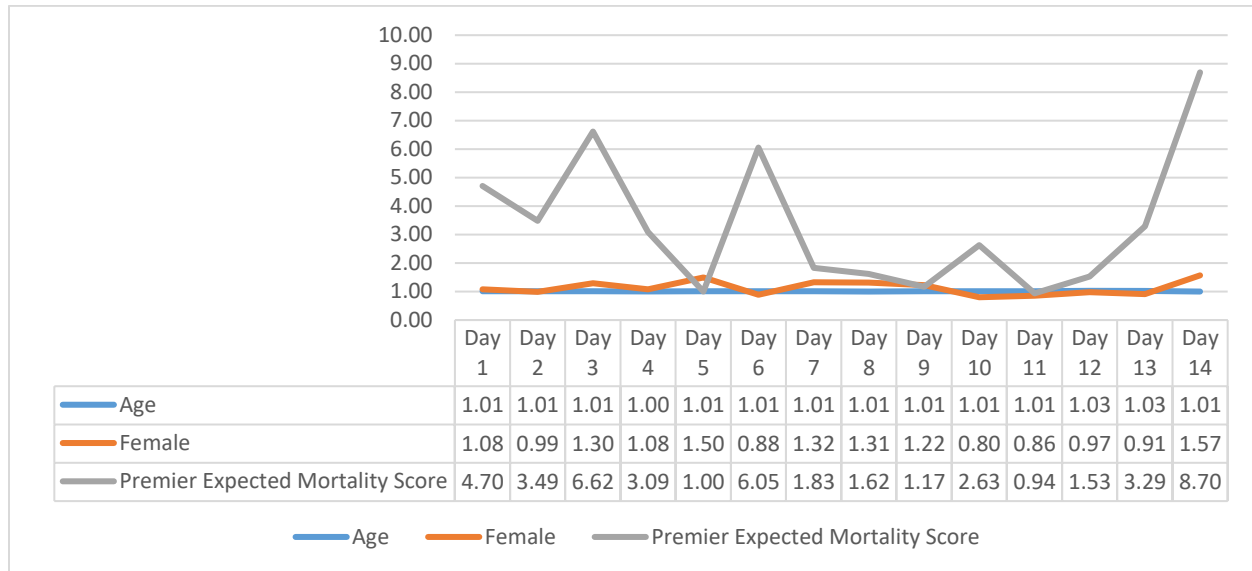
Table 2 – Overall risk factors for *Clostridium difficile* infection – multivariable logistic regression

| Factor | OR | p-value |
|--|--------------|-------------------|
| Age, | 1.015 | 0.000 |
| Gender | | |
| Female | 1.015 | 0.755 |
| Male | (ref) | |
| Facility | | |
| Hospital 1 | (ref) | |
| Hospital 2 | 0.817 | 0.002 |
| Hospital 3 | 0.382 | <0.0001 |
| Hospital 4 | 0.860 | 0.026 |
| Hospital 5 | 0.506 | <0.0001 |
| Premier predicted mortality score (0-1) | 7.158 | <0.0001 |
| PPI DOT | 0.950 | <0.0001 |
| Probiotic, DOT | 1.038 | 0.057 |
| Colonization pressure (1 exposure day) | 1.010 | <0.0001 |
| ICU stay, days | 1.026 | 0.003 |
| Antibiotic class DOT | | |
| Aminoglycoside, DOT | 0.967 | 0.479 |
| Carbapenem, DOT | 1.035 | 0.017 |
| Cephalosporin, DOT | 0.986 | 0.173 |
| Clindamycin, DOT | 0.781 | <0.0001 |
| PCN, DOT | 1.014 | 0.114 |
| Quinolone, DOT | 0.991 | 0.595 |
| Other antimicrobials, DOT | 0.005 | 0.083 |

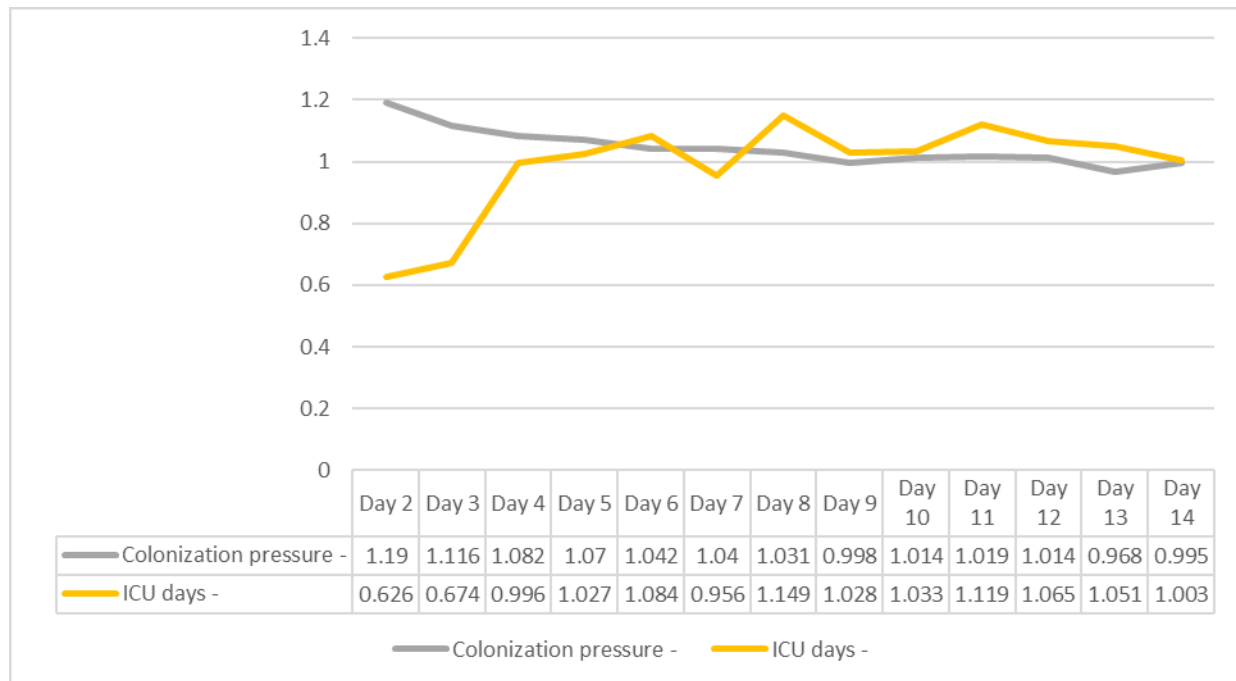
Table 2 Risk factors for CDI by day of admission

| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 |
|--------------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|---------------------|--------------------|--------------------|---------------------|---------------------|
| | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio |
| VARIABLES | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) | (SE) |
| Age | 1.013*** (0.002) | 1.009*** (0.003) | 1.010** (0.004) | 1.003 (0.005) | 1.006 (0.006) | 1.008 (0.007) | 1.014 (0.008) | 1.005 (0.008) | 1.009 (0.010) | 1.010 (0.009) | 1.010 (0.010) | 1.026** (0.012) | 1.025 (0.015) | 1.005 (0.015) |
| Female | 1.078 (0.097) | 0.987 (0.098) | 1.295 (0.195) | 1.079 (0.196) | 1.495** (0.300) | 0.882 (0.199) | 1.324 (0.338) | 1.313 (0.354) | 1.219 (0.388) | 0.799 (0.233) | 0.856 (0.276) | 0.974 (0.334) | 0.912 (0.386) | 1.568 (0.787) |
| Hospital facility | | | | | | | | | | | | | | |
| Hospital 1 | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) | (ref) |
| Hospital 2 | 1.293** (0.165) | 0.808 (0.109) | 0.851 (0.167) | 0.941 (0.241) | 1.196 (0.293) | 0.898 (0.260) | 0.679 (0.276) | 0.822 (0.301) | 1.220 (0.533) | 1.369 (0.551) | 0.923 (0.402) | 0.195** (0.147) | 1.088 (0.605) | 1.079 (0.685) |
| Hospital 3 | 0.782 (0.121) | 0.485*** (0.083) | 0.331*** (0.091) | 0.741 (0.214) | 0.173*** (0.103) | 0.283** (0.151) | 0.460 (0.250) | 0.138 (0.141) | 0.613 (0.389) | 1.419 (0.649) | 0.231 (0.239) | 0.133 (0.138) | 0.228 (0.240) | 0.222 (0.257) |
| Hospital 4 | 2.089*** (0.253) | 0.637*** (0.101) | 0.441*** (0.109) | 0.792 (0.225) | 0.906 (0.270) | 0.427** (0.184) | 1.518 (0.544) | 1.037 (0.426) | 0.869 (0.500) | 1.753 (0.762) | 1.512 (0.682) | 0.472 (0.280) | 0.288 (0.306) | - |
| Hospital 5 | 1.221 (0.190) | 0.499*** (0.102) | 0.347*** (0.112) | 0.463 (0.186) | 0.286** (0.173) | 0.514 (0.293) | 1.067 (0.598) | 1.150 (0.666) | 2.058 (1.203) | 0.420 (0.450) | 0.449 (0.488) | 0.346 (0.310) | - | - |
| Premier Expected Mortality Score | 4.702*** (1.196) | 3.487*** (1.143) | 6.617*** (2.777) | 3.094** (1.753) | 1.001 (0.742) | 6.054*** (3.248) | 1.827 (1.440) | 1.615 (1.144) | 1.171 (1.130) | 2.629 (1.798) | 0.937 (0.785) | 1.533 (1.349) | 3.286 (2.942) | 8.695** (8.290) |
| Proton Pump Inhibitor | - | 0.884 (0.122) | 0.919 (0.096) | 0.911 (0.075) | 1.050 (0.064) | 0.920 (0.054) | 1.022 (0.052) | 1.047 (0.049) | 0.966 (0.048) | 1.079** (0.041) | 0.982 (0.039) | 0.961 (0.038) | 0.967 (0.043) | 0.982 (0.046) |
| Probiotics | - | 2.669*** (0.890) | 1.607 (0.396) | 1.457** (0.245) | 0.889 (0.236) | 1.134 (0.211) | 0.871 (0.178) | 0.946 (0.172) | 0.802 (0.213) | 1.064 (0.122) | 0.986 (0.161) | 1.18 (0.108) | - | 1.399*** (0.113) |
| Colonization pressure | - | 1.190*** (0.023) | 1.116*** (0.024) | 1.082*** (0.020) | 1.070*** (0.015) | 1.042*** (0.017) | 1.040*** (0.015) | 1.031** (0.014) | 0.998 (0.021) | 1.014 (0.014) | 1.019 (0.012) | 1.014 (0.014) | 0.968 (0.030) | 0.995 (0.023) |
| ICU days | - | 0.626*** (0.111) | 0.674*** (0.099) | 0.996 (0.102) | 1.027 (0.083) | 1.084 (0.076) | 0.956 (0.073) | 1.149** (0.063) | 1.028 (0.066) | 1.033 (0.051) | 1.119** (0.050) | 1.065 (0.052) | 1.051 (0.057) | 1.003 (0.062) |
| Aminoglycosides | - | 0.327 (0.232) | 0.265 (0.249) | 1.425 (0.343) | 0.986 (0.300) | 1.092 (0.270) | 1.254 (0.219) | 1.042 (0.244) | 0.862 (0.321) | 1.040 (0.182) | 0.765 (0.313) | 0.678 (0.452) | 0.810 (0.414) | 0.923 (0.262) |
| Carbapenem | - | 2.047*** (0.498) | 1.809*** (0.318) | 1.457*** (0.210) | 1.459*** (0.161) | 1.115 (0.134) | 1.171 (0.115) | 1.140 (0.116) | 1.197** (0.107) | 1.237*** (0.076) | 1.181** (0.081) | 1.044 (0.099) | 0.902 (0.161) | 1.069 (0.111) |
| Cephalosporin | - | 0.835 (0.088) | 1.154 (0.100) | 1.195** (0.089) | 1.149** (0.078) | 1.019 (0.068) | 1.042 (0.066) | 1.055 (0.066) | 1.053 (0.070) | 1.105** (0.055) | 1.096 (0.056) | 1.079 (0.057) | 1.089 (0.065) | 1.083 (0.069) |
| Clindamycin | - | 0.160*** (0.093) | 0.528 (0.198) | 0.426 (0.194) | 0.817 (0.192) | 1.039 (0.166) | 0.558 (0.281) | 1.108 (0.146) | - | 0.956 (0.163) | 0.977 (0.160) | 0.949 (0.179) | - | 1.027 (0.165) |
| Penicillins | - | 1.224 (0.171) | 1.701*** (0.156) | 1.292*** (0.102) | 1.311*** (0.085) | 1.008 (0.072) | 1.045 (0.066) | 1.170*** (0.060) | 1.131** (0.063) | 1.024 (0.054) | 1.030 (0.053) | 1.066 (0.050) | 1.094 (0.056) | 1.049 (0.063) |
| Quinolone | - | 1.662*** (0.297) | 1.502*** (0.230) | 1.488*** (0.166) | 0.919 (0.161) | 1.179 (0.118) | 0.881 (0.132) | 0.927 (0.132) | 0.884 (0.143) | 1.020 (0.094) | 1.035 (0.096) | 1.097 (0.079) | 1.203*** (0.077) | 0.957 (0.125) |
| Other antibiotic | - | 1.889*** (0.131) | 1.127 (0.071) | 1.073 (0.055) | 0.931 (0.049) | 1.023 (0.042) | 1.042 (0.038) | 0.943 (0.042) | 0.988 (0.039) | 0.959 (0.034) | 0.997 (0.030) | 0.981 (0.032) | 0.988 (0.035) | 0.974 (0.038) |
| Cases | 525 | 423 | 187 | 125 | 105 | 81 | 64 | 56 | 41 | 49 | 40 | 35 | 23 | 17 |
| Observations | 179,823 | 175,479 | 146,615 | 106,993 | 77,051 | 57,063 | 44,363 | 35,250 | 26,132 | 23,131 | 19,345 | 16,405 | 12,244 | 10,691 |
| Infection Rate (Per 10,000 Patient D | 29.20 | 24.11 | 12.75 | 11.68 | 13.63 | 14.19 | 14.43 | 15.89 | 15.69 | 21.18 | 20.68 | 21.33 | 18.78 | 15.90 |
| seEform in parentheses | | | | | | | | | | | | | | |
| *** p<0.01, ** p<0.05 | | | | | | | | | | | | | | |

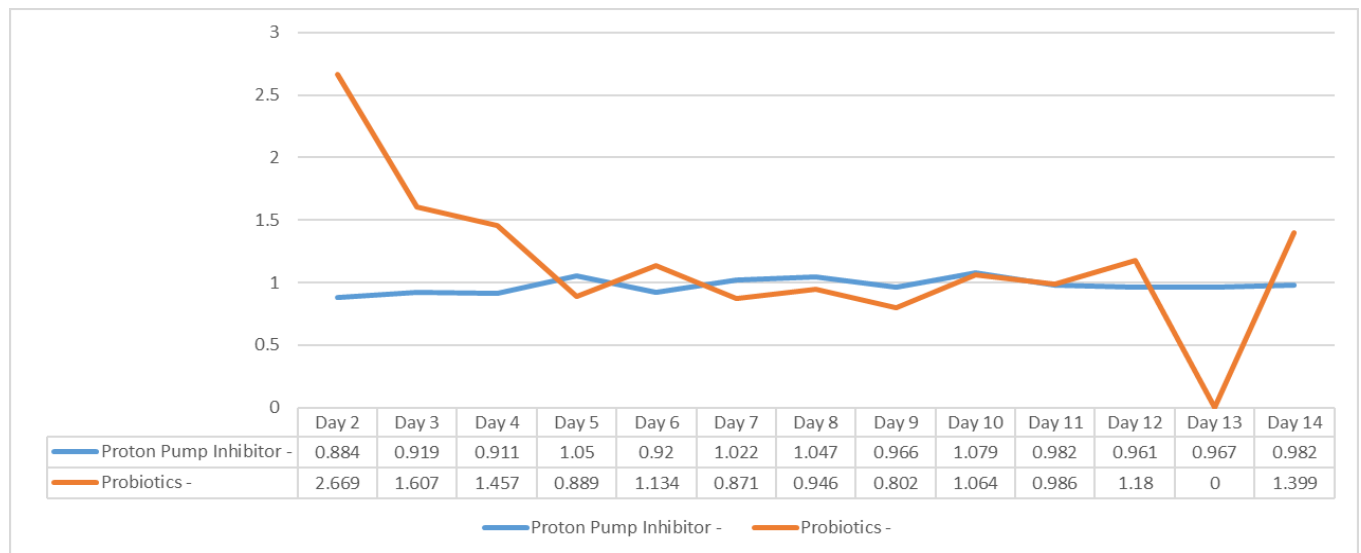
Graph 2 – Patient Characteristics and Association with CDI over time



Graph 3 – Colonization Pressure and ICU days and Association with CDI over time



Graph 4 - Proton Pump Inhibitor use and Probiotic Use and Association with CDI over time



Graph 5 - Antibiotic class and risk of CDI over Time

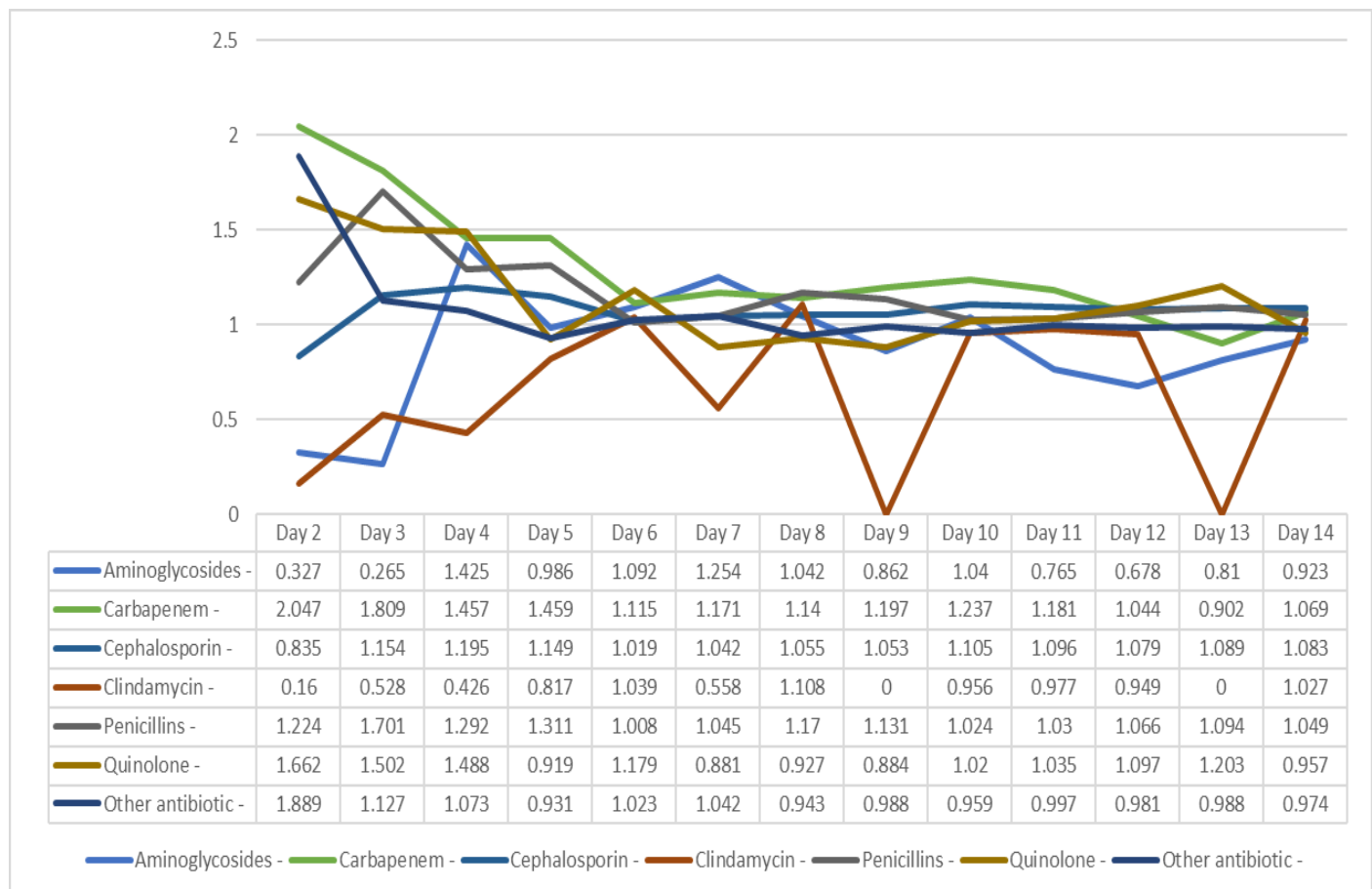


Table 4 – Risk factors for CDI by hospital

| | Day 4 to Day 30 | | | | | |
|------------------------------------|---------------------|---------------------|---------------------|--------------------|----------------------|-----------------------|
| | Overall | Hospital 1 | Hospital 2 | Hospital 3 | Hospital 4 | Hospital 5 |
| VARIABLES | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio | odds ratio |
| Age | 1.009*** (0.002) | 1.012*** (0.003) | 1.005 (0.005) | 1.009 (0.008) | 0.999 (0.006) | 1.029*** (0.011) |
| 1.Female | 0.924 (0.069) | 1.021 (0.104) | 1.074 (0.180) | 1.142 (0.357) | 0.702* (0.135) | 0.394** (0.143) |
| Hospital 1 | ref | | | | | |
| Hospital 2 | 0.855 (0.085) | | | | | |
| Hospital 3 | 0.299*** (0.048) | | | | | |
| Hospital 4 | 0.762** (0.087) | | | | | |
| Hospital 5 | 0.351*** (0.065) | | | | | |
| MortalityExpectedCSStd | 7.726*** (1.416) | 7.193*** (1.918) | 6.680*** (2.468) | 3.940 (3.663) | 13.349*** (5.421) | 29.918*** (33.518) |
| Proton pump inhibitor use | 0.985 (0.008) | 0.983 (0.011) | 0.992 (0.019) | 0.985 (0.044) | 0.995 (0.024) | 0.969 (0.059) |
| Probiotic | 1.062** (0.025) | 1.006 (0.108) | 1.074 (0.074) | 1.048 (0.074) | 1.142*** (0.046) | 0.911 (0.076) |
| Colonization pressure (person/day) | 1.013*** (0.003) | 1.014*** (0.005) | 1.01 (0.006) | 1.035** (0.018) | 1.016** (0.008) | 1.016 (0.031) |
| ICU day | 1.026** (0.011) | 1.008 (0.017) | 1.04 (0.022) | 1.111 (0.066) | 1.031 (0.025) | 0.942 (0.082) |
| Aminoglycoside (per DOT) | 1.012 (0.051) | 0.999 (0.068) | 1.060 (0.095) | 1.131 (0.192) | 0.729 (0.373) | 1.046 (0.364) |
| Carbapenem (per DOT) | 1.054*** (0.019) | 1.027 (0.028) | 1.040 (0.042) | 1.094 (0.087) | 1.096** (0.045) | 1.204** (0.103) |
| Cephalosporin (per DOT) | 1.045*** (0.013) | 1.070*** (0.015) | 0.984 (0.035) | 1.021 (0.073) | 0.969 (0.043) | 1.015 (0.125) |
| Clindamycin (per DOT) | 0.902 (0.065) | 0.822 (0.104) | 0.921 (0.113) | 1.090 (0.307) | 0.889 (0.169) | 1.201 (0.344) |
| Other antibiotic (per DOT) | 0.994 (0.006) | 0.987 (0.008) | 1.016 (0.016) | 0.947 (0.056) | 1.055*** (0.018) | 0.992 (0.055) |
| Penicillin (per DOT) | 1.030** (0.012) | 1.024 (0.015) | 1.043 (0.029) | 1.002 (0.067) | 1.019 (0.032) | 1.144** (0.076) |
| Quinolone (per DOT) | 0.992 (0.023) | 1.019 (0.027) | 0.947 (0.068) | 0.956 (0.116) | 0.900 (0.079) | 0.780 (0.195) |
| Observations | 106,993 | 46,851 | 17,922 | 16,617 | 14,116 | 11,487 |
| seEform in parentheses | | | | | | |
| *** p<0.01, ** p<0.05, | | | | | | |

References

1. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014; **370**(13): 1198-208.
2. Lessa FC, Mu Y, Bamberg WM, et al. Burden of Clostridium difficile infection in the United States. *N Engl J Med* 2015; **372**(9): 825-34.
3. Evans CT, Safdar N. Current Trends in the Epidemiology and Outcomes of Clostridium difficile Infection. *Clin Infect Dis* 2015; **60 Suppl 2**: S66-71.
4. Bartlett JG. Clostridium difficile Infection. *Infect Dis Clin North Am* 2017; **31**(3): 489-95.
5. Leffler DA, Lamont JT. Clostridium difficile infection. *N Engl J Med* 2015; **372**(16): 1539-48.
6. Barker AK, Alagoz O, Safdar N. Interventions to Reduce the Incidence of Hospital-Onset Clostridium difficile Infection: An Agent-Based Modeling Approach to Evaluate Clinical Effectiveness in Adult Acute Care Hospitals. *Clin Infect Dis* 2018; **66**(8): 1192-203.
7. Slimings C, Riley TV. Antibiotics and hospital-acquired Clostridium difficile infection: update of systematic review and meta-analysis. *J Antimicrob Chemother* 2014; **69**(4): 881-91.
8. Brown KA, Fisman DN, Moineddin R, Daneman N. The magnitude and duration of Clostridium difficile infection risk associated with antibiotic therapy: a hospital cohort study. *PLoS One* 2014; **9**(8): e105454.
9. Vardakas KZ, Trigkidis KK, Boukouvala E, Falagas ME. Clostridium difficile infection following systemic antibiotic administration in randomised controlled trials: a systematic review and meta-analysis. *Int J Antimicrob Agents* 2016; **48**(1): 1-10.
10. Doernberg SB, Winston LG, Deck DH, Chambers HF. Does doxycycline protect against development of Clostridium difficile infection? *Clin Infect Dis* 2012; **55**(5): 615-20.
11. Bartoletti M, Tedeschi S, Pascale R, et al. Differences in the rate of carbapenem-resistant Enterobacteriaceae colonisation or Clostridium difficile infection following frontline treatment with tigecycline vs. meropenem for intra-abdominal infections. *Int J Antimicrob Agents* 2018; **51**(3): 516-21.
12. Baur D, Gladstone BP, Burkert F, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2017; **17**(9): 990-1001.
13. DiDiodato G, McArthur L. Evaluating the Effectiveness of an Antimicrobial Stewardship Program on Reducing the Incidence Rate of Healthcare-Associated Clostridium difficile Infection: A Non-Randomized, Stepped Wedge, Single-Site, Observational Study. *PLoS One* 2016; **11**(6): e0157671.
14. Ostrowsky B, Ruiz R, Brown S, et al. Lessons learned from implementing Clostridium difficile-focused antibiotic stewardship interventions. *Infect Control Hosp Epidemiol* 2014; **35 Suppl 3**: S86-95.
15. Tleyjeh IM, Abdulhak AB, Abdulhak AA, et al. The association between histamine 2 receptor antagonist use and Clostridium difficile infection: a systematic review and meta-analysis. *PLoS One* 2013; **8**(3): e56498.
16. Rogers MA, Greene MT, Young VB, et al. Depression, antidepressant medications, and risk of Clostridium difficile infection. *BMC Med* 2013; **11**: 121.
17. Tschudin-Sutter S, Carroll KC, Tamma PD, et al. Impact of Toxigenic Clostridium difficile Colonization on the Risk of Subsequent C. difficile Infection in Intensive Care Unit Patients. *Infect Control Hosp Epidemiol* 2015; **36**(11): 1324-9.
18. Zacharioudakis IM, Zervou FN, Pliakos EE, Ziakas PD, Mylonakis E. Colonization with toxinogenic C. difficile upon hospital admission, and risk of infection: a systematic review and meta-analysis. *Am J Gastroenterol* 2015; **110**(3): 381-90; quiz 91.
19. McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of Clostridium difficile infection. *N Engl J Med* 1989; **320**(4): 204-10.

20. Lin HJ, Hung YP, Liu HC, et al. Risk factors for Clostridium difficile-associated diarrhea among hospitalized adults with fecal toxigenic C. difficile colonization. *J Microbiol Immunol Infect* 2015; **48**(2): 183-9.
21. Truong C, Schroeder LF, Gaur R, et al. Clostridium difficile rates in asymptomatic and symptomatic hospitalized patients using nucleic acid testing. *Diagn Microbiol Infect Dis* 2017; **87**(4): 365-70.
22. Blixt T, Gradel KO, Homann C, et al. Asymptomatic Carriers Contribute to Nosocomial Clostridium difficile Infection: A Cohort Study of 4508 Patients. *Gastroenterology* 2017; **152**(5): 1031-41 e2.
23. Clabots CR, Johnson S, Olson MM, Peterson LR, Gerding DN. Acquisition of Clostridium difficile by hospitalized patients: evidence for colonized new admissions as a source of infection. *J Infect Dis* 1992; **166**(3): 561-7.
24. Samore MH, DeGirolami PC, Tlucko A, Lichtenberg DA, Melvin ZA, Karchmer AW. Clostridium difficile colonization and diarrhea at a tertiary care hospital. *Clin Infect Dis* 1994; **18**(2): 181-7.
25. Alasmari F, Seiler SM, Hink T, Burnham CA, Dubberke ER. Prevalence and risk factors for asymptomatic Clostridium difficile carriage. *Clin Infect Dis* 2014; **59**(2): 216-22.
26. Brazier JS, Fitzgerald TC, Hosein I, et al. Screening for carriage and nosocomial acquisition of Clostridium difficile by culture: a study of 284 admissions of elderly patients to six general hospitals in Wales. *J Hosp Infect* 1999; **43**(4): 317-9.
27. Curry SR, Muto CA, Schlackman JL, et al. Use of multilocus variable number of tandem repeats analysis genotyping to determine the role of asymptomatic carriers in Clostridium difficile transmission. *Clin Infect Dis* 2013; **57**(8): 1094-102.
28. Eyre DW, Griffiths D, Vaughan A, et al. Asymptomatic Clostridium difficile colonisation and onward transmission. *PLoS One* 2013; **8**(11): e78445.
29. Gerding DN, Olson MM, Peterson LR, et al. Clostridium difficile-associated diarrhea and colitis in adults. A prospective case-controlled epidemiologic study. *Arch Intern Med* 1986; **146**(1): 95-100.
30. Guerrero DM, Becker JC, Eckstein EC, et al. Asymptomatic carriage of toxigenic Clostridium difficile by hospitalized patients. *J Hosp Infect* 2013; **85**(2): 155-8.
31. Hung YP, Tsai PJ, Hung KH, et al. Impact of toxigenic Clostridium difficile colonization and infection among hospitalized adults at a district hospital in southern Taiwan. *PLoS One* 2012; **7**(8): e42415.
32. Johnson S, Clabots CR, Linn FV, Olson MM, Peterson LR, Gerding DN. Nosocomial Clostridium difficile colonisation and disease. *Lancet* 1990; **336**(8707): 97-100.
33. Manzoor SE, McNulty CAM, Nakiboneka-Ssenabulya D, Lecky DM, Hardy KJ, Hawkey PM. Investigation of community carriage rates of Clostridium difficile and Hungatella hathewayi in healthy volunteers from four regions of England. *J Hosp Infect* 2017; **97**(2): 153-5.
34. Kyne L, Warny M, Qamar A, Kelly CP. Asymptomatic carriage of Clostridium difficile and serum levels of IgG antibody against toxin A. *N Engl J Med* 2000; **342**(6): 390-7.
35. Dubberke ER, Reske KA, Noble-Wang J, et al. Prevalence of Clostridium difficile environmental contamination and strain variability in multiple health care facilities. *Am J Infect Control* 2007; **35**(5): 315-8.
36. Samore MH, Venkataraman L, DeGirolami PC, Arbeit RD, Karchmer AW. Clinical and molecular epidemiology of sporadic and clustered cases of nosocomial Clostridium difficile diarrhea. *Am J Med* 1996; **100**(1): 32-40.
37. Dumford DM, 3rd, Nerandzic MM, Eckstein BC, Donskey CJ. What is on that keyboard? Detecting hidden environmental reservoirs of Clostridium difficile during an outbreak associated with North American pulsed-field gel electrophoresis type 1 strains. *Am J Infect Control* 2009; **37**(1): 15-9.

38. Shapey S, Machin K, Levi K, Boswell TC. Activity of a dry mist hydrogen peroxide system against environmental *Clostridium difficile* contamination in elderly care wards. *J Hosp Infect* 2008; **70**(2): 136-41.
39. Bender BS, Bennett R, Laughon BE, et al. Is *Clostridium difficile* endemic in chronic-care facilities? *Lancet* 1986; **2**(8497): 11-3.
40. Riggs MM, Sethi AK, Zabarsky TF, Eckstein EC, Jump RL, Donskey CJ. Asymptomatic carriers are a potential source for transmission of epidemic and nonepidemic *Clostridium difficile* strains among long-term care facility residents. *Clin Infect Dis* 2007; **45**(8): 992-8.
41. Jinno S, Kundrapu S, Guerrero DM, Jury LA, Nerandzic MM, Donskey CJ. Potential for transmission of *Clostridium difficile* by asymptomatic acute care patients and long-term care facility residents with prior *C. difficile* infection. *Infect Control Hosp Epidemiol* 2012; **33**(6): 638-9.
42. Eckstein BC, Adams DA, Eckstein EC, et al. Reduction of *Clostridium Difficile* and vancomycin-resistant *Enterococcus* contamination of environmental surfaces after an intervention to improve cleaning methods. *BMC Infect Dis* 2007; **7**: 61.
43. Wilcox MH, Fawley WN, Wigglesworth N, Parnell P, Verity P, Freeman J. Comparison of the effect of detergent versus hypochlorite cleaning on environmental contamination and incidence of *Clostridium difficile* infection. *Journal of Hospital Infection* 2003; **54**(2): 109-14.
44. Barbut F, Menuet D, Verachten M, Girou E. Comparison of the efficacy of a hydrogen peroxide dry-mist disinfection system and sodium hypochlorite solution for eradication of *Clostridium difficile* spores. *Infect Control Hosp Epidemiol* 2009; **30**(6): 507-14.
45. Verity P, Wilcox MH, Fawley W, Parnell P. Prospective evaluation of environmental contamination by *Clostridium difficile* in isolation side rooms. *J Hosp Infect* 2001; **49**(3): 204-9.
46. Varki NM, Aquino TI. Isolation of *Clostridium difficile* from hospitalized patients without antibiotic-associated diarrhea or colitis. *J Clin Microbiol* 1982; **16**(4): 659-62.
47. Kundrapu S, Sunkesula V, Jury LA, Sitzlar BM, Donskey CJ. Daily disinfection of high-touch surfaces in isolation rooms to reduce contamination of healthcare workers' hands. *Infect Control Hosp Epidemiol* 2012; **33**(10): 1039-42.
48. Kaatz GW, Gitlin SD, Schaberg DR, et al. Acquisition of *Clostridium difficile* from the hospital environment. *Am J Epidemiol* 1988; **127**(6): 1289-94.
49. Widmer AF, Frei R, Erb S, et al. Transmissibility of *Clostridium difficile* Without Contact Isolation: Results From a Prospective Observational Study With 451 Patients. *Clin Infect Dis* 2017; **64**(4): 393-400.
50. Freedberg DE, Salmasian H, Cohen B, Abrams JA, Larson EL. Receipt of Antibiotics in Hospitalized Patients and Risk for *Clostridium difficile* Infection in Subsequent Patients Who Occupy the Same Bed. *JAMA Intern Med* 2016; **176**(12): 1801-8.
51. Shaughnessy MK, Micielli RL, DePestel DD, et al. Evaluation of hospital room assignment and acquisition of *Clostridium difficile* infection. *Infect Control Hosp Epidemiol* 2011; **32**(3): 201-6.
52. Echaiz JF, Veras L, Zervos M, Dubberke E, Johnson L. Hospital roommates and development of health care-onset *Clostridium difficile* infection. *Am J Infect Control* 2014; **42**(10): 1109-11.
53. Brown K, Valenta K, Fisman D, Simor A, Daneman N. Hospital ward antibiotic prescribing and the risks of *Clostridium difficile* infection. *JAMA Intern Med* 2015; **175**(4): 626-33.
54. Dubberke ER, Yan Y, Reske KA, et al. Development and validation of a *Clostridium difficile* infection risk prediction model. *Infect Control Hosp Epidemiol* 2011; **32**(4): 360-6.
55. Dubberke ER, Reske KA, Yan Y, Olsen MA, McDonald LC, Fraser VJ. *Clostridium difficile*--associated disease in a setting of endemicity: identification of novel risk factors. *Clin Infect Dis* 2007; **45**(12): 1543-9.
56. Eyre DW, Fawley WN, Rajgopal A, et al. Comparison of Control of *Clostridium difficile* Infection in Six English Hospitals Using Whole-Genome Sequencing. *Clin Infect Dis* 2017; **65**(3): 433-41.

57. Brown KA, Daneman N, Stevens VW, et al. Integrating Time-Varying and Ecological Exposures into Multivariate Analyses of Hospital-Acquired Infection Risk Factors: A Review and Demonstration. *Infect Control Hosp Epidemiol* 2016; **37**(4): 411-9.
58. Nayan M, Jewett MA, Hosni A, et al. Conditional Risk of Relapse in Surveillance for Clinical Stage I Testicular Cancer. *European urology* 2017; **71**(1): 120-7.
59. Kroch E, Duan M. CareScience Risk Assessment Model: Hospital Performance Measurement. *Mortality Measurement* 2008.
60. Brown KA, Khanafer N, Daneman N, Fisman DN. Meta-analysis of antibiotics and the risk of community-associated *Clostridium difficile* infection. *Antimicrob Agents Chemother* 2013; **57**(5): 2326-32.
61. Deshpande A, Pasupuleti V, Thota P, et al. Community-associated *Clostridium difficile* infection and antibiotics: a meta-analysis. *J Antimicrob Chemother* 2013; **68**(9): 1951-61.
62. Kavanagh K, Pan J, Marwick C, et al. Cumulative and temporal associations between antimicrobial prescribing and community-associated *Clostridium difficile* infection: population-based case-control study using administrative data. *J Antimicrob Chemother* 2017; **72**(4): 1193-201.
63. Pakyz AL, Jawahar R, Wang Q, Harpe SE. Medication risk factors associated with healthcare-associated *Clostridium difficile* infection: a multilevel model case-control study among 64 US academic medical centres. *J Antimicrob Chemother* 2014; **69**(4): 1127-31.
64. Stevens V, Dumyati G, Fine LS, Fisher SG, van Wijngaarden E. Cumulative antibiotic exposures over time and the risk of *Clostridium difficile* infection. *Clin Infect Dis* 2011; **53**(1): 42-8.
65. Baxter R, Ray GT, Fireman BH. Case-control study of antibiotic use and subsequent *Clostridium difficile*-associated diarrhea in hospitalized patients. *Infect Control Hosp Epidemiol* 2008; **29**(1): 44-50.
66. Greenberg RG, Cochran KM, Smith PB, et al. Effect of Catheter Dwell Time on Risk of Central Line-Associated Bloodstream Infection in Infants. *Pediatrics* 2015; **136**(6): 1080-6.
67. McLaws ML, Burrell AR. Zero risk for central line-associated bloodstream infection: are we there yet? *Crit Care Med* 2012; **40**(2): 388-93.
68. McLaws ML, Berry G. Nonuniform risk of bloodstream infection with increasing central venous catheter-days. *Infect Control Hosp Epidemiol* 2005; **26**(8): 715-9.
69. Milstone AM, Reich NG, Advani S, et al. Catheter dwell time and CLABSIs in neonates with PICCs: a multicenter cohort study. *Pediatrics* 2013; **132**(6): e1609-15.
70. Milstone AM, Sengupta A. Do prolonged peripherally inserted central venous catheter dwell times increase the risk of bloodstream infection? *Infect Control Hosp Epidemiol* 2010; **31**(11): 1184-7.
71. Raad I, Umphrey J, Khan A, Truett LJ, Bodey GP. The duration of placement as a predictor of peripheral and pulmonary arterial catheter infections. *J Hosp Infect* 1993; **23**(1): 17-26.

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1. **Sood G**, Nyirjesy P, Weitz MV, Chatwani A. Terconazole cream for non-Candida albicans fungal vaginitis: results of a retrospective analysis. *Infect Dis Obstet Gynecol*. 2000;8(5-6):240-3.
2. **Sood G**, Heath D, Adams K, Radu C, Bauernfeind J, Price LA, Zenilman J. Survey of Central Line-Associated Bloodstream Infection Prevention Practices across American Burn Association-Certified Adult Burn Units. *Infect Control Hosp Epidemiol*. 2013 Apr;34(4):439-40.
3. **Sood G**, Huber K, Dam L, Reidel S. A pilot observational study of hydrogen peroxide and alcohol for disinfection of privacy curtains contaminated by MRSA, VRE and Clostridium difficile. *Jnl of Infect Prev*. 2014 Sep; 15(5): 189–193.
4. Argani C, Notis E, Moseley R, Huber K, Lifchez S, Price LA, Zenilman J, Satin A, Perl TM, **Sood G**. Survey of Cesarean Delivery Infection Prevention Practices Across US Academic Centers. *Infect Control Hosp Epidemiol*. 2015 Jul 20:1-3
5. Yang M, Vleck K, Bellantoni M, **Sood G**. Telephone Survey of Infection-Control and Antibiotic Stewardship Practices in Long-Term Care Facilities in Maryland. *J Am Med Dir Assoc*. 2016 Feb 2. pii: S1525-
6. Al Ghamdi M, Alghamdi KM, Ghandoor Y, Alzahrani A, Salah F, Alsulami A, Bawayan MF, Vaidya D, Perl TM, **Sood G**. Treatment outcomes for patients with Middle Eastern Respiratory Syndrome Coronavirus (MERS CoV) infection at a coronavirus referral center in the Kingdom of Saudi Arabia. *BMC Infect Dis*. 2016 Apr 21;16(1):174.
7. **Sood G**, Huber K, Dam L, Riedel S, Grubb L, Zenilman J, Perl TM, Argani C. Pseudo-outbreak of Penicillium in an outpatient obstetrics and gynecology clinic. *Am J Infect Control*. 2017 May 1;45(5):557-558
8. **Sood G**, Caffrey J, Krout K, Khouri-Stevens Z, Gerold K, Riedel S, McIntyre J, Maragakis LL, Blanding R, Zenilman J, Bennett R, Pronovost P. Use of Implementation Science for a Sustained Reduction of Central-Line-Associated Bloodstream Infections in a High-Volume, Regional Burn Unit. *Infect Control Hosp Epidemiol*. 2017 Sep 13:1-6
9. **Sood G**, Vaidya D, Dam L, Grubb LM, Zenilman J, Krout K, Khouri-Stevens Z, Bennett R, Blanding R, Riedel S, Milner S, Price LA, Perl TM. A polymicrobial fungal outbreak in a regional burn center after Hurricane Sandy. *Am J Infect Control*. 2018 Mar 30 pii: S0196-6553(18)30032-4. doi: 10.1016/j.ajic.2018.01.011. [Epub ahead of print]

Review Articles

1. **Sood G**. Fekete T. Lyme disease vaccine in North America. *J Clin Outcome Management*. 2000;7(7):42-46.

2. **Sood G**, O'Donnell JA. Clinical controversies in Lyme disease. J Clin Outcome Management. 2000;7(7):47-55.
3. Bono, BR, Samuel R. **Sood G**, Suh B. The international traveler and infectious diseases: What physicians should know. JKAMA. 2000;6(1):11-19.
4. O'Donnell, JA. **Sood G**. Arthritis-Dermatitis Syndromes. Hospital Physician Rheumatology Board Review Manual. 2002;6(2):1-12.
5. **Sood G**, Perl TM. Outbreaks in Health Care Settings. Infect Dis Clin North Am 2016 Sep;30(3):661-87.
6. **Sood G**, Parrish N. Outbreaks of nontuberculous mycobacteria. Curr Opin Infect Dis. 2017 Aug;30(4):404-409.
7. **Sood G**, Argani C, Ghanem KG, Perl T, Sheffield JS. Infections complicating cesarean delivery. Curr Opin Infect Dis. 2018 May 29. doi: 10.1097

Case report

1. Milner SM, Fauerbach JA, Hahn A, Price LA, Ware L, Krout K, Panter E, Pharm NK, Pfeiffer J, Nguyen H, **Sood G**, Dhanjani K, McKeon G, Gerold K. Cody. Eplasty. 2015 Aug 6;15:e35. eCollection 2015.

FUNDING

EXTRAMURAL Funding

2015-2018 CDC 1U54CK000447D – Pronovost and Maragakis (PI) Epicenter Grant – Funding for aim 2

2018 CDC 200-2018-96313 - Katz and Gurses (PI/ co-PI)

INTRAMURAL Funding

2017 Armstrong Institute at Bayview safety seed grant

2017 EPIC scholars grant

CLINICAL ACTIVITIES

Certification

Board Certified Internal Medicine recertified 2011

Board Certified Infectious Diseases recertified 2011

Medical, other state/government licensure

2011 – present - Maryland D72242

2001-2011 - Pennsylvania – MD-071691-L

[Clinical \(Service\) Responsibilities](#)

2001-2007 – Infectious Disease inpatient service, Albert Einstein Medical Center attending 52 weeks/year

2007-2011 - Infectious Disease inpatient service, Abington Memorial Hospital, attending 52 weeks/year

2011-2013 - Infectious Disease outpatient clinic, Johns Hopkins Bayview, attending –one 1/2 day a week

2011-present - Infectious Disease inpatient service, Johns Hopkins Bayview, attending - 8-10 weeks/year

EDUCATIONAL ACTIVITIES

[Teaching](#)

[Classroom instruction](#)

2001-2007 - Resident Conferences - Albert Einstein Medical Center -

Antibiotics

Skin and Soft Tissue Infection

Gram Stains

UTI

Line sepsis

2001-2007 – Student lectures - Albert Einstein Medical Center - 2 / week

2007-2009 – Resident lectures - Abington Memorial Hospital -Resident Lectures – one/year

2012-2015 - MPH students - Johns Hopkins School of Public Health– Hospital Epidemiology lecture annually

2016–2017 – Course co-director - Johns Hopkins School of Public Health– Hospital Epidemiology course

[Clinical instruction](#)

2001-2006 - Inpatient medicine service. Attending physician, 4 weeks each year. Albert Einstein Medical Center, Philadelphia, PA – residents, medical students

2001-2007 – Inpatient Infectious disease service. Attending physician. 16-20 weeks each year. Albert Einstein Medical Center, Philadelphia, PA – residents, medical students

2007-2010 – Inpatient Infectious disease service. Attending physician. 16-20 weeks each year. Abington Memorial Hospital, Abington, PA – Infectious Disease fellows

2011-2014 – Outpatient Infectious disease clinic preceptor. Attending physician. Johns Hopkins Bayview Medical Center, Baltimore, MD – Infectious Disease fellows

2011-present – Inpatient Infectious disease service. Attending physician. 6-8 weeks each year. Johns Hopkins Bayview Medical Center, Baltimore, MD - Infectious Disease fellows

[CME instruction](#)

Local

2001 – Grand Rounds Lecturer– “Medical Clinicopathologic conference” - Temple University Hospital, Philadelphia PA

2001 – Grand Rounds Lecturer– “Community-acquired pneumonia” - Northeastern Hospital – Philadelphia, PA

2001 – Grand Rounds Lecturer - “New Anti-Infective Agents” – Department of Emergency Medicine; Temple University Hospital, Philadelphia, PA

2001 – Grand Rounds Lecturer “ENT manifestations of HIV infection” - Department of Ear, Nose and Throat Departmental Grand Rounds; Temple University Hospital, Philadelphia, PA

2002 – Grand Rounds Lecturer “ENT manifestations of HIV infection” - - Ear, Nose and Throat Departmental Grand Rounds; Philadelphia College of Osteopathic Medicine; Philadelphia, PA

2002 –Grand Rounds Lecturer “Infections and the Genitourinary tract”, Section of Urology Grand Rounds; Philadelphia College of Osteopathic Medicine, Philadelphia, PA

2002 – Grand Rounds Lecturer “Metal and Bugs” Albert Einstein Medical Center - Orthopedic Grand Rounds - Local

2004 – Grand Rounds Lecturer – “Treatment for Staphylococcal infections” Department of Pediatrics; Albert Einstein Medical Center, Philadelphia, PA

2013 – Grand Rounds Lecturer “Clostridium difficile” Medicine Grand Rounds Johns Hopkins Bayview Medical Center, Baltimore MD

Regional

2012 Lecturer “Antibiotic stewardship” Maryland Nursing Home Medical Directors

2013 Lecturer “Clostridium difficile in the nursing home” Maryland Nursing Home Medical Directors

National

2011 Lecturer “Antimicrobial Resistance” Infectious Diseases for the Primary Care Physician, Johns Hopkins University, Baltimore MD

2012 Lecturer “Upper Respiratory Infections” Infectious Diseases for the Primary Care Physician, Johns Hopkins University, Baltimore MD

2015 Lecturer “The Latest and Greatest on Immunizations for Seniors” Edmund G. Beacham Current Topics in Geriatrics - National

2015 Lecturer “Cleaning, Disinfection and Contact precautions – the Essentials of Infection Control” Society for Healthcare Epidemiology of America (SHEA) fellows course – National

2015 Lecturer “Saturday Night with the Pager” Society for Healthcare Epidemiology of America (SHEA) fellows course - National

2016 Lecturer “Outbreak Investigation” S Society for Healthcare Epidemiology of America (SHEA) fellows course – National

2016 Lecturer “Saturday Night with the Pager” Society for Healthcare Epidemiology of America (SHEA) fellows course – National

2018 Moderator - Society for Healthcare Epidemiology of America (SHEA) Annual meeting

2018 Lecturer “*Clostridium difficile* Infection”; Division of Infectious Diseases, Duke University, Durham, NC

International

2015 Lecturer and curriculum development “Hospital Epidemiology Summer Course” Tel Aviv University
2015 - International

Mentoring

Pre-doctoral Advisees /Mentees

2012 Alexandra Thomas, MPH, capstone Advisor - Infectious Disease Society of America abstract
2015-2017 Morgan Katz, MD – mentorship in hospital epidemiology
2017 Saranya Seetharaman, MBBS MPH - Capstone Advisor
2018 Arti Gharpure MPH - Capstone Advisor
2018 Donna Phantran MPH – Capstone Advisor

Educational Program Building / Leadership

2002-2007 - Associate Program Director Internal Medicine Residency – Albert Einstein Medical Center
2002-2007 - Student Clerkship Site Director Internal Medical – Jefferson Medical School
2002-2007 - Physical Diagnosis Site Course Director affiliate site - Jefferson Medical School
2016-2017 - Course Co-director Healthcare Epidemiology – Johns Hopkins School of Public Health
2018 – present - Society of Healthcare Epidemiology of America - SHEA/CDC Track Vice Chair

RESEARCH ACTIVITIES

SYSTEM INNOVATION AND QUALITY IMPROVEMENT ACTIVITIES

System Innovation Focus –In 2001, I was tasked with developing an antibiotic stewardship program at AEMC. We were able to build local support for this program and save over \$100,000 in antibiotic costs in the first year of implementation. I moved to Abington Memorial Hospital in 2007 as the hospital epidemiologist and in my first year Pennsylvania was the first state to enact mandatory public reporting for healthcare associated infections and require implementation of an infection control software. Within 6 months we successfully implemented all of these requirements. I moved to Johns Hopkins Bayview Medical Center in 2011 and at the time we had one of the highest central line associated bloodstream infection rate in the state. Now after a series of rapid interventions we have the lowest rate among academic hospitals in the state.

System Innovation and Quality Improvement efforts within JHMI:

2011 – current - Hospital epidemiologist, Johns Hopkins Bayview Medical Center - 70% effort

Reduction in CLABSI – 200% in 3 years
Reduction in craniotomy infections – 30% in 4 years
Hand Hygiene compliance - > 88% - in 2 years
Reduction in C section infection rates – 50% - in 2 years

System Innovation and Quality Improvement efforts outside of JHMI:

2014 – Assessment of MERS coronavirus preparedness at multiple hospitals in Saudi Arabia in conjunction with Aramco

2015 - Development of an Infection Prevention Program for the prevention of MERS Coronavirus, National Guard Hospital, Saudi Arabia

2017 – Infection Control Assessment JHAH

ORGANIZATIONAL ACTIVITIES

Institutional Administrative Appointments

2013-current – Co-chair, Surgical Site Infection prevention group (SSIP)

Journal peer review activities

2011-2016 reviewer e-Plasty
2011 present – reviewer BMC Infectious Diseases
2016 reviewer American Journal of Infection control
2017 reviewer Infection Control and Hospital Epidemiology
2018 reviewer Journal of Infection Prevention

Other peer review activities

2016 -2018 Infectious Disease Society of America abstract reviewer

Advisory Committees, Review Groups/Study Sections

2015 Maryland Health Care Commission Healthcare Advisory Committee
2016 Educational Committee Panel - Society of Healthcare Epidemiologists of America/CDC outbreak response training program
2016 The National Academies of Sciences, Engineering, and Medicine - presenter N95 and FXX surgical masks
2016 FDA Advisory Panel – Wound dressings
2016 Society of Healthcare Epidemiology of America/Center for Disease Control Outbreak Response Training Program
2017 Society of Healthcare Epidemiology of America Education Committee Member
2017 Society of Healthcare Epidemiology of America Policy Committee Member
2018 Society of Healthcare Epidemiology of America Planning Committee
2018 The National Academies of Sciences, Engineering, and Medicine – member - Committee on Personal Protective Equipment for Workplace Safety and Health
2018 Council for Outbreak Response: Healthcare-Associated Infections and Antimicrobial Resistant Pathogens (COHRA) – Centers for Disease Control and Council for State and Territorial Epidemiologists

Professional Societies

2007 – current - member, Society of Healthcare Epidemiology Association

2001 – current – member, Infectious Disease Society of America

RECOGNITION

[Awards, Honors](#)

2015 Armstrong Award for Excellence in Quality and Safety

2016 Medical Staff Award – HEIC team Johns Hopkins Bayview Medical Center

2017 Dean’s Excellence in Teaching Johns Hopkins School of Public Health

[Invited Talks](#)

2013 Asahi Memorial Hospital, Japan – Visiting professor.

2016 Washington State Healthcare Advisory Board – CLABSI Reduction in high risk environments