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Characteristics of antibiotic prophylaxis and risk of surgical site infections in open colectomies

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Abstract

Background—Despite numerous trials assessing optimal antibiotic prophylaxis strategies for colorectal surgery, few studies have assessed real-world practice on a national scale with respect to risk of surgical site infections.

Objective—Using a large, national claims database we aimed to describe 1) current use of prophylactic antibiotics (type and duration) and 2) associations with surgical site infection after open colectomies.

Design—Retrospective study using the Premier Perspective database.

Setting—Patient hospitalizations nationwide from January 2006 to December 2013.

Patients—90,725 patients that underwent an open colectomy in 445 different hospitals.

Main Outcome Measures—Multilevel multivariable logistic regressions measured associations between surgical site infection and 1) type of antibiotic used and 2) duration (day of surgery only, day of surgery and the day after, >1 day after surgery).

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Contributors Statement: All authors were involved in attaining data from Premier Perspective Inc. and were involved in designing the study. Nicole Zubizarreta and Isaac Wasserman analyzed data under guidance of Jashvant Poeran and Madhu Mazumdar. All authors contributed to the interpretation of the results, reviewed and approved the final document, and take responsibility for the content of the manuscript. Jashvant Poeran and Nicole Zubizarreta take responsibility for the completeness of the data and the accuracy of the analysis. Jashvant Poeran and Madhu Mazumdar are the study guarantors.

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Results—Overall surgical site infection prevalence was 5.2% (n=4,750). Most patients (41.8%) received cefoxitin for prophylaxis; other choices were ertapenem (18.2%), cefotetan (10.3%), metronidazole+cefazolin (9.9%), ampicillin+sulbactam (7.6%), while 12.2% received other antibiotics. Distribution of prophylaxis duration was: 51.6%, 28.5%, and 19.9% for days 0, 0+1, and 1+, respectively. Compared to cefoxitin, lower odds for surgical site infection were observed for ampicillin+sulbactam (odds ratio 0.71; 95% confidence interval 0.63–0.82), ertapenem (odds ratio 0.65; 95% confidence interval 0.58–0.71) and metronidazole+cefazolin (odds ratio 0.56; 95% confidence interval 0.49–0.64), and “other” (odds ratio 0.81; 95% confidence interval 0.73–0.90); duration was not significantly associated with altered odds for surgical site infection. Sensitivity analyses supported the main findings.

Limitations—Lack of detailed clinical information in the billing dataset used.

Conclusions—In this national study assessing real-world use of prophylactic antibiotics in open colectomies, type of antibiotic used appeared to be associated with up to 44% decreased odds for surgical site infections. While there are numerous trials on optimal prophylactic strategies, studies that particularly focus on factors that influence the choice of prophylactic antibiotic might provide insights into ways of reducing the burden of surgical site infections in colorectal surgeries.

Keywords

Antibiotic prophylaxis; Colectomy; Surgical site infection

INTRODUCTION

In addition to compromising patient safety, surgical site infections (SSI) represent a substantial burden on US healthcare costs. More than serving as a hospital quality measure—increasingly important for hospital reimbursements¹—SSIs are associated with an extended length of hospital stay by 10 days, representing an additional \$1.6 billion annual burden on the health care system.^{2–4} With the highest SSI rates, the >260,000 patients undergoing colorectal surgery each year appear at particular risk despite prophylactic antibiotics, the cornerstone of SSI prevention.⁵ Current guidelines recommend the use of antibiotics covering both aerobic and anaerobic bacteria, however, the relative efficacy of different regimens has yet to be established.⁶ Moreover, despite numerous trials assessing optimal antibiotic prophylaxis strategies for colorectal surgery, few studies have assessed real-world antibiotic prophylaxis practice on a national scale with respect to SSI risk.^{7,8} Notable exceptions are the Veterans Affairs Surgical Quality Improvement Program⁹ (n=5,750) and the Michigan Surgical Quality Collaborative⁵ (n=4,331) studies that compared different antibiotic prophylaxis regimens in colorectal surgery. Although these studies do demonstrate that the type of antibiotic prophylaxis matters in mitigating SSI risk after colorectal surgery, they are burdened by small and localized samples, while also lacking the most recent data.

Using a large, national claims-based database we, therefore, sought to 1) describe the real-world use of antibiotic prophylaxis (type and duration) in open colectomies, and 2) quantify the odds of developing a SSI for each prophylaxis regimen.

MATERIALS AND METHODS

Data Source and Study Design

In this retrospective cohort study we used data from the Premier Perspective database (Premier Inc., Charlotte, NC). This database contains information on patient hospitalizations nationwide from January 2006 to December 2013 and includes International Classification of Diseases-9th revision Clinical Modification (ICD-9 CM) codes, Current Procedural Terminology (CPT) codes, and billed items. These data meet the de-identification requirements as defined by the Health Insurance Portability and Accountability Act and was exempt from consent requirements of the Mount Sinai Medical Center Institutional Review Board (project HS#: 14-00647).

Study Sample

The study sample contained patients that underwent an open colectomy¹⁰ (right hemicolectomy, left hemicolectomy, resection of transverse colon, sigmoidectomy, other; indicated by ICD-9 CM procedure codes 45.7X, 45.82, 45.83). Exclusion criteria were based on previous studies.^{11,12} Patients were excluded (see figure 1) if they had an unknown gender or discharge type (n=321), had systemic antibiotic use prior to surgery (n=77,043), no claims for antibiotic use on the day of surgery (n=20,323), a switch in antibiotic class or gaps in antibiotic use of ≥ 1 days (as to distinguish between treatment and prophylaxis, n=59,510), patients who had multiple procedures during the same hospitalization (n=4,085), were treated at a hospital performing <30 colectomies (to ensure sufficient sample size per cluster) (n=1,274)¹³ or died within two days of surgery (n=861).

Study Variables

The main exposures of interest were 1) the type of prophylactic antibiotic used, and 2) the duration of the use of prophylactic antibiotics. Type of prophylactic antibiotic was categorized into cefotetan, cefoxitin, ampicillin+sulbactam, ertapenem, metronidazole +cefazolin, and other (for a full list of “other” medications, see Appendix Table 1); duration of prophylaxis was categorized into day of surgery only (day 0), day of surgery and the day after (day 0+1), or >1 day after surgery (day 1+).

Patient demographic variables included age, gender, and ethnicity (White, Black, Hispanic, other). Healthcare related variables were insurance type (commercial, Medicaid, Medicare, uninsured, other), hospital location (urban, rural), hospital size (<300 , 300–499, >500 beds), hospital teaching status, and the mean annual number of open colectomies performed per hospital. Procedure related variables included the indication for surgery (neoplasm, diverticular disease, inflammatory bowel disease, other), type of surgery (right hemicolectomy, left hemicolectomy, resection of transverse colon, sigmoidectomy, other), year of procedure, and length of hospitalization. Overall comorbidity burden was assessed using the Quan¹⁴ adaptation of the Charlson Comorbidity Index. In addition, other included variables deemed to influence SSI risk were obesity (ICD-9 278.0, 278.00, 278.01, 649.1, V85.3, V85.4, V85.54, 793.91) and smoking (ICD-9 305.1X, V15.82).

The main outcome of interest was the occurrence of a SSI during the index hospitalization. As different definitions of SSI have been used in previous studies, we assessed three different definitions of SSI in our study: 1) only ICD-9 codes (998.5, 998.51, 998.59, 998.13, 998.3, 998.31, 998.32, 998.83, 998.81),¹⁵ 2) ICD-9 codes AND billing for a wound culture, and 3) only billing for a wound culture. We believe that the use of varying definitions will demonstrate the robustness of our main effects of interest. Unfortunately, the use of billing information does not allow us to reliably differentiate between superficial and deep wound infections; our SSI variables therefore represent a combination of both.

Statistical Analysis

First, we assessed the univariable association between type of antibiotic use and study variables using Chi-square tests and t-tests for categorical and continuous variables, respectively. We then performed multilevel multivariable logistic regressions to measure the association between type and duration of antibiotic use, and the three definitions of SSI. Models included a random intercept term that varies at the level of each hospital, accounting for correlation of patients within hospitals. The multivariable models were adjusted using all variables found significant at the $P < 0.15$ level from the univariable tests and deemed clinically important. Adjusted odds ratio (OR), 95% confidence interval (CI), and P-value are reported. Model discrimination was evaluated using the C-statistic.

All analyses were performed in SAS v9.4 statistical software (SAS Institute, Cary, NC, USA).

RESULTS

The final study cohort consisted of 90,725 patients undergoing an open colectomy at 445 hospitals between January 2006 and December 2013. Overall, 42% ($n=37,883$) of patients received cefoxitin as prophylaxis; this was 18% ($n=16,531$) for ertapenem, 10% ($n=9,388$) for cefotetan, 10% ($n=9,006$) for metronidazole+cefazolin, 8% ($n=6,888$) for ampicillin/sulbactam, and 12% ($n=11,029$) for 'other' antibiotics. Furthermore, 52% ($n=46,788$) received antibiotic prophylaxis only on the day of operation; 29% ($n=25,871$) received prophylaxis on the day of the operation and the following day, and 20% ($n=18,066$) received prophylaxis that lasted longer than the day after the operation. Figure 2 shows the overall distribution of type of antibiotic as well as sub-grouped by day 0, day 0+1, and day 1+. Appendix 1 contains a list of all antibiotics included under "other." The most commonly used "other" medication was metronidazole + quinolone ($n=8,705$; 79% of all "other" medications).

Table 1 provides a breakdown of type of prophylactic antibiotic used by patient, healthcare-related, procedure-related, comorbidity and outcome (SSI) variables. The majority of variables were univariably associated with the type of antibiotic used. Interestingly, the use of ertapenem rapidly increased from 6% of all patients in 2006 to 29% in 2013 (row percentages, not shown in table). In addition, the mean length of hospitalization was highest among patients administered 'other' antibiotics (8.8 days) and ampicillin+sulbactam (8.3 days), while the highest costs of hospitalization were seen for those administered "other" antibiotics (\$19,916), and the highest Charlson comorbidity index was seen for those on

metronidazole+cefazolin (2.51); all $P < 0.0001$. The overall SSI prevalence—defined by only ICD-9 codes—was 5.2% ($n=4,750$), varying from 3.5% (metronidazole+cefazolin) to 5.9% (cefotetan). In general, estimated prevalences were lower for the other SSI definitions.

After adjustment for relevant covariates (Table 2; full model results are depicted in Appendix 2), certain antibiotics remained significantly associated with lower odds for SSI: compared to cefoxitin this was true for ampicillin+sulbactam (OR 0.71 CI 0.63–0.82), ertapenem (OR 0.65 CI 0.58–0.71), and metronidazole+cefazolin (OR 0.56 CI 0.49–0.64); all $P < 0.05$. This pattern did not change when using the varying SSI definitions. The duration of prophylaxis was not significantly associated with SSI risk. The model c-statistics varied between 0.83 and 0.91, indicating good model discrimination.

DISCUSSION

Although several others have assessed differences between antibiotic prophylaxis regimens in open colectomies,⁷ to our knowledge this is the largest nationwide study representing real-world clinical practice among 90,725 patients from 445 US hospitals over eight years. We demonstrated significant variations in antibiotic prophylaxis practices for open colectomies; while cefoxitin was most commonly used (42%) the role of ertapenem increased from 6% in 2006 to 29% in 2013 (of all prophylactics used). Moreover, the type of antibiotic used appeared to be associated with SSI risk: with lower (compared to cefoxitin) odds seen for ampicillin+sulbactam (29% decreased odds), ertapenem (35% decreased odds), and metronidazole+cefazolin (44% decreased odds). These effects remained with varying definitions of SSI. Interestingly, the duration of prophylaxis was not significantly associated with SSI risk.

Previous attempts to describe antibiotic prophylaxis choice and SSI rates suffer from small population size or diverse study design, and the optimal regimen of antibiotic prophylaxis for open colectomies has yet to be established.⁸ The most commonly used prophylactic (cefotetan) in our study differs from what was found in the only other similarly large description of clinical practice in colectomies using Medicare data in 2005. Using a random sample of 5,279 Medicare inpatients undergoing colon surgery, Bratzler et al. found the most commonly used prophylactic to be cefotetan (52.8%), with only 30.7% receiving cefoxitin.¹⁶ Similarly, using data from the Michigan Surgical Quality Collaborative ($n=3,002$) Hendren et al. also found variations in antibiotic choice with cefoxitin used in 20.0% while metronidazole+cefazolin and ertapenem were used in 18.5% and 16.9%, respectively.¹⁷ In addition to this variation, we also demonstrated an increasing use of ertapenem. This may be due to an increasing number of studies in which ertapenem compares favorably to other antibiotics in SSI prevention.^{5,10,18,19} One of the main drivers in particular may have been the highly publicized 2006 trial by Itani et al. which showed ertapenem to be more effective than cefotetan in the prevention of SSIs in patients undergoing elective open colorectal surgery.¹⁰ In addition, ertapenem covers both anaerobes and aerobes found in bowel lumen, has a relatively long half-life (preventing the need for a second administration), and a similar safety profile compared to other prophylaxis choices.^{10,20,21}

Examining real-world clinical practice, we also observed a deviation from recommended antibiotic prophylaxis guidelines. According to the 2013 Surgical Infection Society Guidelines, antibiotic prophylaxis should be “continued for no more than 24 hours and can typically be stopped when the procedure is completed.¹⁹” We found that 48% of patients received prophylactics beyond the day of surgery, meaning in only 52% of cases prophylaxis lasted for just the day of surgery, as recommended by current guidelines. This is higher than the 41% of patients discontinuing prophylaxis within 24 hours of the end of surgery found in the 2005 Medicare study.¹⁶

The overall SSI rate was 5.2% in our study, lower than the rates found in other studies and most probably an underestimation as rates have been shown to vary from 5% up to 30%.^{8,10,22,23} Important factors affecting this variation are differences in clinical case definition,²⁴ differences in definition based on billing information (in our study we varied between ICD-9 codes and billing for wound cultures), and follow-up time.^{25,26} Indeed, 50% of SSI cases have been shown to occur after discharge²⁶ and, thus, were not captured in our data. Importantly, however, this underestimation is likely to be distributed equally among all types of antibiotic prophylaxis. To our knowledge, there is no literature suggesting differing rates of post-discharge incidence of SSI by antibiotic choice. Therefore, although absolute risk of SSI may be underestimated, we expect the comparison of relative odds of SSI to still be valid.

Interestingly, we found that antibiotic choice (after adjustment for relevant covariates) was significantly associated with SSI risk, with lower odds consistently seen for ampicillin+sulbactam, ertapenem, and metronidazole+cefazolin. This is comparable to results found in a study using data from the Michigan Surgical Quality Collaborative including 4,331 patients undergoing a colectomy in twenty-four different Michigan hospitals between 2008 and 2010. Here, the authors compared SSI rates between Surgical Care Improvement Project (SCIP) recommended antibiotic prophylactic choices to those that were non-SCIP-compliant.⁵ The authors found that SCIP compliant antibiotics (ciprofloxacin+metronidazole, metronidazole+cefazolin, ertapenem) were associated with decreased odds of developing a SSI. The favorable comparison of metronidazole+cefazolin and ertapenem against cefotetan and cefoxitin is confirmed by the findings in the present study. Moreover, among 5,750 veterans undergoing a colectomy at 112 different VA hospitals between 2005 and 2009 metronidazole+cefazolin again appeared to be associated with the lowest SSI rates while second-generation cephalosporins accounted for the majority of antibiotic prophylaxis.⁹ Although we do not know the reasons for antibiotic choices in our study, one important factor contributing to differences in effectiveness of antibiotic prophylaxis might be an emerging resistance of common antibiotics used in prophylaxis to *Bacteroides fragilis*, the most commonly isolated organism in these SSIs.²⁷ In particular, *Bacteroides* resistance to clindamycin has been found to range from 20% to 60%, while increased resistance has also been found in cefoxitin, cefotetan, and ampicillin+sulbactam.^{9,28}

While a significant proportion of patients in our study received antibiotic prophylaxis beyond the day of surgery (48%), duration of prophylaxis was not associated with SSI risk, thus supporting the rationale behind current guidelines.^{7,19} Between 1978 and 2011, thirty-three studies examined the association between duration of prophylaxis and SSI; combined,

their data showed no association between duration of antibiotic prophylaxis and SSI risks.⁷ It is unclear what is behind the observed extended use of prophylactic antibiotics; qualitative studies geared towards this question will shed some light on this intriguing issue and thus provide targets for intervention.

Next to replication and validation of our study results using other data sources, we feel that the current study hints towards potentials for improvement in the perioperative care for these patients. This opportunity pertains particularly to the most commonly used prophylactic (cefotetan) being associated with the highest odds for SSIs, and 48% of patients receiving antibiotic prophylaxis beyond the day of surgery, despite this practice not showing altered odds for SSI risk. Despite general consensus on the importance of SSI prevention in hospital policies, there is a lack of studies looking into so-called ‘return on investment’ calculations from the hospital perspective. Using data from the Johns Hopkins Health System for a variety of surgeries, Shepard et al. found the change in annual profit due to SSIs was around \$650,000—a conservative measure given their methodology—thus illustrating the financial incentive for hospitals to reduce SSIs.²⁹ The results from our study suggest that even relatively straightforward alterations in antibiotic prophylaxis strategies may yield substantial patient safety and economic benefits. Future studies should explore the full scope of benefits and harms while also evaluating implementation strategies and their costs.

The main limitation of our study is the lack of detailed clinical information in the billing dataset used; data are collected for the purpose of billing, not specific research questions. Therefore, important information such as reasons behind antibiotic choice and duration of prophylaxis, SSI pathogens, type of SSI (deep or superficial), or other interventions that might influence SSI risk (e.g. mechanical bowel preparation with or without oral antibiotics) cannot be taken into account, and, thus, residual confounding cannot be ruled out. However, while there is evidence on specifically the benefits of the latter on SSI risk, some reports suggest a decrease in the use of oral antibiotics: ³⁰ 92% of surgeons reported using oral antibiotics in 1992³¹ while this was only 36% in 2010.³² Additionally, information from billing databases does not necessarily reflect what is actually administered to the patient as there might be a mismatch between the two. Given the de-identified nature of the dataset auditing was not possible. However, we expect the effect of the mismatch to be minimal as this should be unrelated to SSI risk and type/duration antibiotics. Another limitation—partly due to the lack of clinical information—pertains to the definition of SSI from billing data for the inpatient period only. This appears particularly important as a substantial proportion (almost fifty percent) of infections after colorectal surgery occur after hospital discharge.²⁶ This limitation would theoretically only affect our results when the occurrence of SSI post-discharge is dependent on choice and duration of antibiotic prophylaxis. Although this assumption might be debatable we feel confident in our findings as they confirm those found in previous studies. Our study might also have been burdened by differential definitions of SSI. While we have tried to account for this by assessing the effects of antibiotic choice and duration on three different SSI definitions, the issue of differences in clinical interpretation persists. Hedrick et al. recently showed that there is a poor agreement between the SSI definition put forward by the Centers for Disease Control and Prevention and a more objective SSI scoring system. While this is an important issue for particularly the validity of SSI reporting, we feel that for the current study the comparison between differences in

clinical interpretation and differential (billing) definitions is independent of antibiotic choice, and therefore reducing its effect on the current findings. Also, while the rate of laparoscopic colectomy is increasing, our results only apply to those undergoing open colectomies.³³ We specifically only studied patients undergoing open colectomies as their SSI risk is higher and therefore the effect of antibiotic practices is expected to be more profound.³⁴ As an increasing number of patients is undergoing laparoscopic surgery it would indeed be of interest to assess antibiotic practices in this group in future studies. Adding to the issue of generalizability is the use of multiple exclusion criteria. These were used to minimize confounding (next to covariate adjustment), however, with the risk of compromising generalizability. This indeed is an inevitable limitation of retrospective studies. The explicit statement of our exclusion criteria should ensure the correct interpretation of our results.

In conclusion, in this large, nationwide study, we found significant variations in antibiotic prophylaxis practices for open colectomies, with cefoxitin the most commonly used, and a rapid increase of ertapenem usage. The type of prophylactic antibiotic used appeared to be associated with SSI risk, with 29% to 44% lower odds seen for ampicillin+sulbactam, ertapenem, and metronidazole+cefazolin as compared to the most commonly administered antibiotic, cefoxitin. These effects persisted with varying definitions of SSI. Lending support to current guidelines, the duration of prophylaxis was not significantly associated with SSI risk.

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APPENDIX I

Table 1

List of “Other” antibiotics

<i>Medication</i>	<i>n</i>
Metronidazole + Cefuroxime	83
Metronidazole + Ceftriaxone	639
Clindamycin + Aminoglycoside	764
Clindamycin + Quinolone	441
Clindamycin + Aztreonam	164
Metronidazole + Aminoglycoside	233
Metronidazole + Quinolone	8705

Table 2

SSI rates by year

SSI Definition	2006	2007	2008	2009	2010	2011	2012	2013
<i>ICD 9 + wound culture</i>	0.9%	0.9%	1.0%	1.1%	0.9%	1.0%	1.1%	0.9%
<i>ICD 9</i>	4.8%	4.7%	5.0%	4.9%	4.7%	4.7%	4.9%	4.5%
<i>Wound Culture</i>	1.8%	2.0%	1.9%	1.8%	1.9%	1.8%	1.9%	1.9%

APPENDIX II

Full multivariable model results

	Only ICD-9 codes		ICD-9 codes AND billing for wound culture		Only wound culture billing	
	OR	95% CI	OR	95% CI	OR	95% CI
TYPE OF ANTIBIOTIC USED (Reference = Cefoxitin)						

	Only ICD-9 codes			ICD-9 codes AND billing for wound culture			Only wound culture billing		
	OR	95% CI		OR	95% CI		OR	95% CI	
Cefotetan	0.99	0.89	1.11	0.97	0.74	1.28	0.93	0.76	1.15
Ampicillin/Sulbactam	0.71	0.63	0.82	0.52	0.37	0.73	0.72	0.57	0.90
Ertapenem	0.65	0.58	0.71	0.55	0.42	0.71	0.53	0.43	0.64
Metronidazole/Cefazolin	0.56	0.49	0.64	0.68	0.49	0.94	0.57	0.44	0.73
Other	0.81	0.73	0.90	0.72	0.56	0.92	0.69	0.58	0.83
DURATION OF PROPHYLAXIS (Reference = Day 0)									
Day 0+1	1.05	0.96	1.14	0.98	0.81	1.18	1.01	0.96	1.26
Day 1+	0.93	0.86	1.01	0.90	0.76	1.07	0.90	0.80	1.03
PATIENT DEMOGRAPHICS									
<i>Age (continuous)</i>	1.00	0.99	1.00	1.00	0.99	1.01	1.00	0.99	1.00
<i>Gender (Reference = Male)</i>									
Female	0.80	0.75	0.85	0.80	0.70	0.91	0.76	0.69	0.84
<i>Race (Reference = White)</i>									
Black	0.79	0.70	0.88	0.84	0.64	1.09	0.92	0.76	1.11
Hispanic	1.08	0.89	1.32	1.02	0.63	1.66	1.29	0.93	1.80
Other	1.03	0.94	1.13	1.19	0.95	1.48	1.20	1.01	1.41
HEALTHCARE RELATED									
<i>Insurance type (Reference = Commercial)</i>									
Medicaid	1.00	0.87	1.15	1.19	0.90	1.59	0.99	0.79	1.23
Medicare	0.88	0.88	0.96	0.84	0.69	1.01	0.89	0.78	1.03
Uninsured	0.94	0.94	1.12	0.78	0.51	1.18	1.06	0.81	1.39
Other	1.03	1.03	1.26	1.04	0.64	1.67	0.96	0.67	1.39
<i>Hospital location (Reference = Urban)</i>									
Rural	1.08	0.97	1.20	0.76	0.42	1.37	0.67	0.35	1.25
<i>Hospital size (continuous)</i>									
	1.00	1.00	1.00	1.00	0.98	1.01	0.99	0.98	1.00
<i>Hospital Teaching Status (Reference = Teaching)</i>									
Non-Teaching	0.88	0.81	0.95	1.23	0.73	2.08	1.01	0.58	1.79
PROCEDURE RELATED									
<i>Procedure status (Reference = Elective)</i>									
Emergency	0.95	0.87	1.03	1.21	1.01	1.45	1.28	1.12	1.46
Urgent	0.88	0.79	0.99	1.10	0.85	1.43	1.17	0.96	1.41
<i>Indication for Colectomy</i>									
Neoplasm	1.59	1.05	2.42	2.43	1.20	4.94	1.89	1.04	3.45
Diverticular Disease	2.18	1.43	3.32	3.76	1.83	7.71	2.46	1.34	4.51
Inflammatory Bowel Disease	2.07	1.36	3.13	4.08	2.06	8.11	3.00	1.67	5.39
<i>Type of procedure</i>									
Right Hemicolectomy	0.75	0.69	0.83	0.79	0.65	0.96	0.77	0.67	0.89
Sigmoidectomy	0.96	0.88	1.06	0.89	0.72	1.09	0.91	0.78	1.05
Other	0.95	0.85	1.06	1.14	0.92	1.43	0.99	0.84	1.17
<i>Year of procedure (Reference = 2006)</i>									

	Only ICD-9 codes			ICD-9 codes AND billing for wound culture			Only wound culture billing			
	OR	95% CI		OR	95% CI		OR	95% CI		
2007	0.91	0.80	1.03	0.90	0.68	1.19	0.93	0.76	1.13	
2008	1.02	0.90	1.16	1.10	0.84	1.44	0.92	0.75	1.12	
2009	1.23	1.08	1.39	1.31	1.00	1.73	1.05	0.85	1.28	
2010	1.13	0.99	1.28	1.01	0.75	1.34	1.02	0.83	1.25	
2011	1.05	0.93	1.20	1.07	0.81	1.43	0.93	0.75	1.15	
2012	1.20	1.06	1.36	1.19	0.90	1.59	1.04	0.85	1.29	
2013	1.18	1.04	1.35	1.12	0.83	1.51	1.11	0.90	1.37	
<i>Mean length of hospital stay</i>	1.12	1.12	1.12	1.07	1.07	1.08	1.09	1.09	1.09	
COMORBIDITIES										
<i>Mean Charlson comorbidity index</i>	1.00	0.99	1.01	1.03	1.00	1.05	1.01	0.99	1.03	
<i>Smoking</i>	1.17	1.09	1.25	1.14	0.98	1.33	1.19	1.06	1.33	
<i>Obesity</i>	1.73	1.59	1.88	1.56	1.29	1.89	1.36	1.18	1.58	

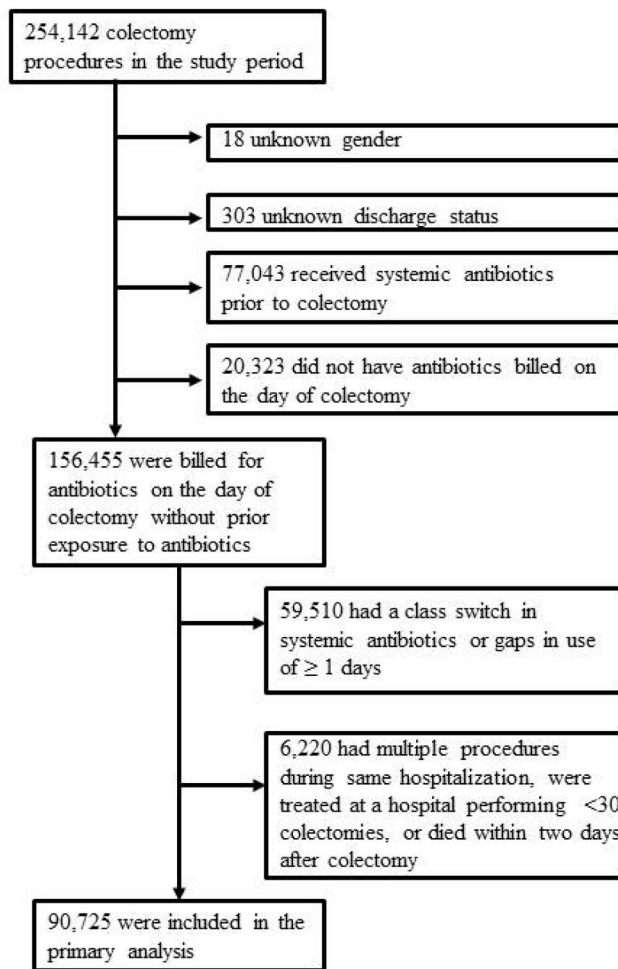
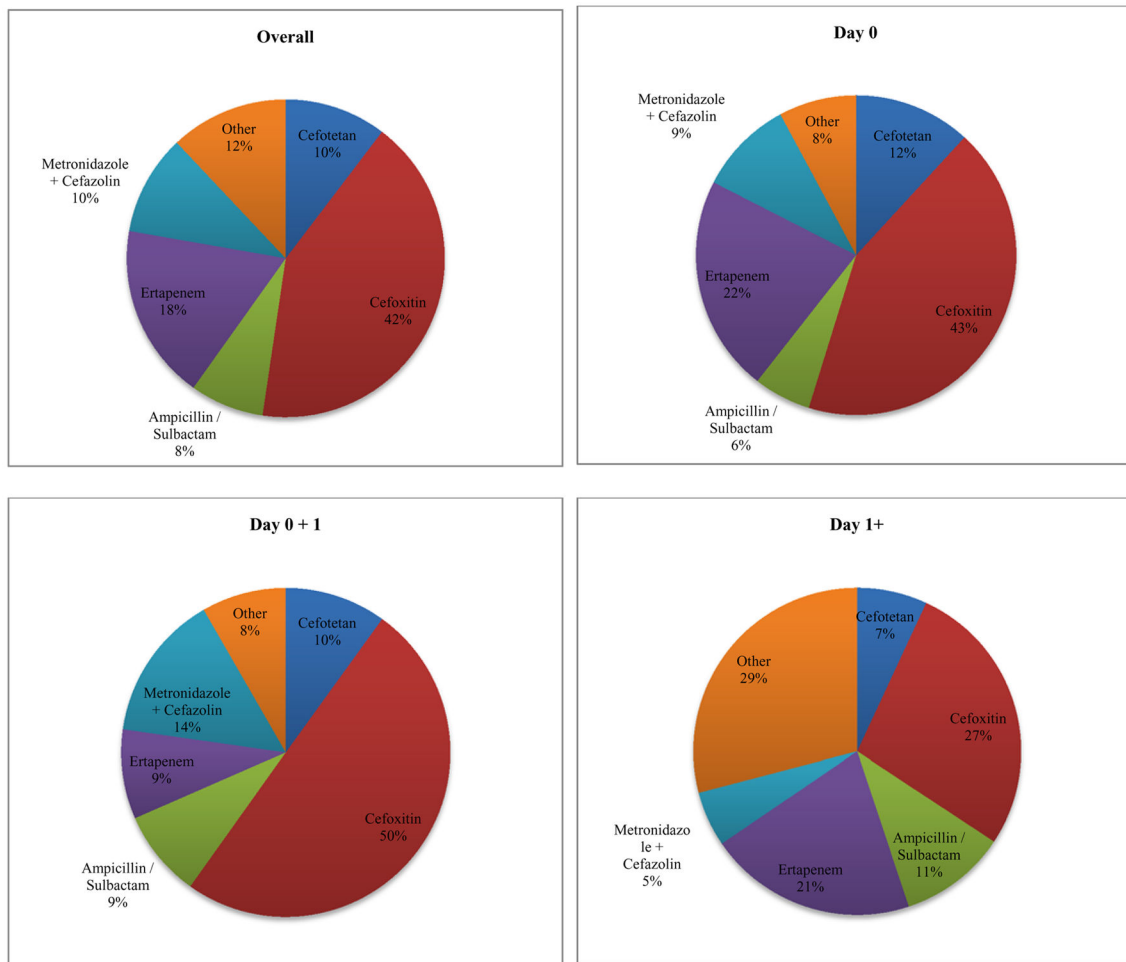


Figure 1.
Patient flow chart



DURATION OF PROPHYLAXIS	Cefotetan		Cefoxitin		Amp + Sulba		Ertapenem		Met + Cefaz		Other		P-value*
	n	%	n	%	n	%	n	%	n	%	n	%	
Day 0	5584	12	19979	43	2678	6	10453	22	4444	9	3650	8	<0.0001
Day 0+1	2577	10	12989	50	2221	9	2340	9	3629	14	2115	8	
Day 1+	1227	7	4915	27	1989	11	3738	21	933	5	5264	29	
Overall	9388	10	37883	42	6888	8	16531	18	9006	10	11029	12	

*Chi-square test

Figure 2. Distribution of type of prophylactic antibiotic used; overall and sub-grouped by day 0, day 0+1, and day 1+

Table 1

Type of antibiotic used by patient, healthcare related, procedure related, comorbidity and outcome (SSI) variables.

TYPE OF ANTIBIOTIC USED N (%)													
	Cefotetan		Cefoxitin		Amp+Salba		Ertapenem		Met+Cefaz		Other		
	n	%	n	%	n	%	n	%	n	%	n	%	
PATIENT DEMOGRAPHICS													
<i>Mean Age *</i>	63.5	15.1	63.4	15.2	62.2	16.2	63.5	15.2	63.3	14.9	63.2	15.5	
<i>Age category</i>												<i>P-value**</i>	
<45 years	1013	10.8	4151	11.0	891	12.9	1842	11.1	999	11.1	1280	11.6	<0.0001
45-54 years	1448	15.4	6042	15.9	1167	16.9	2654	16.1	1418	15.7	1811	16.4	
55-64 years	2162	23.0	8483	22.4	1541	22.4	3647	22.1	2020	22.4	2435	22.1	
65-74 years	2289	24.4	9233	24.4	1561	22.7	4046	24.5	2268	25.2	2567	23.3	
>75 years	2476	26.4	9974	26.3	1728	25.1	4342	26.3	2301	25.5	2936	26.6	
<i>Gender</i>													
Female	4995	53.2	19980	52.7	3570	51.8	8673	52.5	4814	53.5	6737	61.1	<0.0001
Male	4393	46.8	17903	47.3	3318	48.2	7858	47.5	4192	46.5	4292	38.9	
<i>Race</i>													
White	6278	66.9	27519	72.6	5094	74.0	12451	75.3	5944	66.0	8032	72.8	<0.0001
Black	822	8.8	3560	9.4	790	11.5	1563	9.5	986	10.9	997	9.0	
Hispanic	232	2.5	965	2.5	160	2.3	285	1.7	556	6.2	309	2.8	
Other	2056	21.9	5839	15.4	844	12.3	2232	13.5	1520	16.9	1691	15.3	
HEALTHCARE RELATED													
<i>Insurance type</i>													
Commercial	3826	40.8	15133	39.9	2709	39.3	6243	37.8	3650	40.5	4320	39.2	<0.0001
Medicaid	324	3.5	1768	4.7	418	6.1	788	4.8	449	5.0	587	5.3	
Medicare	4606	49.1	19087	50.4	3310	48.1	8513	51.5	4420	49.1	5533	50.2	
Uninsured	286	3.0	1153	3.0	258	3.7	632	3.8	277	3.1	388	3.5	
Other	346	3.7	742	2.0	193	2.8	355	2.1	210	2.3	201	1.8	
<i>Hospital location</i>													
Rural	849	9.0	5407	14.3	758	11.0	3355	20.3	1112	12.3	1097	9.9	<0.0001
Urban	8539	91.0	32476	85.7	6130	89.0	13176	79.7	7894	87.7	9932	90.1	

	TYPE OF ANTIBIOTIC USED N (%)												P-value**
	Cefotetan	Cefoxitin	Amp+Subba	Ertapenem	Met+Cefaz	Other	n	%	n	%	n	%	
Hospital size													
<300 beds	2941	31.3	11675	30.8	2226	32.3	6433	38.9	2430	27.0	3280	29.7	<0.0001
300-499 beds	3495	37.2	14378	38.0	2852	41.4	6263	37.9	3944	43.8	4324	39.2	
500 beds	2952	31.4	11830	31.2	1810	26.3	3835	23.2	2632	29.2	3425	31.1	
Hospital Teaching Status													
Non-Teaching	5034	53.6	23023	60.8	4020	58.4	10835	65.5	5754	63.9	6705	60.8	<0.0001
Teaching	4354	46.4	14860	39.2	2868	41.6	5696	34.5	3252	36.1	4324	39.2	
<i>Mean annual # of colectomies per hospital*</i>													<0.0001
PROCEDURE RELATED													
Procedure status													
Elective	7059	75.2	28807	76.0	4426	64.3	11159	67.5	7210	80.1	6456	58.5	<0.0001
Emergency	1432	15.3	5657	14.9	1749	25.4	3642	22.0	1228	13.6	3547	32.2	
Urgent	897	9.6	3419	9.0	713	10.4	1730	10.5	568	6.3	1026	9.3	
Indication for Colectomy***													
Neoplasm	1958	20.9	8034	21.2	1245	18.1	3205	19.4	2110	23.4	1556	14.1	<0.0001
Diverticular Disease	1183	12.6	4533	12.0	674	9.8	1938	11.7	1284	14.3	1333	12.1	<0.0001
Inflammatory Bowel Disease	235	2.5	814	2.1	113	1.6	452	2.7	290	3.2	209	1.9	<0.0001
Type of procedure***													
Right Hemicolectomy	3503	37.3	14962	39.5	2657	38.6	6018	36.4	3455	38.4	3736	33.9	<0.0001
Left Hemicolectomy	988	10.5	3929	10.4	682	9.9	1808	10.9	967	10.7	1140	10.3	0.18574
Resection of Transverse colon	490	5.2	2024	5.3	345	5.0	770	4.7	483	5.4	515	4.7	0.00415
Sigmoidectomy	2883	30.7	11457	30.2	2090	30.3	5235	31.7	2679	29.7	4006	36.3	<0.0001
Other	1524	16.2	5511	14.5	1114	16.2	2700	16.3	1422	15.8	1632	14.8	<0.0001
Year of procedure													
2006	1701	18.1	5966	15.7	1185	17.2	749	4.5	985	10.9	1842	16.7	<0.0001
2007	151	1.6	7728	20.4	1286	18.7	1164	7.0	1554	17.3	1741	15.8	
2008	1465	15.6	5572	14.7	1177	17.1	2094	12.7	1428	15.9	1549	14.0	
2009	1298	13.8	3864	10.2	751	10.9	1872	11.3	904	10.0	1240	11.2	
2010	1399	14.9	3725	9.8	668	9.7	2237	13.5	1040	11.5	1183	10.7	

	TYPE OF ANTIBIOTIC USED N (%)												P-value**
	Cefotetan		Cefoxitin		Amp+Sulba		Ertapenem		Met+Cefaz		Other		
	n	%	n	%	n	%	n	%	n	%	n	%	
2011	1224	13.0	3932	10.4	688	10.0	2721	16.5	1047	11.6	1255	11.4	
2012	1182	12.6	3759	9.9	633	9.2	2919	17.7	1042	11.6	1183	10.7	
2013	968	10.3	3337	8.8	500	7.3	2775	16.8	1006	11.2	1036	9.4	
<i>Mean length of hospital stay*</i>	7.5	6.3	8.0	6.7	8.3	7.0	7.9	6.2	7.6	6.5	8.8	7.3	<0.0001
<i>Mean Cost of hospitalization*</i>	18472	17620	17415	18908	18902	19474	17840	16143	17096	18002	19916	20389	<0.0001
COMORBIDITIES													
<i>Mean Charlson comorbidity index</i>	2.46	3.1	2.47	3.0	2.31	3.0	2.34	3.0	2.51	3.1	2.12	2.9	<0.0001
<i>Smoking</i>	2483	26.4	9047	23.9	1789	26.0	4429	26.8	2062	22.9	2652	24.0	<0.0001
<i>Obesity</i>	1060	11.3	4061	10.7	707	10.3	1924	11.6	858	9.5	1289	11.7	<0.0001
SURGICAL SITE INFECTIONS													
<i>-Only ICD-9 codes</i>	554	5.9	2216	5.8	334	4.8	704	4.3	311	3.5	631	5.7	<0.0001
<i>-ICD-9 code AND billing for wound culture</i>	144	1.5	457	1.2	58	0.8	115	0.7	79	0.9	115	1.0	<0.0001
<i>-Only wound culture billing</i>	254	2.7	878	2.3	149	2.2	219	1.3	145	1.6	231	2.1	<0.0001

* Continuous variable mean and standard deviation instead of N and %, respectively

** Chi-square test for categorical variables, t-test for continuous variables

*** Overlap between categories

Multivariable associations between type of antibiotic / duration of prophylaxis and three definitions of SSI.

Table 2

	Only ICD-9 codes		ICD-9 codes AND billing for wound culture		Only wound culture billing	
	OR*	95% CI	OR*	95% CI	OR*	95% CI
TYPE OF ANTIBIOTIC USED						
<i>Reference = Cefoxitin</i>						
Cefotetan	0.99	0.89 1.11	0.97	0.74 1.28	0.93	0.76 1.15
Ampicillin/Sulba ctam	0.71**	0.63 0.82	0.52**	0.37 0.73	0.72**	0.57 0.90
Ertapenem	0.65**	0.58 0.71	0.55**	0.42 0.71	0.53**	0.43 0.64
Metronidazole/Cefazolin	0.56**	0.49 0.64	0.68**	0.49 0.94	0.57**	0.44 0.73
Other	0.81**	0.73 0.90	0.72**	0.56 0.92	0.69**	0.58 0.83
DURATION OF PROPHYLAXIS						
<i>Reference = Day 0</i>						
Day 0+1	1.05	0.96 1.14	0.98	0.81 1.18	1.01	0.96 1.26
Day 1+	0.93	0.86 1.01	0.90	0.76 1.07	0.90	0.80 1.03

* OR odds ratio / CI confidence interval; models adjusted for: age, gender, race, insurance type, hospital geographic location, hospital teaching status, hospital size, indication for colectomy, type of procedure, year of procedure, length of hospital stay, comorbidity burden, smoking status, obesity, and emergent/urgent procedure

** P<0.05