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Original Article

Perioperative Antibiotic Choice and Postoperative Infectious Complications in Pelvic Organ Prolapse Surgery

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ABSTRACT **Objective:** The objective of this study was to determine how rates of postoperative infectious complications after pelvic organ prolapse surgery differ based on perioperative antibiotic administered. In particular, we sought to determine whether anaerobic coverage is associated with reduced rates of infectious complications.

Design: This was a retrospective cohort study.

Setting: Premier Healthcare U.S. national database, a comprehensive all-payer dataset capturing patients from urban and rural nonprofit, community, and teaching hospitals.

Participants: Adult patients who underwent vaginal, laparoscopic, and/or abdominal prolapse surgery with or without hysterectomy from January 2000 to March 2020. Procedures with and without mesh were included.

Interventions: Rates of infectious complications were compared among patients who received guideline-concordant antibiotic regimens, including those with anaerobic coverage. The primary outcome was any surgical site infection within 30 days of surgery without mesh or 90 days of surgery involving mesh.

Results: Among 130,198 prolapse surgeries, the most common antibiotic regimens were cefazolin (n = 97,058, 74.5%), second-generation cephalosporin (n = 16,442, 12.6%), clindamycin + aminoglycoside (n = 8,397, 6.4%) and cefazolin + metronidazole (n = 4,328, 3.3%). On multivariable logistic regression, only clindamycin + aminoglycoside was associated with a higher rate of surgical site infections (OR = 1.37; 95% CI 1.09−1.72) and other infectious morbidity (OR = 1.26; 95% CI 1.12−1.42) when compared to cefazolin alone. The addition of metronidazole to cefazolin was not associated with reduced rates of surgical site infections (OR = 1.09; 95% CI 0.82−1.45). Obesity (OR = 1.22; 95% CI 1.03−1.43), diabetes without complication (OR = 1.30; 95% CI 1.08−1.57), Charlson comorbidity score >0 (OR = 1.24; 95% CI 1.06−1.45), and tobacco use (OR = 1.22, 95% CI 1.05−1.40) were also associated with increased composite surgical site infection.

Conclusion: Compared with cefazolin alone, the use of alternative perioperative antibiotics, including those with anaerobic coverage, was not associated with reduced infectious complications after pelvic organ prolapse surgery in this U.S. national sample. Journal of Minimally Invasive Gynecology (2025) 32, 185−193. © 2024 AAGL. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Keywords: Antibiotic prophylaxis; Cefazolin; Postoperative infections; Surgical complications; Urogynecology and reconstructive pelvic surgery

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Introduction

There is limited consensus on perioperative prophylactic antibiotic selection for pelvic organ prolapse (POP) surgery. Historically, antibiotic recommendations for urogynecologic surgery have been extrapolated from other clean-contaminated procedures. Studies indicate that single-dose antibiotic prophylaxis is adequate during mesh-augmented prolapse surgery when compared with multidose regimens, but the optimal regimen remains unknown [1−3].

The primary antibiotic recommendation for colporrhaphy according to the American College of Obstetricians and Gynecologists (ACOG) and the AUGS-IUGA Joint clinical consensus is administration of IV cefazolin within 1 hour before incision [4,5]. The American Urological Association (AUA) recommends antibiotic prophylaxis with a second-generation cephalosporin for all vaginal procedures with consideration of additional anaerobic coverage with metronidazole [6]. Other guidelines recommend using a second-generation cephalosporin for all vaginal procedures [6] or conjure insufficient evidence to guide decision-making regarding antibiotics for vaginal procedures [3].

Postoperative infections after gynecologic surgery are often polymicrobial and include gram-negative and anaerobic bacteria [7]. Evidence suggests adding metronidazole to IV cefazolin during benign hysterectomy [8] and hysterectomy for gynecologic cancer staging [9,10] reduces infection risk, but it is unclear if this benefit applies to patients undergoing urogynecologic surgery. There has been no large-scale investigation of perioperative prophylactic antibiotic choice in surgery for POP. This is of clinical importance as surgical site infection (SSI), particularly in the setting of permanent mesh, can be devastating while antibiotic overuse contributes to resistance. The objective of this study was to determine whether rates of postoperative infectious complications after pelvic organ prolapse surgery differ based on perioperative antibiotic administered. In particular, we sought to determine whether the addition of anaerobic coverage is associated with reduced rates of infectious complications. We hypothesized that antibiotic regimens with anaerobic coverage would be associated with reduced rates of infectious complications.

Materials and Methods

The Institutional Review Board deemed this study (STUDY20231395) to be exempt from review.

Data Source and Exposure of Interest

This was a retrospective cohort study of patients curated from the Premier Healthcare Database, undergoing surgery for POP between January 2000 and March 2020. The Premier Healthcare Database is a comprehensive all-payer U. S. healthcare dataset capturing more than 244 million patients across 1,113 nonprofit hospitals from urban and rural areas. This database includes both inpatient and select outpatient encounters (emergency department, ambulatory surgery centers, alternative sites of care) dating back to January 2000. Outpatient diagnosis codes are accessible when patients represent at a hospital-based encounter (inpatient or outpatient) within the same hospital system and are included in this study. Time from index surgery is approximate as encounter month and year are available. The data is derived from patient encounters. Patient-level data includes demographics, International Classification of Diseases, Current Procedural Terminology (CPT) codes, length of stay, readmissions to the same hospital, and a list of billed items including medications (name/dose/route of administration/frequency), laboratory results, and diagnostic testing [11]. Cost data is derived from billed items and is validated.

Inclusion and Exclusion Criteria

The Premier National Database was queried to include all female patients over age 18 who underwent POP surgery between January 2000 to March 2020 using CPT codes: laparoscopic colpopexy, uterosacral suspension, sacrospinous/iliococcygeus suspension, abdominal sacrocolpopexy, anterior repair, posterior repair, combined anterior/posterior repair, enterocele repair, paravaginal repair, obliterative procedures, and insertion of mesh or other prosthesis. Additional procedures permitted included: cystoscopy, lysis of adhesions, abdominal hysterectomy, laparoscopic-assisted vaginal hysterectomy, laparoscopic hysterectomy with robotic assistance, vaginal hysterectomy, and procedures for incontinence. Full details for coding used for classification and analysis can be found in Appendix 1.

Among these patients, only those who received antibiotic regimens in accordance with national guidelines were included in this study. The exposure of interest was perioperative antibiotic regimen associated with index POP encounter, and the most commonly used regimens were compared. Guideline-concordant regimens were classified as: cefazolin only [4,5,12], second-generation cephalosporin (cefoxitin, cefotetan, or cefuroxime) [6,12], clindamycin + aminoglycoside (gentamicin or tobramycin) [4,12], cefazolin + metronidazole [6,12], and other (ampicillin-sulbactam, clindamycin/vancomycin + aminoglycoside/aztreonam/fluoroquinolone, or metronidazole + aminoglycoside/fluoroquinolone) [12]. Because administering perioperative antibiotics at the time of clean-contaminated procedures is the current standard of care, patients who received nonguideline concordant antibiotics and those without perioperative antibiotic data were excluded. Those undergoing concomitant nongynecologic, oncologic, or colorectal surgery at the time of POP surgery were also excluded.

Outcomes

Perioperative antibiotics are indicated to prevent SSI. As such, the primary outcome was occurrence of any SSI (composite of: wound infection, cellulitis, abscess, and

retroperitoneal infection) within 30 days of surgery for procedures without mesh and within 90 days for procedures involving mesh (mid-urethral sling, vaginal mesh, and/or sacrocolpopexy). This is concordant with the U.S. Centers for Disease Control and Prevention and National Healthcare Safety Network definition of surgical site infection (SSI) [13]. We also evaluated other infectious morbidity as a secondary outcome, which was a composite of: urinary tract infection (UTI), sepsis, pneumonia, and sacral osteomyelitis.

Statistical Analysis

Descriptive statistics were expressed as percentages or means with standard deviations. Comparison among antibiotic groups was performed using the Kruskal−Wallis and Chi-Squared tests. Multivariable logistic regression was used to identify variables independently associated with composite SSI and other infectious morbidity. Cefazolin is the most commonly used antibiotic for prophylaxis at the time of gynecologic surgery [4] and was the referent to which all other antibiotic cohorts were compared in the multivariable logistic regression. To evaluate whether menopause status affected outcomes, age was modeled to allow for a nonlinear relationship. Additional variables (obesity, diabetes, tobacco use, Charlson Comorbidity Index [CCI, calculated using ICD codes from 1 year prior to index procedure], and concomitant surgery) were included in the analysis as they have been associated with postoperative infectious morbidity after urogynecologic surgery [14−16]. Subgroup analysis was performed separately for vaginal surgery and sacrocolpopexy.

To account for possible confounding of the relationship between antibiotic regimen and our outcomes of interest, by age, comorbidities, and surgical procedures, we adopted an inverse probability of treatment weighting (IPTW) approach. The goal of this approach is to estimate the average treatment effect of changing from one antibiotic regimen to another and best approximate the causal effect of antibiotic regimen on outcomes. This is achieved in two steps: the first is to weigh the sample such that potential confounding factors are distributed equally between the antibiotic groups; once balance is achieved, the second step is to compare outcomes in the weighted samples and calculate risk differences and odds ratios (OR). The ability to assess balance before comparing outcomes is a particular strength of IPTW, as it reduces the likelihood that differences in outcomes between groups are due to differences in measured confounders [17].

Antibiotic cohorts were balanced for age, obesity, diabetes, tobacco use, CCI, and concurrent surgery using the weight. It package for R [18]. Differences in covariate values between the treatment groups after weighing were assessed by the maximum absolute standardized mean difference (SMD). Pairwise risk differences and marginal ORs were estimated from a weighted logistic regression model using the marginal effects package [19]. Good balance (max SMDs <0.1) was achieved for all covariates, squared age, and two-way interactions (Appendix 2).

Results

Overall Results (All POP Surgeries Included)

Between January 2000 and March 2020, 130,198 patients underwent POP surgery and met criteria for inclusion (Fig. 1). Cefazolin was the most commonly administered antibiotic (n = 97,058, 74.5%) followed by second-generation cephalosporins (n = 16,442, 12.6%), clindamycin + aminoglycoside (n = 8,397, 6.4%) and cefazolin + metronidazole (n = 4,328, 3.3%). The remaining 3972 patients (3.1%) received an alternative guideline-concordant regimen. The clindamycin + aminoglycoside cohort had a higher prevalence of documented penicillin allergy (20.0%). The study population was on average 59.4 years old (SD 13.4), insured by managed care (39.4%) or Medicare (39.2%), and underwent outpatient surgery (95.1%) predominantly in an urban (88.5%), nonteaching facility (62.6%). The majority of procedures were performed in the US Southern region (50.2%), but the population included all U.S. geographic areas. Demographic data and surgical characteristics are included in Tables 1 and 2, respectively. The preferred regimen across all surgeries was cefazolin alone.

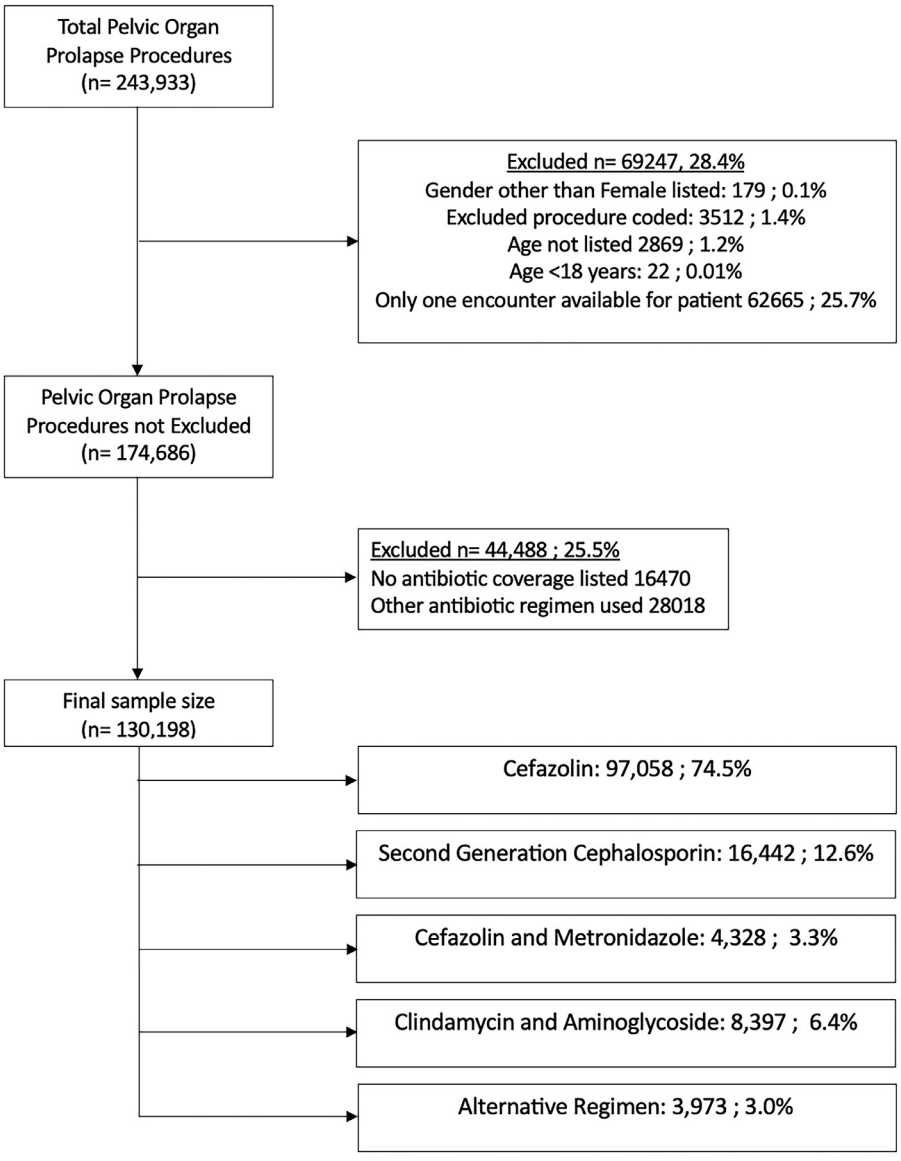
Composite SSI (wound infection, cellulitis, abscess, or retroperitoneal infection) occurred in 1.0% (n = 1,344) of patients. Other infectious morbidity (UTIs, sepsis, pneumonia, and sacral osteomyelitis) occurred in 3.02% (n = 3937) of patients within 30 days which was primarily attributable to UTIs (n = 3767). Table 3 includes detailed complication rates by antibiotic type. Patients receiving cefazolin had significantly fewer other infectious morbidities compared to other antibiotic groups (p <.001). This difference remained significant at 3 months postsurgery (p <.001).

Overall rates of individual complications at 3 months after POP surgery include: 3.7% UTI (n = 4833), 0.33% wound infection (n = 435), 0.25% cellulitis (n = 332), 0.75% abscess (n = 974), 0.24% sepsis (n = 315), 0.03% pneumonia (n = 39), 0.0046% sacral osteomyelitis (n = 6), 3.3% hematoma (n = 4271), 8.5% ER visit (11127), and 1.0% mesh exposure (n = 1301).

After adjusting for covariates (age, obesity, diabetes, tobacco use, CCI score, concomitant procedure type, hysterectomy, insertion of mesh, and antibiotic choice) in a multivariable model, perioperative clindamycin + aminoglycoside was associated with a higher rate of composite SSI (OR = 1.37; 95% CI 1.09−1.72) and other infectious morbidity (OR = 1.26; 95% CI 1.12−1.42) when compared to cefazolin alone. Obesity (OR = 1.22; 95% CI 1.03 −1.43), diabetes without complication (OR = 1.30; 95% CI 1.08−1.57), CCI score >0 (OR = 1.24; 95% CI 1.06−1.45), and tobacco use (OR = 1.22, 95% CI 1.05−1.40) were also

Fig. 1

Flow chart identifying antibiotic groups after exclusion criteria applied.



associated with increased rate of composite SSI (Tables 4 and 5). Antibiotic choice did not significantly interact with age group (≤40, 41−59, and ≥60) (p = .92), suggesting that differences in the odds of the composite SSI outcome between regimens were relatively consistent across age. Hysterectomy was not significantly associated with composite SSI or other infectious morbidity. On IPTW analysis, all antibiotic groups were well-matched for preoperative characteristics, and the probability of composite SSI and other infectious morbidity remained higher with clindamycin + aminoglycoside when compared to cefazolin alone. Details of additional IPTW analyses can be found in Appendix 3.

Vaginal POP Surgery

Of the 108,679 procedures performed vaginally for POP, the unadjusted rate of composite SSI was 1.04%. After adjusting for covariates, only perioperative use of clindamycin + aminoglycoside at the time of vaginal surgery for POP was associated with a higher rate of composite SSI (OR = 1.33; 95% CI 1.04−1.7) and other infectious morbidity (OR = 1.26; 95% CI 1.10−1.44) when compared to cefazolin alone. On IPTW analysis of vaginal procedures, the probability of composite SSI and other infectious morbidity remained higher with clindamycin + aminoglycoside when compared to

Table 1

Demographic characteristics

Characteristic	Perioperative antibiotic regimen received					p-value
	cefazolin (n = 97,058)	Second-generation cephalosporin (n = 16,442)	Clindamycin + aminoglycoside (n = 8,397)	Cefazolin + metronidazole (n = 4,328)	Other (n = 3972)	
Age (y)	59.4 ± 13.4	58.8± 13.5	60.4± 13.2	57.9± 13.5	60.9± 13.3	<.001
Race or ethnicity						<.001
Black	4.8% (4648)	4.1% (669)	5.1% (426)	4.6% (200)	3.5% (140)	
Hispanic	7.5% (7327)	5.6% (921)	6.4% (536)	7.0% (302)	5.1% (203)	
White	78.6% (76300)	81.4% (13389)	79.9% (6706)	77.3% (3346)	82.4% (3271)	
None of the above	9.0% (8783)	8.9% (1463)	8.7% (729)	11.1% (480)	9.0% (359)	
Obesity	10.8% (10503)	10.4% (1705)	11.7% (982)	13.9% (603)	13.3% (527)	<.001
Tobacco use	18.8% (18237)	20.5% (3371)	20.2% (1695)	22.4% (970)	19.6% (778)	<.001
Penicillin allergy	2.1% (2053)	3.2% (529)	20.0% (1682)	2.7% (119)	14.4% (573)	<.001
MRSA colonization	0.05% (47)	0.05% (8)	0.07% (6)	0.02% (1)	0.1% (4)	0.49
Charlson Comorbidity Index Score	1.9 ± 1.5	1.9 ± 1.5	2.1 ± 1.5	1.8 ± 1.5	2.1 ± 1.5	<.001
Insurance type						<.001
Managed care	39.1% (37908)	43.0% (7078)	38.0% (3187)	38.9% (1683)	34.8% (1382)	
Medicare	39.2% (38054)	37.0% (6077)	43.4% (3648)	35.3% (1526)	44.3% (1761)	
Medicaid	6.9% (6675)	7.0% (1159)	6.3% (527)	9.2% (399)	7.5% (296)	
Commercial	9.2% (8959)	8.0% (1311)	7.0% (586)	11.9% (513)	8.5% (338)	
Self-pay	1.2% (1185)	0.86% (142)	0.89% (75)	1.1% (46)	0.68% (27)	
Other	4.4% (4277)	4.1% (675)	4.5% (374)	3.7% (161)	4.3% (169)	
Geographic region						<.001
South	50.5% (48979)	50.2% (8256)	52.5% (4410)	36.5% (1581)	52.6% (2088)	
Midwest	21.6% (20930)	21.4% (3516)	22.4% (1881)	22.2% (959)	20.5% (814)	
West	19.7% (19117)	23.6% (3878)	12.6% (1056)	24.1% (1041)	15.1% (632)	
Northeast	8.3% (8032)	4.8% (792)	12.5% (1050)	17.3% (747)	11.1% (439)	
Procedure setting						<.001
Outpatient	95.1% (92342)	93.3% (15334)	97.4% (8182)	97.3% (4210)	93.6% (3716)	
Inpatient	4.9% (4716)	6.7% (1108)	2.6% (215)	2.7% (118)	6.5% (257)	
Urban-rural						<.001
Urban	89.1% (86456)	83.2% (13683)	90.9% (7636)	93.5% (4048)	86.2% (3424)	
Rural	10.9% (10602)	16.8% (2759)	9.1% (761)	6.5% (280)	13.8% (549)	
Facility type						<.001
Nonteaching Facility	62.1% (60297)	67.3% (11062)	57.8% (4853)	61.8% (2675)	65.3% (2592)	
Teaching facility	37.9% (36761)	32.7% (5380)	42.2% (3544)	38.2% (1653)	34.8% (1381)	

Values are % (n) or mean ± SD.

Table 2

Surgical characteristics

Characteristic	Perioperative antibiotic regimen received					p-value
	Cefazolin (n = 97,058)	Second-generation cephalosporin (n = 16,442)	Clindamycin + aminoglycoside (n = 8,397)	Cefazolin + metronidazole (n = 4,328)	Other (n = 3972)	
Surgery type						
Laparoscopic colpopexy (n = 20513)	16% (15371)	13% (2148)	16% (1356)	25% (1068)	14% (570)	<.001
Abdominal sacrocolpopexy (n = 1011)	0.6% (582)	1.7% (282)	1.1% (92)	0.37% (16)	0.98% (39)	<.001
Uterosacral suspension (n = 11969)	8.7% (8428)	11% (1774)	9.1% (761)	14% (622)	9.7% (384)	<.001
Sacrospinous ligament suspension (n = 16913)	13% (12475)	12% (1981)	17% (1397)	13% (542)	13% (518)	<.001
Anterior repair (n = 29347)	23% (22227)	22% (3574)	21% (1780)	17% (735)	26% (1031)	<.001
Posterior repair (n = 25528)	20% (19096)	19% (3138)	20% (1664)	19% (821)	20% (809)	.21
Combined anterior/posterior repair (n = 41121)	31% (30331)	34% (5642)	33% (2751)	29% (1237)	29% (1160)	<.001
Vaginal enterocele repair (n = 17157)	4.5% (4416)	4.9% (803)	4.7% (398)	3.6% (157)	3.5% (139)	<.001
Additional enterocele repair (n = 11244)	8.4% (8168)	8.9% (1467)	11% (921)	7.8% (336)	8.9% (352)	<.001
Paravaginal repair (n = 3809)	2.8% (2755)	3.4% (137)	3.4% (287)	3.6% (156)	3.4% (137)	<.001
Obliterative procedures (n = 4888)	3.9% (3767)	3.1% (516)	3.8% (317)	3% (132)	3.9% (156)	<.001
Insertion of mesh or other prosthesis (n = 14772)	11% (10680)	11% (1809)	12% (1000)	16% (677)	15% (606)	<.001
Sling procedures (n = 49134)	38% (36653)	36% (5932)	40% (3362)	36% (1542)	41% (1645)	<.001
Concomitant procedures						
Abdominal hysterectomy (n = 931)	0.53% (518)	0.63% (25)	0.63% (25)	0.63% (25)	0.63% (25)	<.001
Laparoscopic hysterectomy (n = 19249)	15% (14167)	12% (2012)	15% (1242)	31% (1323)	13% (505)	<.001
Robot-assisted (n = 5417)	4.2% (4057)	3.4% (555)	4.4% (368)	7% (303)	3.4% (134)	<.001
Laparoscopic assisted vaginal hysterectomy (n = 11334)	8.6% (8390)	9.9% (1635)	8.6% (721)	8.7% (376)	5.3% (212)	<.001
Vaginal hysterectomy (n = 24873)	20% (18935)	19% (3068)	17% (1415)	19% (808)	16% (647)	<.001
Lysis of adhesions (n = 182)	0.13% (123)	0.21% (34)	0.11% (9)	0.25% (11)	0.13% (5)	.024
Burch colposuspension (n = 418)	0.32% (308)	0.42% (69)	0.26% (22)	0.069% (3)	0.4% (16)	.004
Cystoscopy (n = 7767)	5.9% (5731)	5.8% (961)	5.6% (469)	7.6% (328)	7% (278)	<.001

Values are % (n) or mean ± SD.

cefazolin alone and when compared with second-generation cephalosporins (Appendix 3).

Sacrocolpopexy

When analyzing the 11,215 sacrocolpopexy procedures performed, the unadjusted rate of composite SSI was 1.2% (n = 133) and did not differ significantly across cohorts (p 0.11). After adjusting for covariates, no perioperative antibiotic regimen was associated with a higher rate of composite SSI when compared to cefazolin alone. On IPTW analysis of sacrocolpopexy, there was no difference in the probability of composite SSI across antibiotic groups (Appendix 3).

Comment

In this large U.S. study, cefazolin was the most common perioperative antibiotic for POP surgery (74.5%), consistent with ACOG [4] and AUGS-IUGA urogynecology clinical consensus guidelines [5]. Given the predominantly anaerobic nature of the vaginal microbiome [20,21], we hypothesized that the addition of anaerobic coverage to perioperative cefazolin during POP surgery would be beneficial. This approach has been effective in reducing SSIs for hysterectomy [8−10], but our analysis did not support this hypothesis for POP surgeries. Alternative guideline-adherent antibiotics, including those offering additional anaerobic coverage, were not associated with reduced risk of postoperative infections compared with cefazolin alone.

Similar to an analysis of POP surgery using the American College of Surgeons National Surgical Quality Improvement Program database [22] by Erekson et al., our study had a low rate of composite SSI after POP surgery (1.0%) compared to other studies (11%−18.5%) [23,24]. Obesity, tobacco use, diabetes, and CCI score were associated with increased rates of SSI, while concomitant hysterectomy and age were not independently associated. Sacrocolpopexy showed no significant difference in SSI rates among antibiotic groups, possibly due to the relatively small number of SSIs in this subgroup and the resulting lack of statistical power.

Antibiotic prophylaxis has been key to preventing SSIs, but concerns about emergence of antimicrobial resistance necessitate reevaluation [25]. Only two prospective studies have investigated perioperative antibiotics for POP surgery, but neither was powered to detect a difference in

Table 3

Complication rates after POP surgery by perioperative antibiotic cohort

All POP procedures (n = 130,198)	Perioperative antibiotic regimen received					p-value
	Cefazolin (n = 97058)	Second-generation cephalosporin (n = 16442)	Clindamycin + aminoglycoside (n = 8397)	Cefazolin + metronidazole (n = 4328)	Other (n = 3972)	
Composite SSI	1.0% (986)	0.95% (156)	1.4% (115)	1.1% (49)	0.96% (38)	.023
Other infectious morbidity (within 30 days)	2.9% (2837)	3.1% (506)	3.9% (325)	3.1% (136)	3.3% (133)	<.001
Other infectious morbidity (within 90 days)	3.8% (n = 3655)	4.0% (658)	4.8% (407)	3.9% (167)	4.1% (163)	<.001
Vaginal procedures for POP (n = 108,679)	**Perioperative antibiotic regimen received**					**p-value**
	Cefazolin (n = 81110)	Second-generation cephalosporin (n = 14012)	Clindamycin + aminoglycoside (n = 6949)	Cefazolin + metronidazole (n = 3244)	Other (n = 3364)	
Composite SSI	1.0% (840)	0.92% (129)	1.4% (95)	0.99% (32)	0.95% (32)	.049
Other infectious morbidity (within 30 days)	3.0% (2463)	3.2% (443)	4.0% (277)	3.1% (101)	3.5% (118)	<.001
Other infectious morbidity (within 90 days)	3.9% (3184)	4.1% (571)	5.1% (352)	3.9% (128)	4.4% (147)	<.001
Sacrocolpopexy (n = 11,215)	**Perioperative antibiotic regimen received**					**p-value**
	Cefazolin (n = 8068)	Second-generation cephalosporin (n = 1469)	Clindamycin + aminoglycoside (n = 702)	Cefazolin + metronidazole (n = 624)	Other (n = 352)	
Composite SSI	1.1% (89)	1.2% (17)	1.7% (12)	2.1% (13)	0.57% (2)	.11
Other infectious morbidity (within 30 days)	2.0% (160)	3.1% (46)	2.6% (18)	2.2% (17)	2.0% (7)	.083
Other infectious morbidity (within 90 days)	2.6% (210)	4.1% (60)	3.0% (21)	2.7% (17)	2.3% (8)	.034

Table 4

Multivariable logistic regression of composite SSI for POP surgery [1]

Characteristic	Adjusted OR (95% CI)
Obesity	1.22 (1.03−1.43)
Diabetes with complication	0.65 (0.36−1.18)
Diabetes without complication	1.30 (1.08−1.57)
Tobacco use	1.22 (1.05−1.40)
CCI Score >0	1.24 (1.06−1.45)
Laparoscopic colpopexy	0.78 (0.62−0.97)
Uterosacral ligament suspension	0.57 (0.44−0.75)
Sacrospinous ligament suspension	0.66 (0.53−0.81)
Abdominal sacrocolpopexy	1.22 (0.76−1.96)
Anterior repair	0.89 (0.69−1.16)
Posterior repair	1.03 (0.82−1.31)
Combined anterior/ posterior repair	0.93 (0.74−1.16)
Enterocele repair	0.87 (0.65−1.17)
Obliterative procedures	1.04 (0.74−1.46)
Paravaginal repair	1.10 (0.68−1.79)
Insertion of mesh or other prosthesis	1.10 (0.82−1.46)
Hysterectomy	1.20 (0.95−1.52)
Antibiotic Cefazolin*	
Second-generation cephalosporin	0.91 (0.72−1.16)
Clindamycin + aminoglycoside	1.37 (1.09−1.72)
Cefazolin + metronidazole	1.09 (0.82−1.45)
Other regimen	0.94 (0.68−1.31)

OR, odds ratio; CI, confidence interval; CCI, Charlson Comorbidity Index.
In addition to all variables listed in the table, age modeled via a natural cubic spline with six degrees of freedom was included in the final analysis.
* Referent.

Table 5

Multivariable logistic regression of infectious morbidity within 90 days of POP surgery [1]

Characteristic	Adjusted OR (95% CI)
Obesity	1.28 (1.15−1.41)
Diabetes with complication	1.85 (1.57−2.18)
Diabetes without complication	1.33 (1.21−1.46)
Tobacco Use	1.14 (1.05−1.24)
CCI Score >0	1.35 (1.23−1.47)
Laparoscopic colpopexy	0.93 (0.81−1.07)
Uterosacral ligament suspension	0.95 (0.74−1.22)
Sacrospinous ligament suspension	0.98 (0.88−1.10)
Abdominal sacrocolpopexy	0.93 (0.63−1.38)
Anterior repair	1.26 (1.10−1.45)
Posterior repair	0.91 (0.81−1.02)
Combined anterior/posterior repair	1.32 (1.14−1.52)
Enterocele repair	0.97 (0.80−1.17)
Obliterative procedures	1.06 (0.90−1.25)
Paravaginal repair	1.22 (1.00−1.50)
Insertion of mesh or other prosthesis	0.99 (0.86−1.14)
Hysterectomy	0.95 (0.85−1.05)
Antibiotic cefazolin*	
Second-generation cephalosporin	1.06 (0.77−1.47)
Clindamycin + aminoglycoside	1.26 (1.12−1.42)
Cefazolin + metronidazole	1.06 (0.75−1.52)
Other regimen	1.03 (0.85−1.24)

OR, odds ratio; CI, confidence interval; CCI, Charlson Comorbidity Index.
In addition to all variables listed in the table, age modeled via a natural cubic spline with six degrees of freedom was included in the final analysis.
* Referent.

postoperative infections [2,26]. Our study contributes to the literature by demonstrating that alternative antibiotic regimens were not associated with a reduction in composite SSI or other infectious morbidity when compared to cefazolin alone. Despite adjusting for hysterectomy and age at time of POP surgery, the addition of metronidazole to cefazolin did not appear to confer a clinically or statistically significant reduction in postoperative complications, questioning its necessity at the time of POP surgery. Contrary to other literature on broadening antibiotic prophylaxis at time of hysterectomy [8−10], the findings among the predominantly postmenopausal population of this study may support further research into protective features unique to an older cohort. Though overall infectious complications remain low across all antibiotic groups, thoughtful perioperative antibiotic choice remains warranted to minimize harm while continuing to maximize benefit.

For cephalosporin-allergic patients, clindamycin + aminoglycoside is a recommended alternative. Yet, higher rates of composite SSI and other infectious morbidity were seen with clindamycin + aminoglycoside in this study. While gentamicin, an aminoglycoside, broadens gram-negative coverage, its efficacy relies on precise dosing (5 mg/kg) to achieve peak concentrations. Gentamicin underdosing (due to miscalculating weight, rounding down doses, or nephrotoxicity concerns [27]) compromises efficacy and contributes increased infectious morbidity [28]. Clindamycin, a lincosamide targeting gram-positive bacteria and certain anaerobes, has a wider therapeutic window, but judicious prescribing remains crucial to avoid resistance. Further evaluation comparing noncephalosporin and nonpenicillin alternatives is warranted to comprehensively assess surgical prophylaxis in penicillin-allergic patients. Finally, assessing for true allergies remains prudent to optimize appropriate antibiotic choice.

We offer a large dataset (n = 130,198) with patient follow-up across inpatient and outpatient encounters capturing the diverse procedural landscape of POP surgery, including mesh utilization and concurrent hysterectomy. To balance underlying differences and adjust for selection bias, IPTW was performed to supplement regression findings. Limitations include the retrospective design, reliance on chart review where documentation errors are possible, and potential residual confounding by unmeasured factors. The inability to confirm appropriate time-intervals for antibiotic administration remains a critical limitation. Because nonhospital-based clinical encounters are not included in this database, infectious outcomes commonly diagnosed in the office setting (UTIs, cellulitis) may be underestimated while infectious outcomes detected in hospital settings may be overrepresented. Furthermore, patients with complications who were presented to an unaffiliated hospital system would not be captured in this study. We observed significant demographic differences between antibiotic cohorts, suggesting potential selection bias. Finally, because patients without perioperative antibiotics were excluded from this study, no conclusions regarding the necessity of antibiotics at the time of POP surgery can be drawn.

Cefazolin alone is the most widely used regimen and may be sufficient to limit the risk of SSIs and other infectious morbidity after POP surgery. The addition of anaerobic coverage, such as metronidazole, to reduce infectious complications at the time of POP surgery with or without hysterectomy is not supported by the results of this study.

Summation

Compared to cefazolin, alternative guideline-adherent regimens did not significantly reduce the rate of infectious morbidity after prolapse surgery in this U.S. national database of patients.

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Appendix 1: Codes for identification, classification, and analysis

Inclusion

Procedure	CPT Code
Laparoscopic Colpopexy	57425
Uterosacral Suspension	57283
Sacrospinous/Ileococcygeus suspension	57282
Abdominal Sacrocolpopexy	57280
Anterior repair	57240
Posterior Repair	57250
Combined APR	57260, 57265
Vaginal Enterocele Repair	57268
Additional Enterocele codes	57270, 57265
Obliterative Procedures	57110, 57120
Paravaginal repair	57284, 57285
Insertion of Mesh or Other Prosthesis	57267
Cystoscopy	52000
Lysis of adhesions	44180, 44005, 58660, 58740, 44200
Abdominal hysterectomy	58150, 58152, 58180
Laparoscopic-assisted vaginal hysterectomy	58550, 58552, 58553, 58554
Laparoscopic hysterectomy	58570-58573, 58541-58544, 58575
With robotic assistance	S2900
Vaginal hysterectomy	58260, 58262, 58263, 58267, 58270, 58275, 58280, 58285, 58290-58294
Procedures for incontinence	57287, 57288, 51840, 51841

Exclusion

Procedure	CPT Code
Surgery for malignancy	58200, 58943, 58548, 58285, 58210, 56633, 56634, 56630-56632, 179, 180.X, 181, 182.X, 183.X, 184.X, 233.XX, 236.X, C51.X-C58.X
Colorectal surgery	441xx, 442xx, 44xx, 50810, 57307, 445xx, 446xx

Perioperative Complications

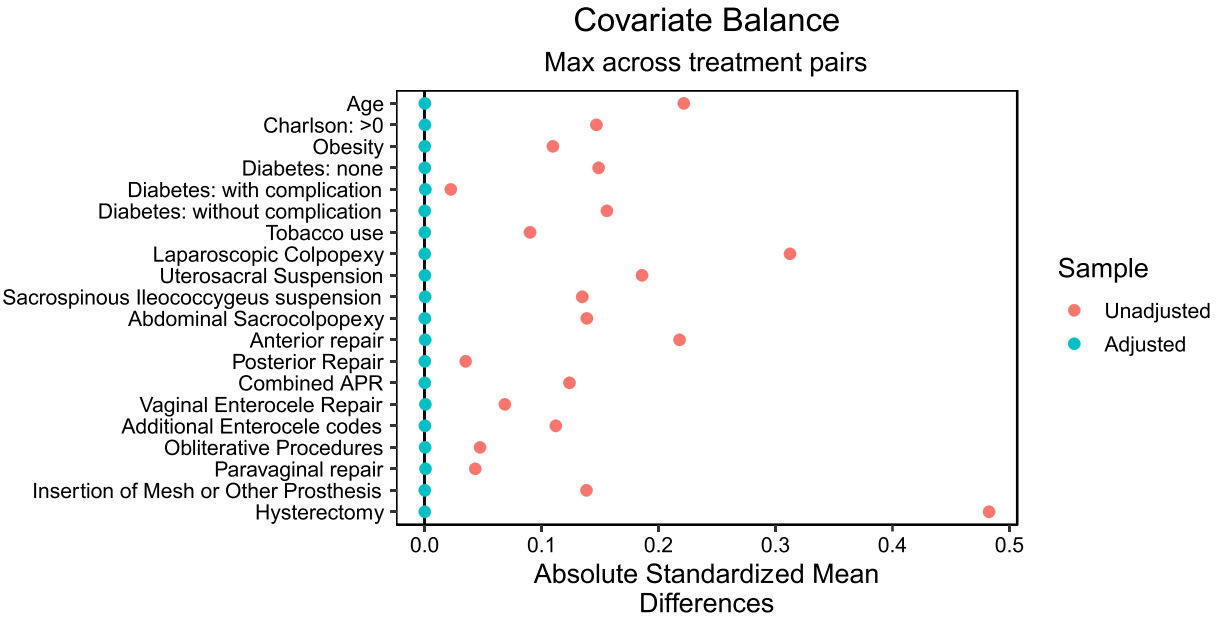
SSI	ICD-9	ICD-10	CPT code
Wound infection	998.5-998.59	T81.4, T81.41 (superficial), T81.42 (Deep), T81.43(organ), T81.49 (NOS) (All have letters XA, XD, XS to follow)	
Cellulitis	682.2, 682.9		
Abscess	567.2, 567.9, 614.3, 614.4, 682.2, 567.21, 567.22, 567.29, 616.10	K65.1, K63.0, K65.0, K65.8, K68.9, K68.19, K68.12, K67.19, L02.212, L02.215, L02.216, N34.0, L02.214	Abscess drainage: 51080, 10060, 10061, 10180, 10140−10180, 11000, 11001, 11005 11008 11040 −11044, 20000, 49040, 49041, 49060, 4906
Retroperitoneal infection	567.3-567.39		
Erosion of mesh into pelvic and non-pelvic organs	629.31, 629.32	T83.711, T83.712, T83.7, T83.718	
Urinary tract infection	599.0	N39.0	

Charge Codes for Individual Antibiotics

Antibiotic	Std_chg_code
Cefazolin	250250010110000
	250250010120000
	250250010130000
	250250010140000
	250250010150000
	250250010160000
	250250010170000
	250250010180000
	250250010190000
	250250010200000
	250250010210000
	250250010220000
	250888003440000
	250999002770000
Cefotetan	250999002850000
	250250010580000
	250250010590000
	250250010600000
	250250010610000
	250250010620000
	250888003520000
	250999002850000
Cefoxitin	250250010630000
	250250010640000
	250250010650000
	250250010660000
	250250010670000
	250250010680000
	250250010690000
	250250010700000
	250250010710000
	250888003530000
	250999002860000
Cefuroxime	250999002930000
	250250011320000
	250250011330000
	250250011340000
	250250011350000
	250250011360000
	250250011370000
	250888003640000
Ampicillin-sulbactam	250250003320000
	250250003330000
	250250003340000
	250250003350000
	250250003360000
	250250003370000
Metronidazole	250250042720000
	250250042730000
	250250042740000
	250250042750000
	250888013810000
	250999011510000
Clindamycin	250250014050000
	250250014060000
	250250014070000
	250250014080000
	250250014170000
	250250014180000
	250250014190000
	250250014200000
	250888004430000
Aminoglycoside (Gentamicin or tobramycin)	Gentamicin: 250250028490000
	250250028500000
	250250028510000
	250250028530000
	250250028540000
	250250028550000
	250250028560000
	250250028570000
	250250028580000
	250250028590000

	250250028600000
	250250028610000
	250250028620000
	250250028630000
	250888009410000
	Tobramycin:
	250250063150000
	250250063160000
	250250063170000
	250250063180000
	250250063190000
	250250063200000
	250250063210000
	250250063220000
	250250063230000
	250250063240000
	250250063250000
	250250063260000
	250250063270000
	250250063280000
	250250063290000
	250250101820000
	250888021000000
Vancomycin	250250065800000
	250250065810000
	250250065840000
	250250065850000
	250250065860000
	250250065870000
	250250065930000
	250250065940000
	250250065950000
	250250065960000
	250888022050000
	250999018570000
Aztreonam	250888001860000
	250999001360000
	250250005250000
	250250005260000
	250250005270000
	250250005280000
	250250005290000
	250250005300000
Fluoroquinolone	Ciprofloxacin:
(Ciprofloxacin or Levofloxacin)	250250013620000
	250250013630000
	250250013680000
	250250013690000
	250888004280000
	250999003480000
	Levofloxacin:
	250250037000000
	250250037010000
	250250037040000
	250250103790000
	250250104050000
	250250108380000
	250888012010000
	250999010110000

Appendix 2: Covariate Balance of Standardized Mean Differences



Appendix 3: Inverse Probability of Treatment Weighing Analysis

Appendix Table 1: Pairwise ORs of composite SSI after IPTW for entire sample

Antibiotic cohort comparisons	OR	95% CI	p value
ln(odds(Other regimen)/odds(Cefazolin))	0.99	0.72−1.39	.986
ln(odds(Second Gen. Cephalosporins)/odds(Cefazolin))	0.92	0.77−1.09	.310
ln(odds(Clindamycin + Aminoglycoside)/odds(Cefazolin))	1.38	1.13−1.68	.001
ln(odds(Cefazolin + Metronidazole)/odds(Cefazolin))	1.05	0.77−1.44	.757
ln(odds(Second Gen. Cephalosporins)/odds(Other regimen))	0.92	0.64−1.32	.644
ln(odds(Clindamycin + Aminoglycoside)/odds(Other regimen))	1.38	0.95−2.01	.093
ln(odds(Cefazolin + Metronidazole)/odds(Other regimen))	1.05	0.67−1.66	.818
ln(odds(Clindamycin + Aminoglycoside)/odds(Second Gen. Cephalosporins))	1.51	1.18−1.93	.001
ln(odds(Cefazolin + Metronidazole)/odds(Second Gen. Cephalosporins))	1.15	0.81−1.63	.435
ln(odds(Cefazolin + Metronidazole)/odds(Clindamycin + Aminoglycoside))	0.76	0.53−1.10	.144

CI = confidence interval; SSI = surgical site infection; IPTW = inverse probability of treatment weighing.

Appendix Table 2: Pairwise ORs of other infectious morbidity after IPTW in entire sample

Antibiotic Cohort Comparisons	OR	95% CI	p value
ln(odds(Other regimen)/odds(Cefazolin))	0.97	0.82−1.15	.722
ln(odds(Second Gen. Cephalosporins)/odds(Cefazolin))	1.05	0.96- 1.14	.263
ln(odds(Clindamycin + Aminoglycoside)/odds(Cefazolin))	1.27	1.14−1.42	.000
ln(odds(Cefazolin + Metronidazole)/odds(Cefazolin))	0.99	0.84−1.18	.965
ln(odds(Second Gen. Cephalosporins)/odds(Other regimen))	1.08	0.90−1.30	.394
ln(odds(Clindamycin + Aminoglycoside)/odds(Other regimen))	1.31	1.08−1.59	.006
ln(odds(Cefazolin + Metronidazole)/odds(Other regimen))	1.03	0.81−1.30	.826
ln(odds(Clindamycin + Aminoglycoside)/odds(Second Gen. Cephalosporins))	1.21	1.07−1.38	.003
ln(odds(Cefazolin + Metronidazole)/odds(Second Gen. Cephalosporins))	0.95	0.79−1.14	.579
ln(odds(Cefazolin + Metronidazole)/odds(Clindamycin + Aminoglycoside))	0.78	0.64−0.95	.015

CI = confidence interval; SSI = surgical site infection; IPTW = inverse probability of treatment weighing.

Appendix Table 3: Pairwise ORs of composite SSI after IPTW in vaginal procedures

Antibiotic Cohort Comparisons	ORs	95% CI	p value
ln(odds(Other regimen)/odds(Cefazolin))	0.96	0.67−1.37	.808
ln(odds(Second Gen. Cephalosporins)/odds(Cefazolin))	0.88	0.73−1.06	.182
ln(odds(Clindamycin + Aminoglycoside)/odds(Cefazolin))	1.34	1.08−1.66	.009
ln(odds(Cefazolin + Metronidazole)/odds(Cefazolin))	0.95	0.66−1.37	.787
ln(odds(Second Gen. Cephalosporins)/odds(Other regimen))	0.92	0.62−1.37	.686
ln(odds(Clindamycin + Aminoglycoside)/odds(Other regimen))	1.40	0.93−2.11	.112
ln(odds(Cefazolin + Metronidazole)/odds(Other regimen))	0.99	0.60−1.65	.984
ln(odds(Clindamycin + Aminoglycoside)/odds(Second Gen. Cephalosporins))	1.52	1.16−1.98	.002
ln(odds(Cefazolin + Metronidazole)/odds(Second Gen. Cephalosporins))	1.08	0.73−1.61	.706
ln(odds(Cefazolin + Metronidazole)/odds(Clindamycin + Aminoglycoside))	0.71	0.47−1.08	.108

CI = confidence interval; SSI = surgical site infection; IPTW = inverse probability of treatment weighing.

Appendix Table 4: Pairwise ORs of other infectious morbidity after IPTW in vaginal procedures

Antibiotic Cohort Comparisons	OR	95% CI	p value
ln(odds(Other regimen)/odds(Cefazolin))	1.01	0.84−1.20	.955
ln(odds(Second Gen. Cephalosporins)/odds(Cefazolin))	1.04	0.95−1.13	.460
ln(odds(Clindamycin + Aminoglycoside)/odds(Cefazolin))	1.26	1.12−1.41	.000
ln(odds(Cefazolin + Metronidazole)/odds(Cefazolin))	0.96	0.80−1.16	.676
ln(odds(Second Gen. Cephalosporins)/odds(Other regimen))	1.03	0.85−1.25	.763
ln(odds(Clindamycin + Aminoglycoside)/odds(Other regimen))	1.25	1.02−1.53	.031
ln(odds(Cefazolin + Metronidazole)/odds(Other regimen))	0.96	0.75−1.23	.727
ln(odds(Clindamycin + Aminoglycoside)/odds(Second Gen. Cephalosporins))	1.21	1.06−1.39	.006
ln(odds(Cefazolin + Metronidazole)/odds(Second Gen. Cephalosporins))	0.93	0.76−1.14	.470
ln(odds(Cefazolin + Metronidazole)/odds(Clindamycin + Aminoglycoside))	0.77	0.62−0.95	.013

CI = confidence interval; SSI = surgical site infection; IPTW = inverse probability of treatment weighing.

Appendix Table 5: Pairwise ORs of composite SSI after IPTW in sacrocolpopexy

Antibiotic Cohort Comparisons	OR	95% CI	p value
ln(odds(Other regimen)/odds(Cefazolin))	0.58	0.13−2.55	.469
ln(odds(Second Gen. Cephalosporins)/odds(Cefazolin))	0.92	0.54−1.56	.757
ln(odds(Clindamycin + Aminoglycoside)/odds(Cefazolin))	1.55	0.84−2.85	.163
ln(odds(Cefazolin + Metronidazole)/odds(Cefazolin))	1.60	0.80−3.21	.182
ln(odds(Second Gen. Cephalosporins)/odds(Other regimen))	1.59	0.339−7.46	.556
ln(odds(Clindamycin + Aminoglycoside)/odds(Other regimen))	2.67	0.55−12.93	.221
ln(odds(Cefazolin + Metronidazole)/odds(Other regimen))	2.77	0.56−12.87	.214
ln(odds(Clindamycin + Aminoglycoside)/odds(Second Gen. Cephalosporins))	1.68	0.79−3.57	.177
ln(odds(Cefazolin + Metronidazole)/odds(Second Gen. Cephalosporins))	1.74	0.77−3.96	.184
ln(odds(Cefazolin + Metronidazole)/odds(Clindamycin + Aminoglycoside))	1.04	0.43−2.49	.934

CI = confidence interval; SSI = surgical site infection; IPTW = inverse probability of treatment weighing.

Appendix Table 6: Pairwise ORs of other infectious morbidity after IPTW in sacrocolpopexy

Antibiotic Cohort Comparisons	OR	95% CI	p value
ln(odds(Other regimen)/odds(Cefazolin))	0.66	0.31−1.38	.268
ln(odds(Second Gen. Cephalosporins)/odds(Cefazolin))	1.63	1.21−2.19	.001
ln(odds(Clindamycin + Aminoglycoside)/odds(Cefazolin))	1.14	0.72−1.81	.578
ln(odds(Cefazolin + Metronidazole)/odds(Cefazolin))	1.29	0.71−2. 34	.404
ln(odds(Second Gen. Cephalosporins)/odds(Other regimen))	2.48	1.14−5.42	.022
ln(odds(Clindamycin + Aminoglycoside)/odds(Other regimen))	1.74	0.74−4.10	.206
ln(odds(Cefazolin + Metronidazole)/odds(Other regimen))	1.97	0.77−5.02	.157
ln(odds(Clindamycin + Aminoglycoside)/odds(Second Gen. Cephalosporins))	0.70	0.42−1.17	.173
ln(odds(Cefazolin + Metronidazole)/odds(Second Gen. Cephalosporins))	0.79	0.42−1.50	.474
ln(odds(Cefazolin + Metronidazole)/odds(Clindamycin + Aminoglycoside))	1.13	0.55−2.35	.740

CI = confidence interval; SSI = surgical site infection; IPTW = inverse probability of treatment weighing.