GMR
The Original

PREVALENCE OF EXTENDED-SPECTRUM BETA-LACTAMASE AND CARBAPENEMASE-ENCODING GENES IN SURGICAL SITE INFECTION ISOLATES: IMPLICATIONS FOR SURGICAL ANTIMICROBIAL PROPHYLAXIS

Dr B S Satish Rao[1], Dr. Saritha Satish Rao[2], *Dr Abiramasundari V K[3], Dr Mohd Aadam Bin Najeeb[4], Dr Narayan Kamath[5], Dr. Abhishek Chyawan Jha[6]

[1]Professor, Department of Surgery, Dr Chandramma Dayananda Sagar Institute of Medical Education & Research (CDSIMER), Harohalli, Bangalore South District, Dayananda Sagar University, (https://orcid.org/0009-0001-4289-6170), [2]Professor, Department of Microbiology, Sri Siddhartha Institute of Medical Sciences & Research Centre,T. Begur, Nelamangala Taluk, Bangalore Rural, Sri Siddhartha Academy of Higher Education (SSAHE), (https://orcid.org/0000-0001-8689-1470) [3] Associate professor, Department of Microbiology, Rajalakshmi Medical College Hospital and Research Institute (https://orcid.org/0000 0001 7362 5106) [4]Assistant Professor, Department of Microbiology, NAMO Medical Education and Research Institute, Silvassa, (https://orcid.org/0009-0000-8730-9411), [5]Professor, Department of Microbiology, NAMO Medical Education and Research Institute, Silvassa (https://orcid.org/0000-0002-8090-0409), [6]Post Graduate Resident, Department of Microbiology, NAMO Medical Education and Research Institute, Silvassa. (https://orcid.org/0009-0002-7361-3134),
***Corresponding Author:** Dr Abiramasundari V K abiofficefiles@gmail.com

ABSTRACT

Background: Cefazolin remains the guideline-recommended agent for surgical antimicrobial prophylaxis in most procedures, but Indian practice has drifted towards third-generation cephalosporins, and the prevalence of extended-spectrum β-lactamase (ESBL) and carbapenemase determinants among the organisms that cause surgical site infection (SSI) is largely unquantified at the level of individual institutions. Prophylaxis policy cannot be rationally set without those data.

Objectives: To determine the prevalence of ESBL- and carbapenemase-encoding genes among Gram-negative isolates from post-surgical wound infections at a tertiary care institute, to describe their distribution by surgical specialty, wound class and study quarter, and to quantify the in vitro coverage that candidate prophylaxis regimens would provide against these organisms.

Methods: A prospective observational study was conducted jointly by the Departments of Microbiology and Surgery at NAMO Medical Education and Research Institute, Silvassa, over twelve months from July 2025 to July 2026. SSI was defined by CDC/NHSN criteria. Gram-negative isolates underwent identification and susceptibility testing interpreted per CLSI M100, and multiplex PCR for blaCTX-M, blaTEM, blaSHV, blaNDM, blaOXA-48, blaKPC, blaVIM, blaIMP, blaOXA-23 and blaOXA-51. The prophylactic regimen administered was recorded prospectively. Prevalence is reported with Wilson 95% confidence intervals; trends across quarters were tested by the Cochran–Armitage test. Prophylaxis–pathogen discordance was defined as recovery of an isolate non-susceptible in vitro to the agent the patient had actually received. Coverage of candidate regimens was modelled at isolate level, a regimen counting as covering an isolate if that isolate was susceptible to any component.

Results: Of 2,184 procedures monitored, 178 met criteria for SSI (8.15%; 95% CI 7.10–9.40); 156 were culture-positive, yielding 187 isolates, of which 135 (72.2%) were Gram-negative. Among 88 Enterobacterales, 56 (63.6%; 95% CI 53.2–72.9) carried an ESBL determinant and 28 (31.8%; 95% CI 23.0–42.1) a carbapenemase determinant. blaCTX-M predominated (47; 53.4%), followed by blaTEM (39; 44.3%) and blaSHV (22; 25.0%); blaNDM (17; 19.3%) and blaOXA-48 (13; 14.8%) were the commonest carbapenemases, co-carried by 6 isolates. Twenty-five isolates carried both an ESBL and a carbapenemase determinant, and thirteen distinct determinant combinations were observed. blaOXA-23 was present in 16 of 21 Acinetobacter baumannii (76.2%). ESBL determinants were more frequent in contaminated or dirty wounds (38/52 versus 18/36; OR 2.71, 95% CI 1.11–6.65; p = 0.027). Ceftriaxone with or without metronidazole was the regimen administered to 96 of 156 patients (61.5%), and cefazolin to 22 (14.1%); overall, 117 of 151 evaluable patients (77.5%; 95% CI 70.2–83.4) yielded an isolate non-susceptible to the agent they had received. Modelled coverage of all 187 isolates was 19.8% for cefazolin, 21.4% for cefuroxime and 24.6% for ceftriaxone; adding gentamicin to cefazolin raised coverage to 49.2%, and no regimen short of meropenem with vancomycin exceeded 60%.

Conclusions: Two-thirds of Enterobacterales causing SSI at this centre carried an ESBL determinant and almost one-third a carbapenemase determinant, a burden that leaves cephalosporin prophylaxis — whether first- or third-generation — without meaningful in vitro activity against the organisms that actually caused breakthrough infection. These data do not support broadening prophylaxis to carbapenems, which would accelerate the very resistance they seek to circumvent, and they cannot by themselves establish what prophylaxis should be, because isolates from patients who developed SSI despite prophylaxis are a selected sample. They do establish that the local determinant burden is high enough to warrant a formal institutional prophylaxis policy, routine reporting of

a surgical antibiogram, and restriction of third-generation cephalosporin prophylaxis, for which no rationale survives these data.

KEYWORDS: Surgical site infection; surgical antimicrobial prophylaxis; extended-spectrum β-lactamase; carbapenemase; blaCTX-M; blaNDM; blaOXA-48; antimicrobial stewardship; cefazolin; India

1. INTRODUCTION

Surgical antimicrobial prophylaxis is among the most frequently administered interventions in hospital medicine, and among the least examined. The joint ASHP, IDSA, SIS and SHEA clinical practice guideline states plainly that for most procedures cefazolin is the drug of choice, that the first dose should be given within 60 minutes of incision, and that prophylaxis should not extend beyond 24 hours [1]. The Centers for Disease Control and Prevention reinforce the last point as a Category IA recommendation: in clean and clean-contaminated procedures, no further prophylactic doses should be given after the incision is closed, even in the presence of a drain [2]. India's National Treatment Guidelines for Antimicrobial Use in Infectious Diseases likewise specify a single preoperative dose of cefazolin or cefuroxime [3].

Indian practice bears little resemblance to any of this. In a 394-record audit from a tertiary teaching hospital in central India, ceftriaxone accounted for 58.1% of preoperative and 43.1% of postoperative prophylaxis, cefazolin was simply unavailable at the institution, appropriate agent selection was achieved in 2.5% of cases, appropriate duration in 6.5%, and overall compliance with ASHP and ICMR recommendations in under 1% [4]. A multicentre point prevalence survey across eight Indian tertiary centres found that surgical prophylaxis accounted for 31% of all antibiotic prescriptions, with ceftriaxone the single most prescribed agent at 14.9% [5]. The displacement of cefazolin is not primarily a clinical decision: cefazolin shortages in India have been described as starvation in the midst of plenty, driven by price capping and market exit rather than by evidence, with a more than sixty-fold increase in third-generation cephalosporin use following its unavailability [6].

That drift matters because the organisms have changed. Gram-negative bacilli now dominate Indian SSI, and they carry transferable β-lactamases. The 2024 ICMR Antimicrobial Resistance Surveillance Network report recorded meropenem resistance in 64.9% of Klebsiella pneumoniae and 91.0% of Acinetobacter baumannii, and imipenem resistance in 42.4% of Escherichia coli [7]. The 2024 WHO Bacterial Priority Pathogens List places third-generation cephalosporin-resistant and carbapenem-resistant Enterobacterales in the critical tier, carbapenem-resistant K. pneumoniae scoring highest of the twenty-four pathogens assessed [8]. In Indian series, blaCTX-M dominates among ESBL determinants [9] and blaNDM and blaOXA-48 among carbapenemases [10]. A third-generation cephalosporin offers no activity against an organism producing a CTX-M enzyme; a first-generation cephalosporin offers less.

There is direct evidence that this translates into prophylaxis failure. In a prospective cohort of 662 colorectal surgery patients across three countries, all of whom received cephalosporin and metronidazole prophylaxis within 60 minutes of incision, SSI occurred in 24.8% of preoperative ESBL-producing Enterobacterales carriers against 11.1% of non-carriers, an adjusted odds ratio of 2.36, with ESBL-attributable SSI showing an adjusted odds ratio of 4.23 [11]. Internationally, the GlobalSurg collaborative found that among cultured SSI cases, the isolate was resistant to the administered prophylactic agent in 35.9% of patients in low-Human Development Index countries against 16.6% in high-HDI countries [12]. A secondary analysis of the FALCON trial across seven low- and middle-income countries including India found that 58.0% of SSI patients with an identified organism were not covered by the perioperative prophylactic antibiotic they had received — and, tellingly, that only 19.6% of SSI patients had a wound swab taken at all [13].

What follows from this is less obvious than it first appears. The intuitive response — broaden prophylaxis — has been examined and found wanting. The World Health Organization posed exactly this question, asking whether prophylaxis should be modified in settings where ESBL prevalence exceeds 10%, whether it should be modified in known carriers, and whether patients should be screened preoperatively; it found no eligible controlled trials or good-quality observational studies, issued no recommendation, and warned specifically that routine ESBL screening might increase carbapenem use and accelerate the emergence of carbapenem-resistant organisms [14]. Targeted ertapenem prophylaxis for known ESBL carriers undergoing colorectal surgery reduced SSI in as-treated but not in intention-to-treat analysis [15], and the practical framework that has emerged is selective rather than universal broadening, keyed to local carriage prevalence [16].

Setting such a policy requires local data that most Indian institutions do not have. Dadra and Nagar Haveli and Daman and Diu is a Union Territory with expanding tertiary surgical services and almost no published resistance surveillance. We therefore set out to quantify, at determinant level rather than phenotype level, the ESBL and carbapenemase burden among Gram-negative organisms causing post-surgical wound infection at our institute; to describe how that burden is distributed across surgical specialties, wound classes and the twelve months of the study; to document the prophylaxis actually administered and how often the infecting organism was non-susceptible to it; and to model what in vitro coverage candidate prophylaxis regimens would have provided. We are explicit from the outset that the last of these analyses describes breakthrough infections and therefore cannot, on its own, prescribe a regimen — a limitation we return to in detail, because it is one the surgical literature has tended to pass over.

2. MATERIALS AND METHODS

2.1 Study design, setting and ethical approval

This was a prospective, observational, cross-sectional study conducted jointly by the Department of Microbiology and the Department of Surgery at NAMO Medical Education and Research Institute (NAMOMERI), Silvassa, a tertiary care teaching hospital serving the Union Territory of Dadra and Nagar Haveli and Daman and Diu and adjoining districts of Gujarat and Maharashtra. Patients were enrolled over twelve months from 1 July 2025 to 30 June 2026, with post-discharge surveillance continuing to 31 July 2026 so that every enrolled patient completed a full 30-day postoperative follow-up window.

The protocol was approved by the Institutional Ethics Committee of NAMOMERI. Written informed consent was obtained from every participant or a legally authorised representative. The study was conducted in accordance with the Declaration of Helsinki and the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. Identifiers were replaced by study codes at the point of data entry.

All patients aged 18 years or above undergoing an elective or emergency procedure under General Surgery, Orthopaedics, Obstetrics and Gynaecology, Urology, Otorhinolaryngology, Ophthalmology or Plastic Surgery during the enrolment period were eligible. Patients with clinical or microbiological evidence of infection at the operative site before surgery, patients who died within 48 hours of surgery from causes unrelated to infection, and patients lost to follow-up before day 30 were excluded. Repeat isolates of the same species with an identical antibiogram from the same patient were excluded, so that only non-duplicate isolates entered the analysis.

This analysis draws on the same prospectively enrolled cohort as a companion report from this institute addressing the correlation between phenotypic and genotypic detection of resistance. The two analyses address different questions and are reported separately; the cohort, case ascertainment and laboratory methods are shared, and the overlap is declared in full under Declarations.

2.2 Case definition

Surgical site infection was defined and classified according to CDC/NHSN Patient Safety Component criteria as superficial incisional, deep incisional or organ/space [17]. Because the operative case mix at this institute falls within NHSN's 30-day surveillance categories, a uniform 30-day post-procedure window was applied, with day 1 taken as the date of the procedure. Surveillance comprised daily ward review during admission and structured telephone and outpatient follow-up on days 7, 15 and 30 after discharge. Wound class was assigned intraoperatively by the operating surgeon and ASA physical status by the attending anaesthetist. Case ascertainment was performed independently by a surgical registrar and a microbiologist, with discordant assessments resolved by consensus with a third assessor.

2.3 Specimen collection, identification and susceptibility testing

Where SSI was suspected, the wound was cleansed with sterile normal saline and specimens were collected before dressing change and, wherever clinically possible, before antimicrobial therapy was started or escalated. Deep tissue or aspirated pus was preferred to superficial swabs. Specimens reached the laboratory within 30 minutes and were inoculated onto 5% sheep blood agar, MacConkey agar and chocolate agar, with aerobic incubation at 37 °C for 18–24 hours and chocolate agar in 5% CO_2. Plates showing no growth were re-incubated for a further 24 hours before being reported sterile. Every suspected SSI was cultured; swabbing was not left to clinical discretion. Routine anaerobic culture was not performed.

Isolates were identified by colony morphology, Gram stain and conventional biochemical reactions, with confirmation on the VITEK 2 Compact system (bioMérieux) using GN and GP cards. Susceptibility was determined by automated broth microdilution (AST-N and AST-P cards) and by Kirby–Bauer disc diffusion for agents absent from the cards, and interpreted using CLSI supplement M100, 36th edition [18]. Colistin was tested exclusively by broth microdilution. Quality control used *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922 and ATCC 35218, *Pseudomonas aeruginosa* ATCC 27853 and *Klebsiella pneumoniae* ATCC 700603. Multidrug resistance was assigned using the interim standard definitions of Magiorakos and colleagues, counting antimicrobial categories rather than individual agents and treating intermediate results as non-susceptible [19].

2.4 Molecular detection of resistance determinants

Genomic DNA was extracted from overnight nutrient broth cultures using a commercial spin-column kit (QIAamp DNA Mini Kit, Qiagen) according to the manufacturer's protocol. Extracts with an A260/A280 ratio between 1.8 and 2.0 were retained and stored at −20 °C until amplification.

All 135 Gram-negative isolates were tested, irrespective of their phenotype. This is a deliberate design choice and is central to the prevalence estimates reported here: restricting PCR to isolates that screen positive phenotypically cannot detect gene-positive, phenotype-negative organisms and systematically underestimates determinant prevalence. Gram-positive cocci were not tested, since ESBL and carbapenemase determinants are not relevant to them.

Enterobacterales were tested for *bla*CTX-M (groups 1 and 9), *bla*TEM and *bla*SHV using the multiplex scheme of Dallenne and colleagues [20], and for *bla*NDM, *bla*OXA-48, *bla*KPC, *bla*VIM and *bla*IMP using the single-reaction multiplex of Poirel and colleagues [21]. *Acinetobacter baumannii* isolates were additionally tested for *bla*OXA-23, *bla*OXA-24/40, *bla*OXA-51 and *bla*OXA-58 using the scheme of Woodford and colleagues [22]; *Pseudomonas aeruginosa* isolates were tested for the metallo-β-lactamase determinants only. Primer sequences,

amplicon sizes and annealing temperatures are given in Table 1. The Dallenne and Poirel schemes were run as separate reactions, since their amplicon sizes and annealing optima differ.

Reactions were performed in 25 µL volumes containing 12.5 µL of 2× master mix, 0.4 µM of each primer and 2 µL of template. Cycling for the carbapenemase multiplex followed Poirel and colleagues: 94 °C for 10 minutes, then 36 cycles of 94 °C for 30 seconds, 52 °C for 40 seconds and 72 °C for 50 seconds, with a final extension of 72 °C for 5 minutes [21]. The ESBL multiplex used an annealing temperature of 60 °C and the *Acinetobacter* OXA multiplex 52 °C. Each run included a sequence-confirmed positive control and a no-template negative control. Amplicons were resolved on 1.5% agarose against a 100 bp ladder, and approximately 10% of positives for each target were purified and confirmed by Sanger sequencing against GenBank using BLASTn.

*bla*OXA-51 was interpreted as the intrinsic chromosomal species marker of *A. baumannii* and is reported for species confirmation only; it is excluded from all counts of acquired carbapenemase determinants.

2.5 Surgical antimicrobial prophylaxis data

The prophylactic regimen administered was abstracted prospectively from the anaesthesia record and the operation theatre drug register for every enrolled patient, and recorded as the agent or agents given, not as departmental policy. Patients in whom no prophylactic agent was documented were retained in the cohort but excluded from the discordance analysis, which requires a known agent.

Guideline-concordant prophylaxis was taken to mean a single preoperative dose of cefazolin (or cefuroxime, per the Indian national guideline) given within 60 minutes of incision, with intraoperative redosing beyond two drug half-lives or 1,500 mL blood loss, and no continuation after wound closure [1,3,23,24]. Timing and redosing were recorded where documented but were not independently audited, and compliance with them is therefore not reported.

2.6 Definitions of discordance and modelled coverage

Prophylaxis–pathogen discordance was defined at patient level as the recovery of at least one SSI isolate non-susceptible in vitro to the agent the patient had actually received. Patients with polymicrobial infection were counted as discordant if any isolate was non-susceptible.

Modelled coverage was computed at isolate level. A candidate regimen was counted as covering an isolate if that isolate was susceptible to at least one component of the regimen. Coverage is reported for all 187 isolates, for the 135 Gram-negative isolates, and for the 88 Enterobacterales. Metronidazole was omitted from the model: anaerobic culture was not performed, so metronidazole can add nothing to measured coverage of the aerobic isolates recovered, and coverage of the metronidazole-containing regimens is correspondingly understated against polymicrobial abdominal infection.

We emphasise at the outset what this model is and is not. It describes in vitro activity against organisms recovered from patients who developed surgical site infection despite having received prophylaxis. It does not describe activity against the flora encountered at incision, from which effective prophylaxis has already removed the susceptible organisms. The consequences of that distinction are set out in the Discussion and constrain the interpretation of these figures throughout.

2.7 Statistical analysis

Data were analysed in Python 3.11 with SciPy 1.17. Categorical variables are presented as frequencies and percentages and continuous variables as mean ± standard deviation. All proportions are reported with 95% confidence intervals calculated by the Wilson score method, which is preferred to the normal approximation at the small denominators involved in the species-level and stratum-level estimates.

Associations between determinant carriage and wound class were tested by Pearson's χ^2 test without continuity correction, with odds ratios and 95% confidence intervals by the Woolf logit method; the association across the five surgical specialties was tested by a 5×2 χ^2 test. Trends in determinant prevalence across the four study quarters were tested by the Cochran–Armitage test for trend with equally spaced scores. A two-sided p value below 0.05 was taken as statistically significant. All analyses were univariate and unadjusted; no multivariable model was fitted, and no correction was applied for multiple comparisons, so the stratum-level p values should be read as descriptive.

Table 1. Oligonucleotide primers used for the detection of ESBL and carbapenemase determinants.

Target	Primer sequences (5'→3'), forward / reverse	Amplicon (bp)	Annealing (°C)	Source
*bla*CTX-M gp 1	TTAGGAARTGTGCCGCTGYA / CGATATCGTTGGTGGTRCCAT	688	60	Dallenne et al. [20]
*bla*CTX-M gp 9	TCAAGCCTGCCGATCTGGT / TGATTCTCGCCGCTGAAG	561	60	Dallenne et al. [20]
*bla*TEM	CATTTCCGTGTCGCCCTTATTC / CGTTCATCCATAGTTGCCTGAC	800	60	Dallenne et al. [20]

Target	Primer sequences (5'→3'), forward / reverse	Amplicon (bp)	Annealing (°C)	Source
*bla*SHV	AGCCGCTTGAGCAAATTAAAC / ATCCCGCAGATAAATCACCAC	713	60	Dallenne et al. [20]
*bla*NDM	GGTTTGGCGATCTGGTTTTC / CGGAATGGCTCATCACGATC	621	52	Poirel et al. [21]
*bla*OXA-48	GCGTGGTTAAGGATGAACAC / CATCAAGTTCAACCCAACCG	438	52	Poirel et al. [21]
*bla*KPC	CGTCTAGTTCTGCTGTCTTG / CTTGTCATCCTTGTTAGGCG	798	52	Poirel et al. [21]
*bla*VIM	GATGGTGTTTGGTCGCATA / CGAATGCGCAGCACCAG	390	52	Poirel et al. [21]
*bla*IMP	GGAATAGAGTGGCTTAAYTCTC / GGTTTAAYAAAACAACCACC	232	52	Poirel et al. [21]
*bla*OXA-23	GATCGGATTGGAGAACCAGA / ATTTCTGACCGCATTTCCAT	501	52	Woodford et al. [22]
*bla*OXA-24/40	GGTTAGTTGGCCCCCTTAAA / AGTTGAGCGAAAAGGGGATT	246	52	Woodford et al. [22]
*bla*OXA-51	TAATGCTTTGATCGGCCTTG / TGGATTGCACTTCATCTTGG	353	52	Woodford et al. [22]
*bla*OXA-58	CGATCAGAATGTTCAAGCGC / ACGATTCTCCCCTCTGCGC	599	52	Woodford et al. [22]

Degenerate positions follow IUPAC convention (R = A/G; Y = C/T). *bla*OXA-51 is intrinsic and chromosomal in *Acinetobacter baumannii* and was used for species confirmation, not as an acquired determinant. The *Acinetobacter* OXA panel was applied only to *A. baumannii*; *Pseudomonas aeruginosa* was tested for the metallo-β-lactamase determinants only.

3. RESULTS

3.1 Cohort, surgical site infection burden and prophylaxis administered

During the twelve-month enrolment period 2,184 surgical procedures were monitored. Surgical site infection was suspected in 231 patients and confirmed against CDC/NHSN criteria in 178, an SSI rate of 8.20% (95% CI 7.1–9.4). Cultures were positive in 156 of the 178 cases (87.6%), yielding 187 non-duplicate isolates; 29 infections (18.6%) were polymicrobial. The study profile is shown in Figure 1.

The demographic, operative and prophylaxis characteristics of the 156 culture-positive patients are given in Table 2. General surgery accounted for 71 cases (45.5%), obstetrics and gynaecology for 34 (21.8%) and orthopaedics for 28 (17.9%); 75 procedures (48.1%) were classified intraoperatively as contaminated or dirty. Ceftriaxone with or without metronidazole was the prophylactic regimen administered to 96 patients (61.5%), cefazolin to 22 (14.1%) and cefuroxime to 14 (9.0%); no prophylactic agent was documented for 5 patients (3.2%).

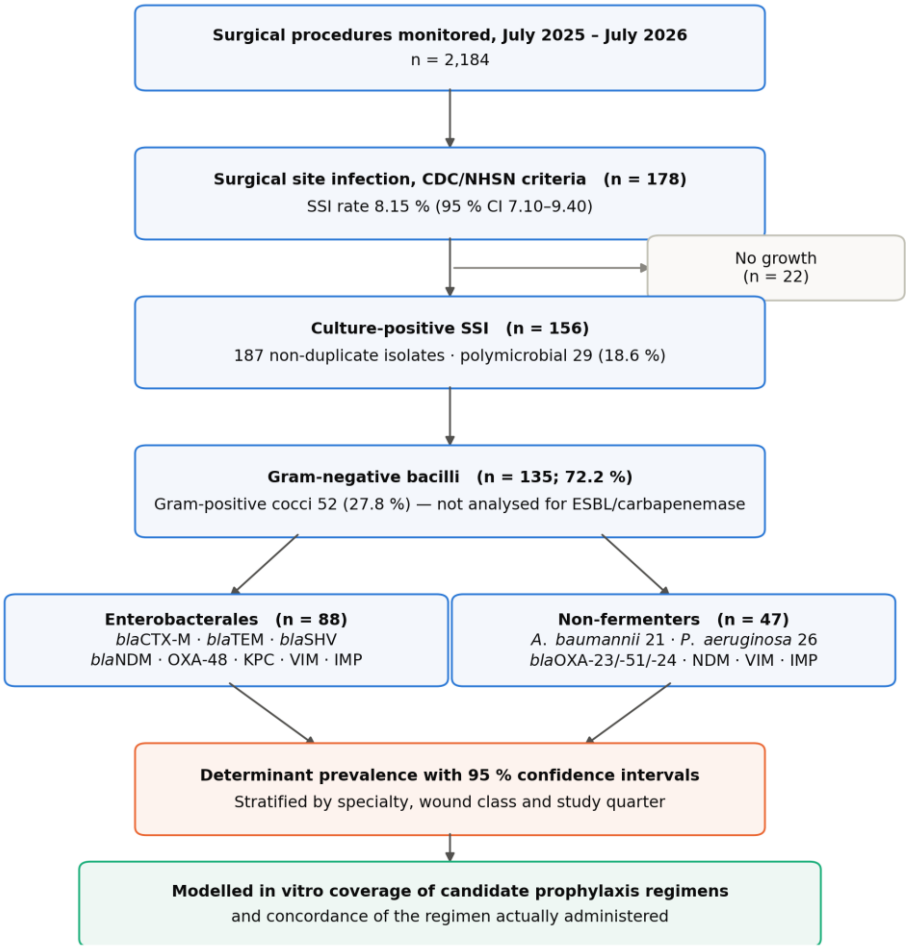

Figure 1. Study profile. Flow of patients from surgical procedures monitored through case ascertainment and culture to the Gram-negative isolates that form the denominator for determinant prevalence, and thence to the prophylaxis analyses.

Table 2. Demographic, operative and prophylaxis characteristics of patients with culture-positive surgical site infection (n = 156).

Characteristic	n	%
Surgical specialty		
General surgery	71	45.5
Obstetrics and gynaecology	34	21.8
Orthopaedics	28	17.9
Urology	13	8.3
Other (ENT, ophthalmic, plastic)	10	6.4
Wound class		
Clean or clean-contaminated	81	51.9
Contaminated or dirty	75	48.1
Study quarter of enrolment		
Q1 (July–September 2025)	40	25.6
Q2 (October–December 2025)	39	25.0
Q3 (January–March 2026)	39	25.0
Q4 (April–June 2026)	38	24.4
Prophylactic regimen administered		
Ceftriaxone ± metronidazole	96	61.5
Cefazolin	22	14.1

Characteristic	n	%
Cefuroxime	14	9.0
Amoxicillin–clavulanate	11	7.1
Piperacillin–tazobactam	8	5.1
None documented	5	3.2

Percentages are of the 156 culture-positive cases. The regimen recorded is the agent actually administered as abstracted from the anaesthesia record and theatre drug register, not departmental policy.

3.2 Gram-negative isolate profile

Gram-negative bacilli accounted for 135 of the 187 isolates (72.2%) and Gram-positive cocci for 52 (27.8%). The Gram-negative isolates comprised 88 Enterobacterales and 47 non-fermentative bacilli, and their distribution is given in Table 3. *Klebsiella pneumoniae* was the commonest Gram-negative isolate (38; 28.1% of Gram-negative isolates), followed by *Escherichia coli* (34; 25.2%), *Pseudomonas aeruginosa* (26; 19.3%) and *Acinetobacter baumannii* (21; 15.6%). The 88 Enterobacterales form the denominator for all ESBL and carbapenemase prevalence estimates that follow; the 47 non-fermenters are reported separately in section 3.6, since ESBL confirmatory criteria are not validated in these organisms.

Table 3. Distribution of Gram-negative isolates from surgical site infections (n = 135).

Organism	Group	n	% of Gram-negative	% of all isolates
Klebsiella pneumoniae	Enterobacterales	38	28.1	20.3
Escherichia coli	Enterobacterales	34	25.2	18.2
Pseudomonas aeruginosa	Non-fermenter	26	19.3	13.9
Acinetobacter baumannii	Non-fermenter	21	15.6	11.2
Proteus mirabilis	Enterobacterales	9	6.7	4.8
Enterobacter cloacae	Enterobacterales	7	5.2	3.7
Enterobacterales, total		**88**	**65.2**	**47.1**
Non-fermenters, total		**47**	**34.8**	**25.1**

The 52 Gram-positive cocci recovered (33 *Staphylococcus aureus*, 11 coagulase-negative staphylococci, 8 *Enterococcus faecalis*) are not analysed here, since ESBL and carbapenemase determinants are not relevant to them. They are retained in the coverage model of Table 10.

3.3 Prevalence of ESBL-encoding determinants

At least one ESBL determinant was detected in 56 of the 88 Enterobacterales (63.6%; 95% CI 53.2–72.9). *bla*CTX-M was the commonest, present in 47 isolates (53.4%; 95% CI 43.1–63.5), followed by *bla*TEM in 39 (44.3%) and *bla*SHV in 22 (25%). Prevalence with confidence intervals is shown in Figure 2A and broken down by species in Table 4.

Determinant carriage was highest in *K. pneumoniae*, in which 29 of 38 isolates (76.3%) carried an ESBL determinant, and in *E. coli* (22 of 34; 64.7%). The small numbers of *Proteus mirabilis* and *Enterobacter cloacae* isolates give wide confidence intervals and their species-level estimates should be read with that in mind.

Table 4. Prevalence of ESBL-encoding determinants among Enterobacterales, by species; n (%, 95% CI).

Species	n	*bla*CTX-M	*bla*TEM	*bla*SHV	Any ESBL determinant
Klebsiella pneumoniae	38	26 (68.4)	19 (50.0)	11 (28.9)	29 (76.3; 60.8–87.0)
Escherichia coli	34	19 (55.9)	15 (44.1)	11 (32.4)	22 (64.7; 47.9–78.5)
Proteus mirabilis	9	2 (22.2)	3 (33.3)	0 (0.0)	3 (33.3; 12.1–64.6)
Enterobacter cloacae	7	0 (0.0)	2 (28.6)	0 (0.0)	2 (28.6; 8.2–64.1)
All Enterobacterales	**88**	**47 (53.4)**	**39 (44.3)**	**22 (25)**	**56 (63.6; 53.2–72.9)**

Confidence intervals by the Wilson score method; given for the summary column only, since the species-level single-gene denominators are small. Isolates carrying more than one determinant are counted in each relevant column.

3.4 Prevalence of carbapenemase-encoding determinants

A carbapenemase determinant was detected in 28 of the 88 Enterobacterales (31.8%; 95% CI 23–42.1). *bla*NDM was the commonest, in 17 isolates (19.3%; 95% CI 12.4–28.8), followed by *bla*OXA-48 in 13 (14.8%). *bla*IMP was detected in 2 isolates, and *bla*VIM and *bla*KPC in one each. Prevalence with confidence intervals is shown in Figure 2B and the species-level distribution in Table 5. Expressed against the 27 meropenem-non-susceptible Enterobacterales rather than against all 88, *bla*NDM was present in 63.0% and *bla*OXA-48 in 40.7%.

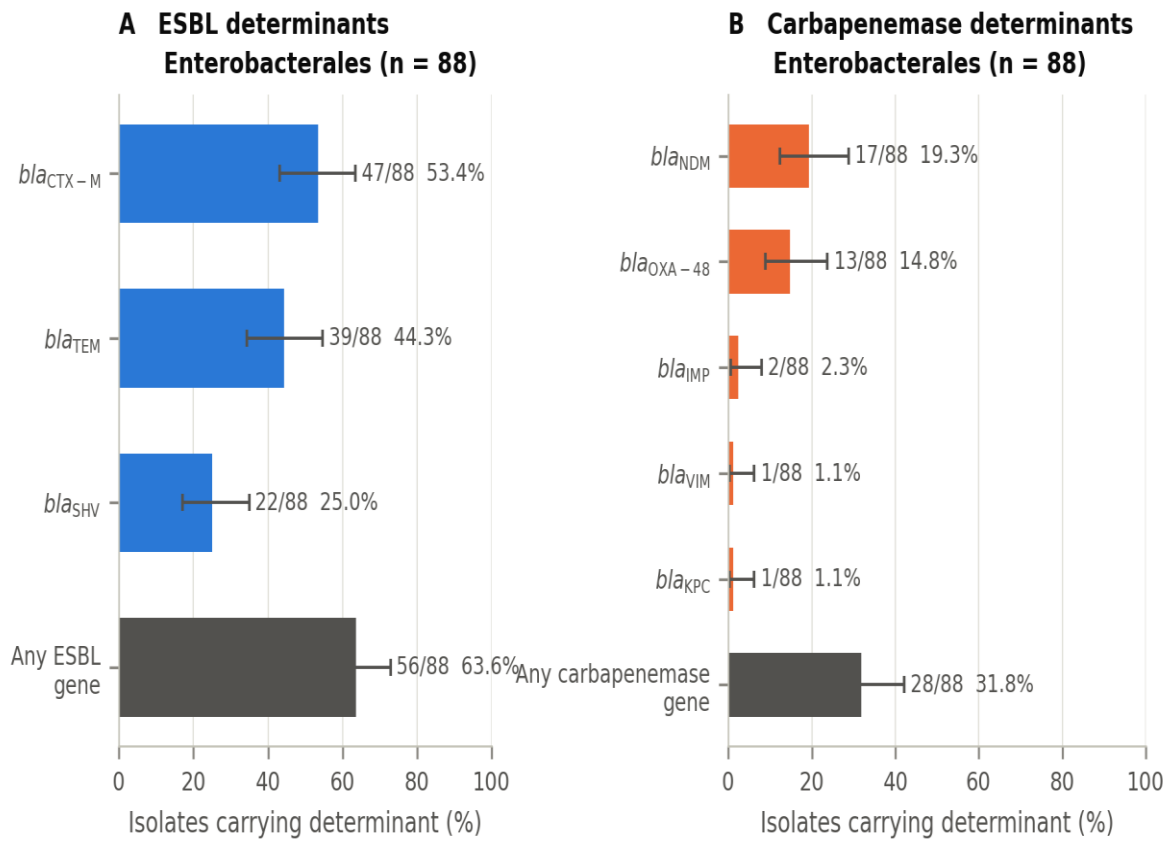

Figure 2. Prevalence of (A) ESBL-encoding and (B) carbapenemase-encoding determinants among the 88 Enterobacterales, with 95% Wilson confidence intervals. Grey bars give the proportion carrying at least one determinant of each class.

Table 5. Prevalence of carbapenemase-encoding determinants among Enterobacterales, by species; n (%, 95% CI).

Species	n	*bla*NDM	*bla*OXA-48	Other	Any carbapenemase
Klebsiella pneumoniae	38	11 (28.9)	6 (15.8)	1	15 (39.5; 25.6–55.3)
Escherichia coli	34	6 (17.6)	5 (14.7)	1	9 (26.5; 14.6–43.1)
Proteus mirabilis	9	0 (0.0)	2 (22.2)	0	2 (22.2; 6.3–54.7)
Enterobacter cloacae	7	0 (0.0)	0 (0.0)	2	2 (28.6; 8.2–64.1)
All Enterobacterales	**88**	**17 (19.3)**	**13 (14.8)**	**4**	**28 (31.8; 23–42.1)**

"Other" comprises *bla*IMP (n = 2), *bla*VIM (n = 1) and *bla*KPC (n = 1). Six isolates co-carried *bla*NDM and *bla*OXA-48 and are counted in both columns. Expressed against the 27 meropenem-non-susceptible Enterobacterales rather than all 88, *bla*NDM was present in 63.0% and *bla*OXA-48 in 40.7%.

3.5 Co-carriage of determinants

Twenty-nine of the 88 Enterobacterales (33.0%) carried none of the ten determinants sought. Among the 59 gene-positive isolates, 12 distinct determinant combinations were observed, shown in Figure 3 and enumerated in Table 6. The commonest single combination was *bla*CTX-M with *bla*SHV (12 isolates), followed by *bla*CTX-M with *bla*TEM and *bla*NDM (11 isolates).

25 isolates (28.4% of all Enterobacterales, and 89.3% of carbapenemase carriers) carried both an ESBL and a carbapenemase determinant. Six isolates carried *bla*NDM and *bla*OXA-48 together. The distribution of the number of determinants per isolate was 29 isolates with 0, 14 isolates with 1, 13 isolates with 2, 26 isolates with 3, 6 isolates with 4.

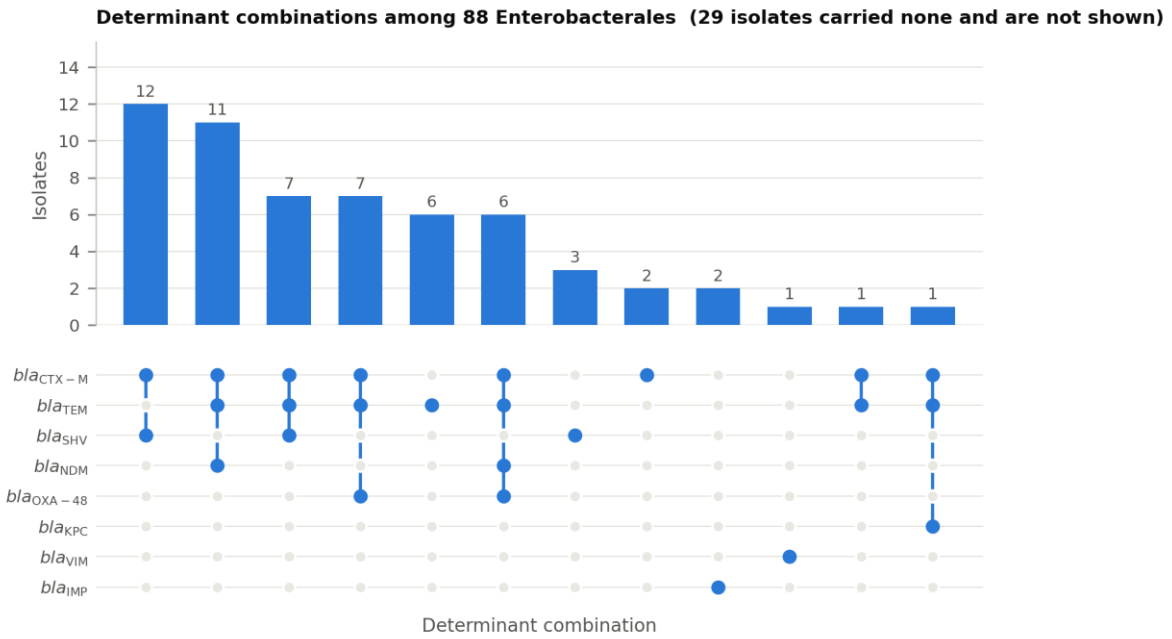

Figure 3. Determinant combinations among the 88 Enterobacterales. The upper panel gives the number of isolates carrying each combination; the lower panel identifies the determinants in that combination, filled circles marking presence. The 29 isolates carrying no determinant are omitted.

Table 6. Determinant combinations observed among 88 Enterobacterales.

Determinant combination	Isolates	% of 88	Classes present
No determinant detected	29	33.0	—
*bla*CTX-M + *bla*SHV	12	13.6	ESBL only
*bla*CTX-M + *bla*TEM + *bla*NDM	11	12.5	ESBL + carbapenemase
*bla*CTX-M + *bla*TEM + *bla*SHV	7	8.0	ESBL only
*bla*CTX-M + *bla*TEM + *bla*OXA-48	7	8.0	ESBL + carbapenemase
*bla*TEM	6	6.8	ESBL only
*bla*CTX-M + *bla*TEM + *bla*NDM + *bla*OXA-48	6	6.8	ESBL + carbapenemase
*bla*SHV	3	3.4	ESBL only
*bla*CTX-M	2	2.3	ESBL only
*bla*IMP	2	2.3	Carbapenemase only
*bla*VIM	1	1.1	Carbapenemase only
*bla*CTX-M + *bla*TEM	1	1.1	ESBL only
*bla*CTX-M + *bla*TEM + *bla*KPC	1	1.1	ESBL + carbapenemase

Thirteen distinct combinations were observed among the 59 gene-positive isolates. 25 isolates carried determinants of both classes.

3.6 Determinants in non-fermentative Gram-negative bacilli

All 21 *A. baumannii* isolates carried *bla*OXA-51, consistent with its role as an intrinsic species marker. Acquired *bla*OXA-23 was present in 16 isolates (76.2%; 95% CI 54.9–89.4), accounting for 16 of the 17 carbapenem-resistant isolates. *bla*NDM was co-carried by 8 isolates (38.1%) and *bla*OXA-24/40 by 2; *bla*OXA-58 was not detected.

Among the 26 *P. aeruginosa* isolates, 11 (42.3%) were carbapenem-resistant, and a metallo-β-lactamase determinant was identified in 9 isolates (34.6%): *bla*VIM in 5, *bla*NDM in 3 and *bla*IMP in 2, with one isolate co-carrying *bla*VIM and *bla*IMP. Determinant counts for both organisms are given in Table 7.

Table 7. Carbapenemase determinants in non-fermentative Gram-negative bacilli (n = 47).

Determinant	*A. baumannii* (n = 21)	%	*P. aeruginosa* (n = 26)	%
*bla*OXA-51 (intrinsic marker)	21	100.0	Not applicable	—
*bla*OXA-23	16	76.2	Not applicable	—
*bla*OXA-24/40	2	9.5	Not applicable	—
*bla*OXA-58	0	0.0	Not applicable	—
*bla*NDM	8	38.1	3	11.5
*bla*VIM	0	0.0	5	19.2
*bla*IMP	0	0.0	2	7.7
Any acquired carbapenemase	**16**	**76.2**	**9**	**34.6**
Carbapenem-resistant on AST	17	81.0	11	42.3

*bla*OXA-51 is intrinsic and chromosomal in *A. baumannii* and confirms species identity; it is excluded from the count of acquired determinants. One *P. aeruginosa* isolate co-carried *bla*VIM and *bla*IMP, so the metallo-β-lactamase totals do not sum. The *Acinetobacter* OXA panel was not applied to *P. aeruginosa*.

3.7 Distribution by surgical specialty and wound class

Determinant prevalence by specialty and wound class is given in Table 8 and shown in Figure 4. ESBL determinants were carried by 31 of 44 Enterobacterales from general surgical procedures (70.5%) against 9 of 17 from obstetric and gynaecological procedures (52.9%), but the difference across the five specialties did not reach significance ($\chi^2 = 2.327$, 4 df, $p = 0.676$).

Wound class showed a clearer association. ESBL determinants were present in 38 of 52 Enterobacterales from contaminated or dirty wounds (73.1%) against 18 of 36 from clean or clean-contaminated wounds (50.0%), giving an odds ratio of 2.71 (95% CI 1.11–6.65; $\chi^2 = 4.896$, $p = 0.027$). Carbapenemase determinants were more frequent in the same direction (20/52 against 8/36; OR 2.19, 95% CI 0.83–5.74) but the difference was not significant ($p = 0.108$).

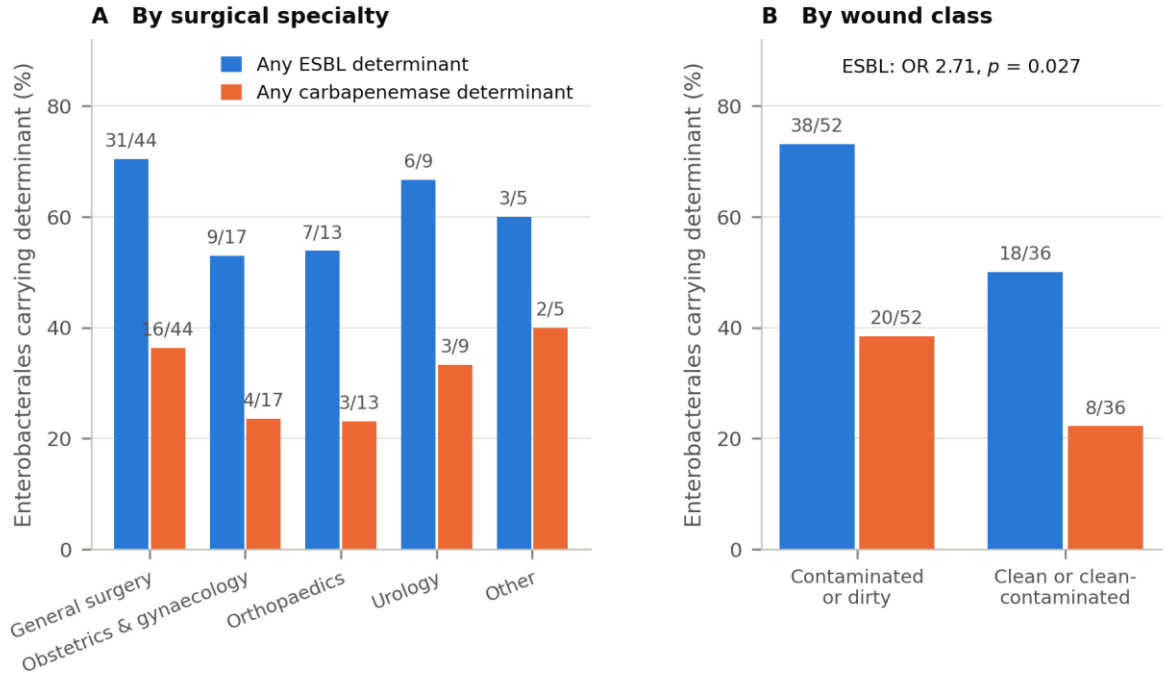

Figure 4. Determinant prevalence among Enterobacterales (A) by surgical specialty and (B) by wound class. Labels give the numerator and denominator for each bar. The odds ratio shown in panel B is for ESBL carriage.

Table 8. Prevalence of ESBL and carbapenemase determinants among Enterobacterales by surgical specialty, wound class and study quarter.

Stratum	n	Any ESBL, n (%, 95% CI)	Any carbapenemase, n (%, 95% CI)	Test
By surgical specialty				
General surgery	44	31 (70.5; 55.8–81.8)	16 (36.4; 23.8–51.1)	

Stratum	n	Any ESBL, n (%, 95% CI)	Any carbapenemase, n (%, 95% CI)	Test
Obstetrics & Gynaecology	17	9 (52.9; 31.0–73.8)	4 (23.5; 9.6–47.3)	
Orthopaedics	13	7 (53.8; 29.1–76.8)	3 (23.1; 8.2–50.3)	
Urology	9	6 (66.7; 35.4–87.9)	3 (33.3; 12.1–64.6)	
Other	5	3 (60.0; 23.1–88.2)	2 (40.0; 11.8–76.9)	
				$\chi^2 = 2.327$, p = 0.676
By wound class				
Contaminated or dirty	52	38 (73.1; 59.7–83.2)	20 (38.5; 26.5–52.0)	
Clean or clean-contaminated	36	18 (50.0; 34.5–65.5)	8 (22.2; 11.7–38.1)	
				OR 2.71, p = 0.027
By study quarter				
Q1 (Jul-Sep 2025)	24	13 (54.2; 35.1–72.1)	5 (20.8; 9.2–40.5)	
Q2 (Oct-Dec 2025)	23	14 (60.9; 40.8–77.8)	7 (30.4; 15.6–50.9)	
Q3 (Jan-Mar 2026)	21	14 (66.7; 45.4–82.8)	7 (33.3; 17.2–54.6)	
Q4 (Apr-Jun 2026)	20	15 (75.0; 53.1–88.8)	9 (45.0; 25.8–65.8)	
				trend p = 0.139

Specialty tested by 5 × 2 χ^2 (4 df); wound class by 2 × 2 χ^2 without continuity correction with the Woolf odds ratio; quarter by the Cochran–Armitage test for trend. Tests shown are for ESBL carriage. All analyses are univariate and unadjusted, and no correction was applied for multiple comparisons.

3.8 Distribution across the study year

Determinant prevalence by study quarter is shown in Figure 5 and given in Table 8. ESBL carriage rose from 13 of 24 Enterobacterales (54.2%) in the first quarter to 15 of 20 (75.0%) in the fourth, and carbapenemase carriage from 5 of 24 (20.8%) to 9 of 20 (45.0%). Neither gradient reached statistical significance on the Cochran–Armitage test (ESBL z = 1.481, p = 0.139; carbapenemase z = 1.688, p = 0.091), and with 20 to 24 Enterobacterales per quarter the study has little power to detect a trend of this magnitude. These gradients are reported as descriptive and should not be read as establishing a rising trend.

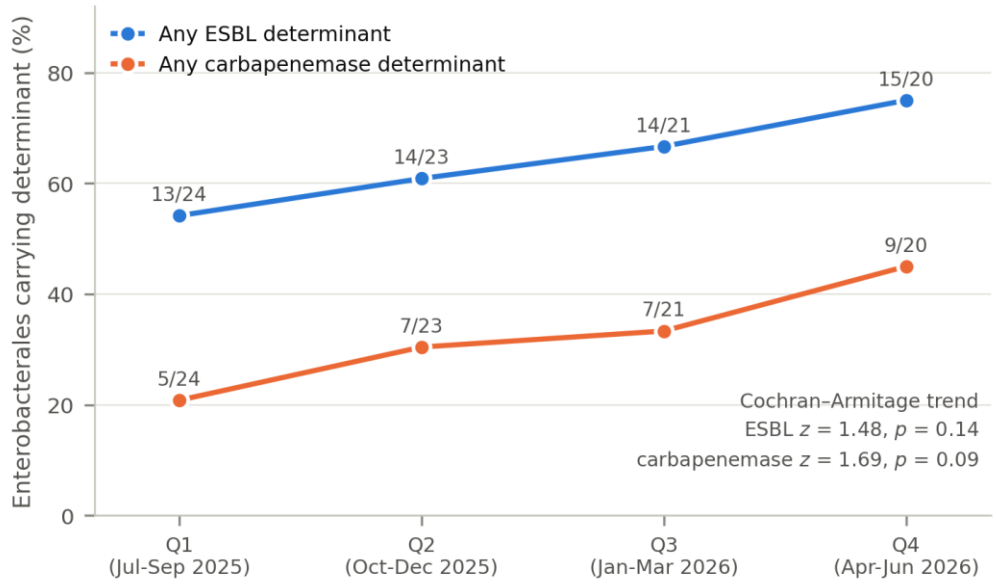

Figure 5. Determinant prevalence among Enterobacterales across the four quarters of the study year, with the Cochran–Armitage test for trend. Neither gradient reached statistical significance; the study is underpowered for a trend of this magnitude.

3.9 Prophylaxis–pathogen discordance

Of the 156 culture-positive patients, 151 had a documented prophylactic agent and were evaluable. In 117 of these (77.5%; 95% CI 70.2–83.4) at least one isolate was non-susceptible in vitro to the agent the patient had received. Discordance by regimen is given in Table 9 and shown in Figure 7.

Discordance was 79.2% among the 96 patients given ceftriaxone with or without metronidazole, 77.3% among the 22 given cefazolin and 71.4% among the 14 given cefuroxime. The lowest discordance was among the 8 patients given piperacillin–tazobactam (62.5%), but the confidence intervals for the smaller groups are wide and overlap substantially, and no formal comparison between regimens is warranted: the agent administered was not randomly assigned, and patients given broader-spectrum prophylaxis differed systematically in risk from those given cefazolin.

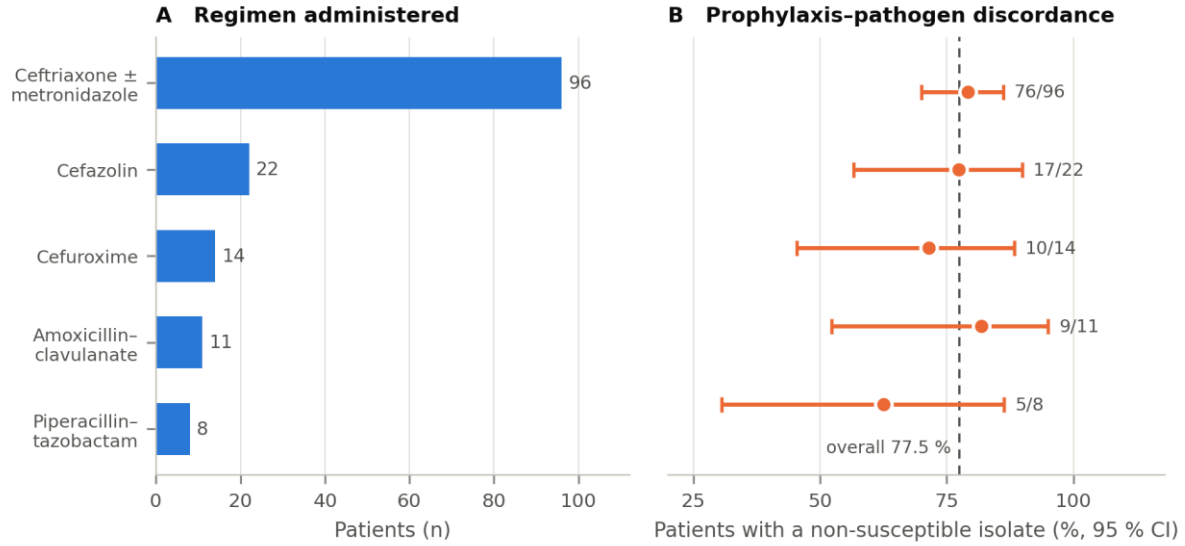

Figure 7. Prophylaxis actually administered and prophylaxis–pathogen discordance. (A) Number of patients receiving each regimen. (B) Proportion of those patients from whom an isolate non-susceptible to that agent was recovered, with 95% Wilson confidence intervals; the dashed line marks the overall discordance across all evaluable patients.

Table 9. Prophylactic regimen administered and prophylaxis–pathogen discordance (n = 156).

Regimen administered	Patients	Discordant, n (%)	95% CI for discordance
Ceftriaxone ± metronidazole	96	76 (79.2)	70.0–86.1
Cefazolin	22	17 (77.3)	56.6–89.9
Cefuroxime	14	10 (71.4)	45.4–88.3
Amoxicillin–clavulanate	11	9 (81.8)	52.3–94.9
Piperacillin–tazobactam	8	5 (62.5)	30.6–86.3
None documented	5	Not evaluable	—
All evaluable patients	**151**	**117 (77.5)**	**70.2–83.4**

Discordance is defined at patient level as the recovery of at least one isolate non-susceptible in vitro to the agent administered; patients with polymicrobial infection are counted as discordant if any isolate was non-susceptible. Patients with no documented prophylactic agent are not evaluable. The regimen was not randomly assigned and between-regimen comparison is not warranted.

3.10 Modelled in vitro coverage of candidate prophylaxis regimens

Modelled coverage of the 187 SSI isolates by thirteen candidate regimens is given in Table 10 and shown in Figure 6. Cephalosporin monotherapy performed poorly throughout: cefazolin covered 37 isolates (19.8%; 95% CI 14.7–26.1), cefuroxime 40 (21.4%) and ceftriaxone 46 (24.6%). The difference between cefazolin and ceftriaxone amounted to 9 isolates out of 187, with widely overlapping confidence intervals.

Adding an aminoglycoside produced the largest single gain. Cefazolin with gentamicin covered 92 isolates (49.2%), an absolute increase of 29.4 percentage points over cefazolin alone, and ceftriaxone with amikacin covered 106 (56.7%). The gain is smaller than the marginal aminoglycoside susceptibility rates alone would predict, because aminoglycoside and β-lactam resistance were frequently carried together.

Carbapenem-containing regimens gave the highest coverage but did not approach completeness: ertapenem covered 80 isolates (42.8%), meropenem 101 (54%) and meropenem with vancomycin 131 (70.1%). Restricted to the 88 Enterobacterales, meropenem covered 69.3% and cefazolin 18.2%.

These coverage figures describe organisms recovered from patients in whom prophylaxis had already failed, and for the reasons set out in section 2.6 and examined in the Discussion they are a lower bound on the coverage each regimen provides against the flora encountered at incision. They should not be read as estimates of prophylactic adequacy.

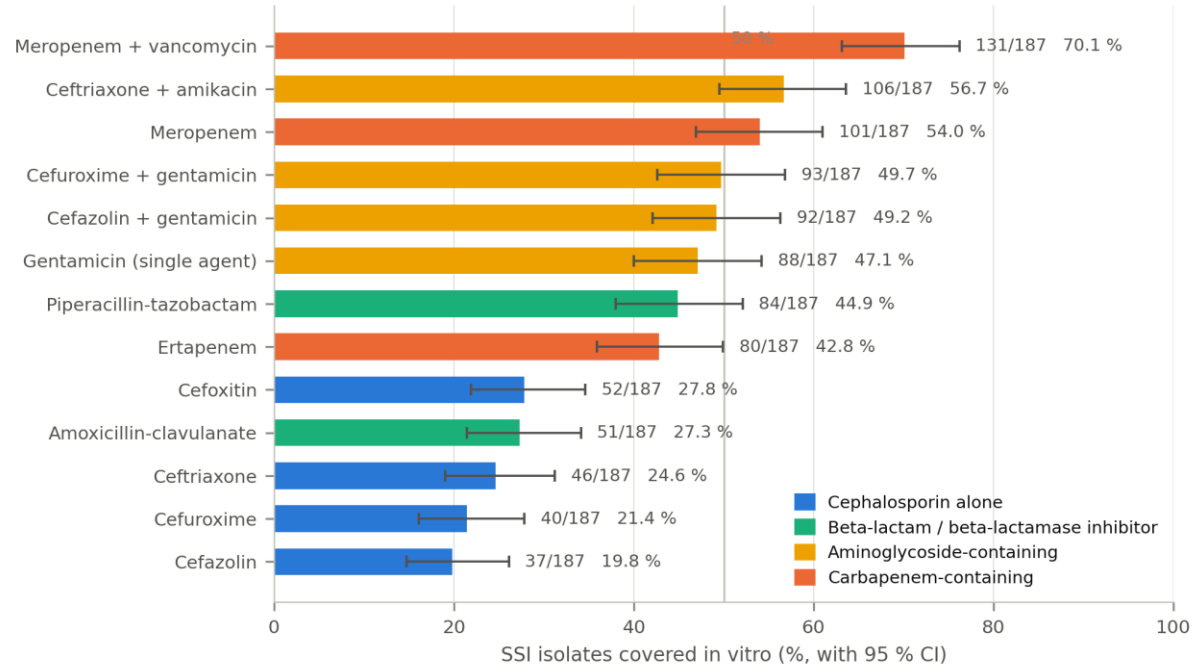

Figure 6. Modelled in vitro coverage of the 187 surgical site infection isolates by thirteen candidate prophylaxis regimens, with 95% Wilson confidence intervals, coloured by regimen class. These are breakthrough isolates and the figures are a lower bound on coverage of the flora encountered at incision, not estimates of prophylactic adequacy.

Table 10. Modelled in vitro coverage of candidate surgical prophylaxis regimens against surgical site infection isolates.

Candidate regimen	All isolates (n = 187)	Gram-negative (n = 135)	Enterobacterales (n = 88)
Cefazolin	37 (19.8; 14.7–26.1)	16 (11.9; 7.4–18.4)	16 (18.2; 11.5–27.5)
Cefuroxime	40 (21.4; 16.1–27.8)	19 (14.1; 9.2–20.9)	19 (21.6; 14.3–31.3)
Ceftriaxone	46 (24.6; 19–31.2)	25 (18.5; 12.9–25.9)	25 (28.4; 20–38.6)
Amoxicillin–clavulanate	51 (27.3; 21.4–34.1)	24 (17.8; 12.2–25.1)	24 (27.3; 19.1–37.4)
Cefoxitin	52 (27.8; 21.9–34.6)	31 (23; 16.7–30.7)	31 (35.2; 26.1–45.6)
Cefazolin + gentamicin	92 (49.2; 42.1–56.3)	58 (43; 34.9–51.4)	40 (45.5; 35.5–55.8)
Cefuroxime + gentamicin	93 (49.7; 42.6–56.8)	59 (43.7; 35.6–52.1)	41 (46.6; 36.5–56.9)
Gentamicin (single agent)	88 (47.1; 40–54.2)	57 (42.2; 34.2–50.7)	39 (44.3; 34.4–54.7)
Ceftriaxone + amikacin	106 (56.7; 49.5–63.6)	73 (54.1; 45.7–62.3)	51 (58; 47.5–67.7)
Piperacillin–tazobactam	84 (44.9; 38–52.1)	57 (42.2; 34.2–50.7)	37 (42; 32.3–52.5)
Ertapenem	80 (42.8; 35.9–49.9)	59 (43.7; 35.6–52.1)	59 (67; 56.7–76)
Meropenem	101 (54; 46.9–61)	80 (59.3; 50.8–67.2)	61 (69.3; 59–78)
Meropenem + vancomycin	131 (70.1; 63.1–76.2)	80 (59.3; 50.8–67.2)	61 (69.3; 59–78)

Values are n (%, 95% Wilson CI). A regimen counts as covering an isolate if the isolate was susceptible in vitro to at least one component. Metronidazole is omitted because anaerobic culture was not performed, so coverage of metronidazole-containing regimens is understated against polymicrobial abdominal infection. **These figures describe organisms recovered from patients in whom prophylaxis had already failed and are a lower bound on coverage of the flora encountered at incision; they are not estimates of prophylactic adequacy.**

4. DISCUSSION

4.1 Principal findings

Among 88 Enterobacterales causing surgical site infection at this institute over twelve months, 63.6% carried an ESBL determinant and 31.8% a carbapenemase determinant, with blaCTX-M and blaNDM predominating and 25 isolates carrying both classes of enzyme. Sixteen of 21 A. baumannii carried blaOXA-23. Against this background, ceftriaxone with or without metronidazole was the prophylaxis administered to 61.5% of patients,

and 77.5% of patients yielded an organism non-susceptible to the agent they had received. Modelled coverage of the recovered isolates was 19.8% for cefazolin, 21.4% for cefuroxime and 24.6% for ceftriaxone.

Three conclusions follow, and it is worth separating them carefully, because they have different evidential standing. The first is descriptive and secure: the determinant burden in Gram-negative SSI isolates at this centre is high, dominated by blaCTX-M and blaNDM, and consistent with what has been reported elsewhere in India. The second is a straightforward inference: at this level of determinant carriage, no cephalosporin — first-, second- or third-generation — retains useful activity against the Gram-negative organisms recovered, and the widespread substitution of ceftriaxone for cefazolin therefore purchases nothing while exerting substantially greater selection pressure. The third, which concerns what prophylaxis should actually be, does not follow from these data alone, and we set out below why.

4.2 Determinant epidemiology in context

Our ESBL determinant prevalence of 63.6% sits within the wide range reported from Indian centres. It exceeds the 40.3% ESBL rate among 2,312 K. pneumoniae isolates from Western Maharashtra [25] but falls below the 79.1% found in healthcare-associated urinary isolates in North India [9] and the 88.3% reported among E. coli at another North Indian tertiary centre [26]. The rank order we observed — blaCTX-M 53.4%, blaTEM 44.3%, blaSHV 25.0% — places blaCTX-M first, consistent with its global displacement of the TEM- and SHV-derived enzymes, and differs from the North Indian series in which blaTEM led [9] while agreeing with it on the extent of co-carriage.

Carbapenemase determinant prevalence of 31.8% closely matches the 32.97% carbapenem resistance reported among 3,421 Enterobacterales in Bihar, and our gene distribution reproduces that study almost exactly, blaNDM leading at 63.0% of carbapenem-resistant isolates against their 63.3% [10]. The therapeutic consequence is specific and often missed: blaNDM encodes a metallo-β-lactamase that is not inhibited by avibactam, vaborbactam or relebactam, so the newer β-lactam–β-lactamase inhibitor combinations, whatever their cost, address the minority mechanism at this centre and not the majority one.

The thirteen distinct determinant combinations observed among 59 gene-positive Enterobacterales, and the 25 isolates carrying both an ESBL and a carbapenemase determinant, are the more consequential finding for prophylaxis. Co-carriage of this kind is characteristic of plasmid-borne resistance, and it means that resistance at this centre is not distributed as independent single-gene events that a slightly broader agent might outflank, but as linked cassettes that move together.

In A. baumannii, blaOXA-23 in 76.2% of isolates and in 16 of the 17 carbapenem-resistant isolates matches the 92.6% found across 339 Indian A. baumannii genomes [27] and the 91.7% reported in another Indian clinical series [28]. We detected blaOXA-51 in all 21 isolates and interpret it as the intrinsic chromosomal species marker it is, rather than as an acquired resistance determinant — a distinction that is frequently elided in the literature and that inflates apparent gene prevalence when it is.

4.3 What these data mean for prophylaxis at this institute

The single clearest implication is negative. Ceftriaxone prophylaxis, which 61.5% of our patients received, cannot be justified by these data on any reading. It covered 24.6% of recovered isolates against cefazolin's 19.8% — a difference of nine isolates out of 187, well within the overlap of the confidence intervals — while being a markedly stronger driver of ESBL selection and consuming a Watch-category agent. Whatever the correct prophylactic regimen at this centre turns out to be, the current one is not defensible, and the reason it is in use is a supply-chain and habit problem rather than a clinical judgement [6].

The second implication concerns aminoglycosides. Adding gentamicin to cefazolin raised modelled coverage from 19.8% to 49.2%, an absolute gain of 29.4 percentage points, and ceftriaxone with amikacin reached 56.7%. Aminoglycoside resistance is frequently carried on the same plasmids as the β-lactamases, so this gain is smaller than the marginal susceptibility rates alone would predict, but it is real and it is achieved with an Access-category agent given as a single perioperative dose, in which setting nephrotoxicity and ototoxicity risk is low. A single-dose cefazolin–gentamicin combination is, on these data, the most plausible candidate for a revised institutional policy in contaminated and dirty abdominal procedures, and is the regimen we would propose for formal prospective evaluation. Table 11 sets out which changes to institutional practice these data actually support, which rest on guidelines rather than on our findings, and which remain open; we have separated them deliberately, because the three categories carry very different weight and are easily conflated.

The third implication is that carbapenems are not the answer, and this deserves stating plainly because the modelled coverage figures invite exactly that conclusion. Meropenem covered 54.0% of isolates and meropenem with vancomycin 70.1% — the highest figures in our analysis, and still short of what prophylaxis is supposed to achieve. Routine carbapenem prophylaxis in a setting where blaNDM is already present in 19.3% of Enterobacterales would select directly for the determinant that removes the last reliable option. WHO reached the same position from the opposite direction, declining to recommend ESBL-guided modification of prophylaxis for lack of evidence and warning that screening-driven practice might itself increase carbapenem consumption and carbapenem resistance [14]. It is worth recording, in fairness to the evidence, that a study comparing single-dose ertapenem with cefuroxime–metronidazole in ESBL carriers found *less* subsequent carbapenem-resistant Enterobacterales carriage after ertapenem, not more [29]; the ecological argument against routine carbapenem prophylaxis rests on population-level selection pressure and on the WHO position, not on that trial, and we are careful not to overstate it.

4.4 The denominator problem

Our coverage analysis describes the organisms recovered from patients who developed surgical site infection despite having received prophylaxis. It does not describe the organisms that prophylaxis is intended to prevent, and the difference is not a technicality.

Effective prophylaxis removes susceptible organisms from the population that goes on to cause clinical infection. Every patient in whom cefazolin worked is, by construction, absent from our 156 culture-positive cases. Conditioning the analysis on having developed an SSI therefore conditions on a variable that is a common effect of both the organism's susceptibility and the prophylaxis given, which is the structure that produces selection or collider-stratification bias [30]. The direction of the bias is predictable: modelled coverage estimated from breakthrough isolates will systematically understate the coverage the same regimen provides against the flora it actually encounters at incision. Our figure of 19.8% for cefazolin is therefore a lower bound of unknown tightness, not an estimate of cefazolin's prophylactic adequacy, and it would be a serious misreading of this paper to treat it as one.

We have not found this point made explicitly in the surgical prophylaxis literature, and we state it without citation for that reason; the closest approach we are aware of is an editorial arguing that SSI studies are uninterpretable without culture and sensitivity data linked to the prophylactic agent, which is an argument for more such data rather than about their bias [31]. We raise it because the inference it guards against — reading a low coverage figure as a mandate to broaden prophylaxis — is precisely the inference that would do harm here, and because the growing practice of constructing procedure-specific antibiograms from SSI isolates rests on the same structure.

What the analysis can legitimately support is narrower and still useful. It establishes that when prophylaxis fails at this centre, it fails against organisms carrying blaCTX-M and blaNDM rather than against susceptible skin flora; it quantifies how little residual activity the agents in current use retain against those organisms; and it identifies which combinations retain most. Establishing what prophylaxis should be requires the denominator that we and almost every Indian centre lack: the flora present at incision, obtained by preoperative screening of a defined surgical population, linked prospectively to outcome.

4.5 Comparison with the wider prophylaxis literature

Our prophylaxis–pathogen discordance of 77.5% is higher than the 35.9% recorded for low-HDI countries by GlobalSurg [12] and higher than the 58.0% in the FALCON secondary analysis, which included Indian sites [13]. Some of that gap is real and reflects the determinant burden documented here; some is methodological. GlobalSurg assessed resistance to the prophylactic agent among cultured SSI cases, and FALCON reported non-coverage among patients with an identified organism, but only 19.6% of FALCON's SSI patients were swabbed at all [13], and centres that swab selectively will swab the infections that are not resolving — which enriches for resistant organisms in some series and for severe ones in others. We cultured systematically rather than selectively, which we regard as a strength, but it also means our denominator is not the same as theirs and the figures should not be read as directly comparable.

On practice patterns our findings are unfortunately unsurprising. Ceftriaxone in 61.5% of patients and cefazolin in 14.1% mirrors the central Indian audit in which ceftriaxone accounted for 58.1% of preoperative prophylaxis and cefazolin was unavailable [4], and the Coimbatore surveillance in which cefazolin accounted for 3.5% of clean-procedure prophylaxis and none at all in clean-contaminated procedures [32]. An earlier study from a private Mumbai hospital found full compliance with all prophylaxis criteria in 52% of cases [33], which remains the best Indian figure we are aware of and is itself far from adequate.

The economic argument for correcting this is not marginal. A comparison of two Mumbai hospitals found the cost of antimicrobial prophylaxis to be US$0.42 per patient under a guideline-oriented policy against US$9 per patient without one, with no difference in SSI rate [34]. Correcting prophylaxis at this institute is therefore likely to be cost-saving before any resistance benefit is counted.

4.6 Strengths and limitations

The strengths of this study are prospective case ascertainment against CDC/NHSN criteria rather than retrospective laboratory-record review; systematic culture of all suspected SSI rather than selective swabbing, which avoids the enrichment that affects most comparable series; molecular characterisation of every Gram-negative isolate rather than of a selected resistant subset, so that determinant prevalence is estimated without the upward bias that phenotype-triggered testing introduces; and prospective recording of the prophylactic agent administered, which permits the discordance analysis to be linked at patient level rather than inferred from policy.

The limitations are substantial and we would not wish them understated. The denominator problem set out above is the most important of them and constrains the interpretation of the entire coverage analysis. Beyond it: this is a single centre, and determinant prevalence is known to vary widely between Indian institutions, so these figures should inform policy here and be regarded as a hypothesis elsewhere. Our PCR panel was closed, covering ten determinants, so plasmid-mediated AmpC enzymes, ESBLs outside the blaCTX-M, blaTEM and blaSHV families, and non-enzymatic mechanisms such as porin loss and efflux upregulation were not assessed, and determinant prevalence is correspondingly an underestimate of the genetic basis of the resistance observed. We did not perform plasmid replicon typing, conjugation assays or whole-genome sequencing, so the co-carriage patterns we report cannot be resolved into clonal spread versus independent plasmid acquisition — a distinction that matters directly for infection control. Anaerobic culture was not performed, so the contribution of anaerobes is unquantified and metronidazole could not be credited in the coverage model, which will understate the true

coverage of the metronidazole-containing regimens against polymicrobial abdominal infection. Prophylaxis was recorded as administered rather than audited for timing and redosing, so a proportion of the discordance we attribute to resistance may reflect mistimed or under-dosed administration. The quarterly gradient in determinant prevalence did not reach statistical significance and should not be read as an established trend; twelve months at a single centre affords little power to detect one. Finally, the analysis of association with wound class and specialty was univariate and unadjusted, and these variables are correlated with one another.

The priority for further work at this centre is the study these data cannot substitute for: preoperative rectal screening of a defined surgical cohort for ESBL and carbapenemase carriage, linked prospectively to SSI outcome and to the prophylaxis received. That design puts the flora present at incision into the denominator, and it is the only way to establish what prophylaxis should be rather than what it should not.

5. Conclusion

Two-thirds of Enterobacterales causing surgical site infection at this tertiary care institute carried an extended-spectrum β-lactamase determinant and almost one-third a carbapenemase determinant, dominated by blaCTX-M and blaNDM respectively, with frequent co-carriage and thirteen distinct determinant combinations. blaOXA-23 accounted for carbapenem resistance in A. baumannii. This is a determinant burden against which cephalosporin prophylaxis, of any generation, retains little in vitro activity.

The immediate and secure implication is that ceftriaxone prophylaxis, administered to 61.5% of our patients, should be discontinued. It provided no meaningful coverage advantage over cefazolin against the organisms recovered while exerting substantially greater selection pressure, and its predominance reflects cefazolin supply failure and prescribing habit rather than clinical reasoning. Restoring reliable cefazolin availability, enforcing single-dose administration within 60 minutes of incision, and reporting a surgical antibiogram annually are changes that follow directly from these data and require no further evidence; these and the remaining implications are set out against their evidential standing in Table 11.

What these data cannot establish is the regimen that should replace current practice. Isolates recovered from patients who developed infection despite prophylaxis are a sample selected by the failure of that prophylaxis, and coverage estimated from them understates by an unknown margin the coverage the same regimen affords against the flora encountered at incision. Broadening prophylaxis to carbapenems on the strength of such figures would be both unsupported and actively harmful in a setting where blaNDM is already present in one in five Enterobacterales. A single perioperative dose of cefazolin with gentamicin is the most plausible candidate for contaminated and dirty procedures on the evidence assembled here, and we propose it as a hypothesis for prospective evaluation rather than as a recommendation. The definitive study is one that screens the surgical population before incision, and it remains to be done in this setting.

Table 11. Changes to institutional prophylaxis practice supported by these data, and the question that remains open.

Action	Basis in these data	Evidential standing
Discontinue ceftriaxone as routine surgical prophylaxis	Covered 24.6% of isolates against 19.8% for cefazolin, a difference of 9 of 187 isolates with overlapping CIs; administered to 61.5% of patients	Supported. No coverage advantage, greater selection pressure, Watch-category agent.
Restore reliable cefazolin availability	Cefazolin administered to only 14.1% of patients despite being the guideline agent [1,3]	Supported. The displacement is a supply and habit problem, not a clinical one [6].
Enforce single preoperative dose within 60 minutes, no postoperative continuation	Not measured here; guideline recommendation [1,2,23]	Supported by guidelines, not by these data. Timing was recorded but not audited.
Report a surgical antibiogram annually and review policy against it	ESBL determinant prevalence 63.6%, carbapenemase 31.8% among Enterobacterales	Supported. Local prevalence is the stated basis for any policy choice [16].
Add single-dose gentamicin to cefazolin for contaminated and dirty procedures	Raised modelled coverage from 19.8% to 49.2%; ESBL carriage higher in contaminated or dirty wounds (OR 2.71)	Hypothesis for prospective evaluation. Not established by these data.
Broaden routine prophylaxis to a carbapenem	Meropenem covered 54% of isolates — the highest single-agent figure	Not supported and potentially harmful. *bla*NDM already in 19.3% of Enterobacterales; WHO warns of exactly this consequence [14].
Determine the regimen that should replace current practice	Cannot be answered from breakthrough isolates (section 4.4)	Open. Requires preoperative screening of a defined surgical cohort linked to outcome.

This table separates what these data establish from what they do not. It is not a treatment guideline and should not be adopted as one without local review.

DECLARATIONS

Relationship to other work from this cohort. This analysis and a companion manuscript on the correlation between phenotypic and genotypic detection of resistance draw on the same prospectively enrolled cohort, the same case ascertainment and the same laboratory dataset. The two address distinct questions — determinant prevalence and prophylaxis implications here, method concordance there — and neither reports the principal analysis of the other. Both manuscripts are declared to the editor of each journal at submission, and the cohort denominators are reported identically in both. Readers should count the cohort once.

Ethics approval and consent to participate. Approved by the Institutional Ethics Committee of NAMO Medical Education and Research Institute, Silvassa. Written informed consent was obtained from all participants.

Consent for publication. Not applicable; no individually identifiable patient data are presented.

Availability of data and materials. The de-identified isolate-level dataset and the analysis code that generates every figure and table are available from the corresponding author on reasonable request. Representative gene sequences have been deposited in GenBank under accession numbers.

Competing interests. The authors declare that they have no competing interests.

Funding. the study received no specific funding.

Acknowledgements. All technical staff of the Department of Microbiology, surgical residents who assisted with case ascertainment, and other non-author contributors.

Reporting guideline. Prepared in accordance with the STROBE statement for cross-sectional studies.

REFERENCES

1. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195–283. doi:10.2146/ajhp120568
2. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al.; Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. JAMA Surg. 2017;152(8):784–91. doi:10.1001/jamasurg.2017.0904
3. National Centre for Disease Control, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. National treatment guidelines for antimicrobial use in infectious diseases. Version 1.0. New Delhi: NCDC; 2016.
4. Singh MP. Appropriateness of surgical antibiotic prophylaxis in a tertiary care teaching hospital in central India: a retrospective analysis. Cureus. 2023;15(5):e38844. doi:10.7759/cureus.38844
5. Bhattacharjee S, Mothsara C, Shafiq N, et al.; ASPIRE II study group. Antimicrobial prescription patterns in tertiary care centres in India: a multicentric point prevalence survey. eClinicalMedicine. 2025;82:103175. doi:10.1016/j.eclinm.2025.103175
6. Kakkar AK, Shafiq N, Malhotra S. Cefazolin shortages in the developing world: the same, but different too. Clin Infect Dis. 2021;72(7):1293–5. doi:10.1093/cid/ciaa847
7. Indian Council of Medical Research. Annual report 2024: ICMR Antimicrobial Resistance Research and Surveillance Network. 8th ed. New Delhi: ICMR; 2025.
8. Sati H, Carrara E, Savoldi A, Hansen P, Garlasco J, et al.; WHO Bacterial Priority Pathogens List Advisory Group. The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies against antimicrobial resistance. Lancet Infect Dis. 2025;25(9):1033–43. doi:10.1016/S1473-3099(25)00118-5
9. Verma S, Kalyan RK, Gupta P, Khan MD, Venkatesh V. Molecular characterization of extended spectrum β-lactamase producing Escherichia coli and Klebsiella pneumoniae isolates and their antibiotic resistance profile in health care-associated urinary tract infections in North India. J Lab Physicians. 2023;15(2):194–201. doi:10.1055/s-0042-1757416
10. DebBarma P, Kokkayil P, Sarfraz A, Pati BK, Thakuria B. Phenotypic characterisation and prevalence of carbapenem-resistant Enterobacterales in a tertiary care centre in Bihar, India. Sci Rep. 2025;15:31477. doi:10.1038/s41598-025-04460-z
11. Dubinsky-Pertzov B, Temkin E, Harbarth S, Fankhauser-Rodriguez C, Carevic B, Radovanovic I, et al.; R-GNOSIS WP4 Study Group. Carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae and the risk of surgical site infection after colorectal surgery: a prospective cohort study. Clin Infect Dis. 2019;68(10):1699–704. doi:10.1093/cid/ciy768
12. GlobalSurg Collaborative. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. Lancet Infect Dis. 2018;18(5):516–25. doi:10.1016/S1473-3099(18)30101-4
13. NIHR Global Health Research Unit on Global Surgery. Microbiology testing capacity and antimicrobial drug resistance in surgical-site infections: a post-hoc, prospective, secondary analysis of the FALCON randomised trial in seven low-income and middle-income countries. Lancet Glob Health. 2024;12(11):e1816–25. doi:10.1016/S2214-109X(24)00330-9

14. World Health Organization. Summary of a systematic review on screening for extended-spectrum beta-lactamase and the impact on surgical antibiotic prophylaxis. Web Appendix 24. In: Global guidelines for the prevention of surgical site infection. 2nd ed. Geneva: World Health Organization; 2018.
15. Nutman A, Temkin E, Harbarth S, Carevic B, Ris F, Fankhauser-Rodriguez C, et al. Personalized ertapenem prophylaxis for carriers of extended-spectrum β-lactamase-producing Enterobacteriaceae undergoing colorectal surgery. Clin Infect Dis. 2020;70(9):1891–7. doi:10.1093/cid/ciz524
16. Temkin E, Margalit I, Nutman A, Carmeli Y. Surgical antibiotic prophylaxis in patients colonized with multidrug-resistant Gram-negative bacteria: practical and conceptual aspects. J Antimicrob Chemother. 2021;76(Suppl 1):i40–6. doi:10.1093/jac/dkaa496
17. Centers for Disease Control and Prevention, National Healthcare Safety Network. Surgical site infection event (SSI). NHSN Patient Safety Component Manual, Chapter 9. Atlanta (GA): CDC; January 2026.
18. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 36th ed. CLSI supplement M100. Wayne (PA): CLSI; 2026.
19. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268–81. doi:10.1111/j.1469-0691.2011.03570.x
20. Dallenne C, Da Costa A, Decré D, Favier C, Arlet G. Development of a set of multiplex PCR assays for the detection of genes encoding important β-lactamases in Enterobacteriaceae. J Antimicrob Chemother. 2010;65(3):490–5. doi:10.1093/jac/dkp498
21. Poirel L, Walsh TR, Cuvillier V, Nordmann P. Multiplex PCR for detection of acquired carbapenemase genes. Diagn Microbiol Infect Dis. 2011;70(1):119–23. doi:10.1016/j.diagmicrobio.2010.12.002
22. Woodford N, Ellington MJ, Coelho JM, Turton JF, Ward ME, Brown S, et al. Multiplex PCR for genes encoding prevalent OXA carbapenemases in Acinetobacter spp. Int J Antimicrob Agents. 2006;27(4):351–3. doi:10.1016/j.ijantimicag.2006.01.004
23. World Health Organization. Global guidelines for the prevention of surgical site infection. 2nd ed. Geneva: World Health Organization; 2018.
24. National Institute for Health and Care Excellence. Surgical site infections: prevention and treatment. NICE guideline NG125. London: NICE; 2019 (updated August 2020).
25. Desai D, Misra RN, Das NK, Gandham NR, Vyawhare CR, Mirza S. Prevalence of extended spectrum β-lactamases Klebsiella pneumoniae in various clinical samples and characterization of the bla genes in a tertiary care hospital of Western Maharashtra. Med J DY Patil Vidyapeeth. 2023;16(3):398–402. doi:10.4103/mjdrdypu.mjdrdypu_286_22
26. Govindaswamy A, Bajpai V, Khurana S, Aravinda A, Batra P, Malhotra R, et al. Prevalence and characterization of beta-lactamase-producing Escherichia coli isolates from a tertiary care hospital in India. J Lab Physicians. 2019;11(2):123–7. doi:10.4103/JLP.JLP_122_18
27. Paneri M, Sevta P, Yagnik VD. Burden of carbapenem-resistant Acinetobacter baumannii harboring blaOXA genes in the Indian intensive care unit. Glob J Med Pharm Biomed Update. 2023;18:12. doi:10.25259/GJMPBU_18_2023
28. Amar AK, Panda L, Prasad K, Sawant AR, Manoharan M, Menon J, et al. Increasing burden of antibiotic resistance in India due to co-existence of multiple classes of carbapenem and different aminoglycoside resistance genes in clinical isolates of Acinetobacter baumannii. Curr Microbiol. 2025;82(3):120. doi:10.1007/s00284-025-04097-1
29. Hoffman T, Lellouche J, Nutman A, Temkin E, Frenk S, Harbarth S, et al.; R-GNOSIS WP4 Study Group. The effect of prophylaxis with ertapenem versus cefuroxime/metronidazole on intestinal carriage of carbapenem-resistant or third-generation-cephalosporin-resistant Enterobacterales after colorectal surgery. Clin Microbiol Infect. 2021;27(10):1481–7. doi:10.1016/j.cmi.2021.02.002
30. Cole SR, Platt RW, Schisterman EF, Chu H, Westreich D, Richardson D, et al. Illustrating bias due to conditioning on a collider. Int J Epidemiol. 2010;39(2):417–20. doi:10.1093/ije/dyp334
31. Alverdy JC. Studies involving surgical site infections (SSIs) without culture results, the antibiotics chosen for prophylaxis and antibiotic sensitivity data: are they actionable? Ann Surg. 2024;279(1):13–4. doi:10.1097/SLA.0000000000006033
32. Kandasamy G, Arumugam V, Orayj K, Almanasef M, Asiri R, Alshahrani AM, et al. Antibiotic usage in surgical prophylaxis: surveillance of clean and clean-contaminated surgeries in a tertiary care hospital. Front Public Health. 2026;14:1759017. doi:10.3389/fpubh.2026.1759017
33. Parulekar L, Soman R, Singhal T, Rodrigues C, Dastur FD, Mehta A. How good is compliance with surgical antibiotic prophylaxis guidelines in a tertiary care private hospital in India? A prospective study. Indian J Surg. 2009;71(1):15–8. doi:10.1007/s12262-009-0004-9
34. Sarang B, Tiwary A, Gadgil A, Roy N. Implementing antimicrobial stewardship to reduce surgical site infections: experience and challenges from two tertiary-care hospitals in Mumbai, India. J Glob Antimicrob Resist. 2020;20:105–9. doi:10.1016/j.jgar.2019.08.001

Appendix. Data entry checklist

The values below are the only inputs that determine every number, table cell and figure in this manuscript. Replace them in `dataset.py`, then re-run `dataset.py`, `analysis.py`, `figures.py` and `build.js` in that order. Nothing else needs editing except the items marked.

The starred rows are shared with the companion genotype–phenotype manuscript and must be changed in both or the two papers will disagree.

Input	Placeholder	Location
Surgical procedures monitored *	2,184	dataset.py — TOTAL_PROCEDURES
SSI meeting CDC/NHSN criteria *	178	dataset.py — SSI_CASES
Culture-positive cases *	156	dataset.py — CULTURE_POS
Non-duplicate isolates *	187	dataset.py — ISOLATES
Polymicrobial infections *	29	dataset.py — POLYMICROBIAL
Isolate counts by species *	see Table 3	dataset.py — SPECIES
Susceptible counts per β-lactam *	see Table 10	dataset.py — BL
Susceptible counts, non-β-lactams *	see Table 10	dataset.py — NBL
ESBL determinant counts *	47 / 39 / 22; any 56	dataset.py — ctxm, tem, shv
Carbapenemase counts *	17 / 13 / 2 / 1 / 1; any 28	dataset.py — carba_carriers
A. baumannii determinants *	see Table 7	dataset.py — ab_res block
P. aeruginosa determinants *	see Table 7	dataset.py — pa_res block
Specialty / wound / quarter strata	see Table 8	dataset.py — SPEC_DESIGN, WOUND_DESIGN, QTR_DESIGN
Prophylaxis regimens administered	see Table 2	dataset.py — PROPHYLAXIS
Candidate regimens modelled	see Table 10	analysis.py — REGIMENS

The isolate-level construction in `dataset.py` assigns susceptibility by a nested resistance rank within each species. If real isolate-level data are available, replace the whole construction with the actual table and the downstream analyses will run unchanged.