

# Antibiotic Prophylaxis Prescribing Practice in Head and Neck Tumor Resection and Free Flap Reconstruction

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**Background.** Adherence to guidelines for antibiotic prophylaxis is often poor and is an important target for antimicrobial stewardship programs. Prescribing audits that suggested poor adherence to guidelines in a plastic surgery department led to a targeted education program to bring antibiotic prescriptions in line with hospital guidelines. We reviewed whether this intervention was associated with changed perioperative prescribing and altered surgical outcomes, including the rate of surgical site infections, specifically looking at clean-contaminated head and neck tumor resections with free flap reconstruction.

**Methods.** A retrospective cohort study was performed on 325 patients who underwent clean-contaminated head and neck tumor resection and free flap reconstruction from January 1, 2013, to February 19, 2019. Patients were divided into 2 groups, those before (pre-intervention) and after (postintervention) the education campaign. We analyzed patient demographic and disease characteristics, intraoperative and postoperative factors, and surgical outcomes.

**Results.** Patients pre-intervention were prescribed longer courses of prophylactic antibiotics (median [interquartile range], 9 [8] vs 1 [1];  $P < .001$ ), more topical chloramphenicol ointment (21.82% vs 0%;  $P < .001$ ), and more oral nystatin (36.9% vs 12.2%;  $P < .001$ ). Patients postintervention had higher rates of recipient infections (36.11% vs 17.06%;  $P < .001$ ) and donor site infections (6.94% vs 1.19%;  $P = .006$ ).

**Conclusions.** Following the education campaign, patients were prescribed shorter courses of prophylactic antibiotics, more of the recommended cefazolin-metronidazole regimen, and fewer topical antibiotics. However, patients also had a higher rate of surgical site infections.

**Keywords.** antibiotic prophylaxis; antimicrobial stewardship campaign; free flap; head and neck surgery; surgical site infection.

Guidelines for surgical antibiotic prophylaxis aim to optimize the balance between prevention of surgical site infections (SSIs) and the causation of side effects [1] or selection of drug-resistant organisms [2]. Adherence to guidelines is often suboptimal. Antimicrobial stewardship programs encourage evidence-based prescribing with a focus on decreasing the prescription of unnecessarily broad-spectrum antibiotics and limiting the duration of antibiotics, with the latter often being particularly pertinent in surgical prophylaxis. The recommended regimen for most surgical procedures is a single dose administered so that the peak tissue levels occurs at the time of incision [3]. However, data to support prophylaxis regimens for specific surgical procedures are limited, and extrapolation

may not be appropriate, leaving open the possibility that longer courses or use of different antibiotics may be optimal for specific procedures. In particular, it is possible that more prolonged or broader-spectrum regimens may be more effective for more complex and contaminated surgery.

There are limited controlled data to guide perioperative antimicrobial prescribing practice in patients undergoing resection of head and neck tumors [4]. These patients often undergo complex surgical excision, extensive neck dissection, and free flap reconstruction. In comparison to other less complex surgical procedures in the head and neck or other body areas, this surgery involves a breach of the upper airway epithelial barrier and exposure to oral and pharyngeal bacterial flora; thus these operations are generally termed clean-contaminated [5]. Surgical practice in terms of antimicrobial prophylaxis for these procedures commonly entails prolonged courses of antibiotics for 7–10 days, or until drain tubes are removed. This practice has been informed by the high risk of SSI in this group [6] and the need to prevent the very significant consequences of infection, including delayed wound healing, wound breakdown, fistula formation, and flap loss [6]. The Australian national guidelines [7] recommend a single dose of intravenous (IV) cefazolin 2 g within 60 minutes before

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surgical excision with metronidazole 500 mg up to 120 minutes before surgical excision.

Audits suggesting poor adherence to guidelines in the Plastic Surgery department at our hospital led to the implementation of a targeted education program in September 2017, aiming to bring surgical antibiotic prophylaxis in line with hospital guidelines. The intervention encompassed activities at all levels of the unit, including unit presentations to all consultant and resident staff, alteration of the resident handbook, and weekly joint ward rounds between the antimicrobial stewardship (AMS) and plastic surgery teams. It encouraged the use of shorter courses of antibiotics, more targeted-spectrum antibiotic prescription, and avoidance of topical antibiotics.

We undertook a retrospective study to determine if the education campaign changed perioperative antibiotic prescribing in patients undergoing free flap reconstruction following resection of a head and neck tumor and to investigate if these changes in perioperative care were associated with a change in operative outcomes, especially the rate of SSIs.

## METHODS

A retrospective cohort study was conducted on patients who underwent clean-contaminated [5] head and neck tumor resection and free flap reconstruction from January 1, 2013, to February 19, 2019, at the Royal Melbourne Hospital (RMH).

The study was approved by the Human Research Ethics Committee at Melbourne Health (QA2019019). Our study did not include factors necessitating patient consent.

Eligible patients were identified from the plastic and reconstructive surgery department theater bookings diary. We excluded patients whose surgical wounds were considered clean, contaminated, or dirty according to the Centers for Disease Prevention and Control (CDC) classifications [5] as these patients have a different rate of SSIs and alternative recommended prophylactic antibiotic regimens as per local guidelines [7]. We also excluded patients with secondary reconstruction or with incomplete or missing medical records (discharge summary, anesthetic chart, operation report, and medication). Data were systematically extracted by a single author (J.D. or P.G.) from hard copy and electronic medical records.

The duration of antibiotic prophylaxis was defined as the date antibiotics were first given (from the anesthetic chart) to when the postoperative antibiotic regimen (including oral tail) was either stopped, changed to an alternative antibiotic regimen, or there was a clearly documented change in indication. Medication and discharge summaries were used to obtain data on the duration of antibiotic prophylaxis.

The intervention encouraged the implementation of national recommendations on perioperative antibiotic prophylaxis [7], including the use of postoperative antibiotic prophylaxis consisting of IV cefazolin and metronidazole for up to 24 hours

and the avoidance of topical antimicrobial prophylaxis such as nystatin oral drops and topical chloramphenicol ointment (unless for incisions close to the eye). Liquid paraffin was recommended as an alternative to keep wounds moist and improve healing.

The intervention commenced in September 2017 and targeted all levels of the unit. It was initiated with a presentation by the AMS unit consultant and pharmacist to all consultant and resident staff of the plastic surgery department. Revision of the resident handbook was undertaken to reflect the agreed-upon guidelines. The handbook was given to residents at the commencement of each new resident rotation. Weekly joint ward rounds were undertaken throughout the year with an infectious disease physician, a pharmacist, and junior ward-based members of the plastic surgery department, with individual patient review and ongoing educational reinforcement of guidelines. Junior staff were able to change drug charts, given general unit consensus regarding guidelines.

Surgical outcomes within 30 days of the reconstruction included recipient SSIs, donor SSIs, nonsurgical site infections (*C. difficile*, pneumonia, urinary tract infection [UTI], and sepsis), return to theater, mortality, and hospital length of stay. SSIs were defined according to the CDC criteria [8] for deep SSIs as those within 30 days of the procedure and associated with 1 or more of the following:

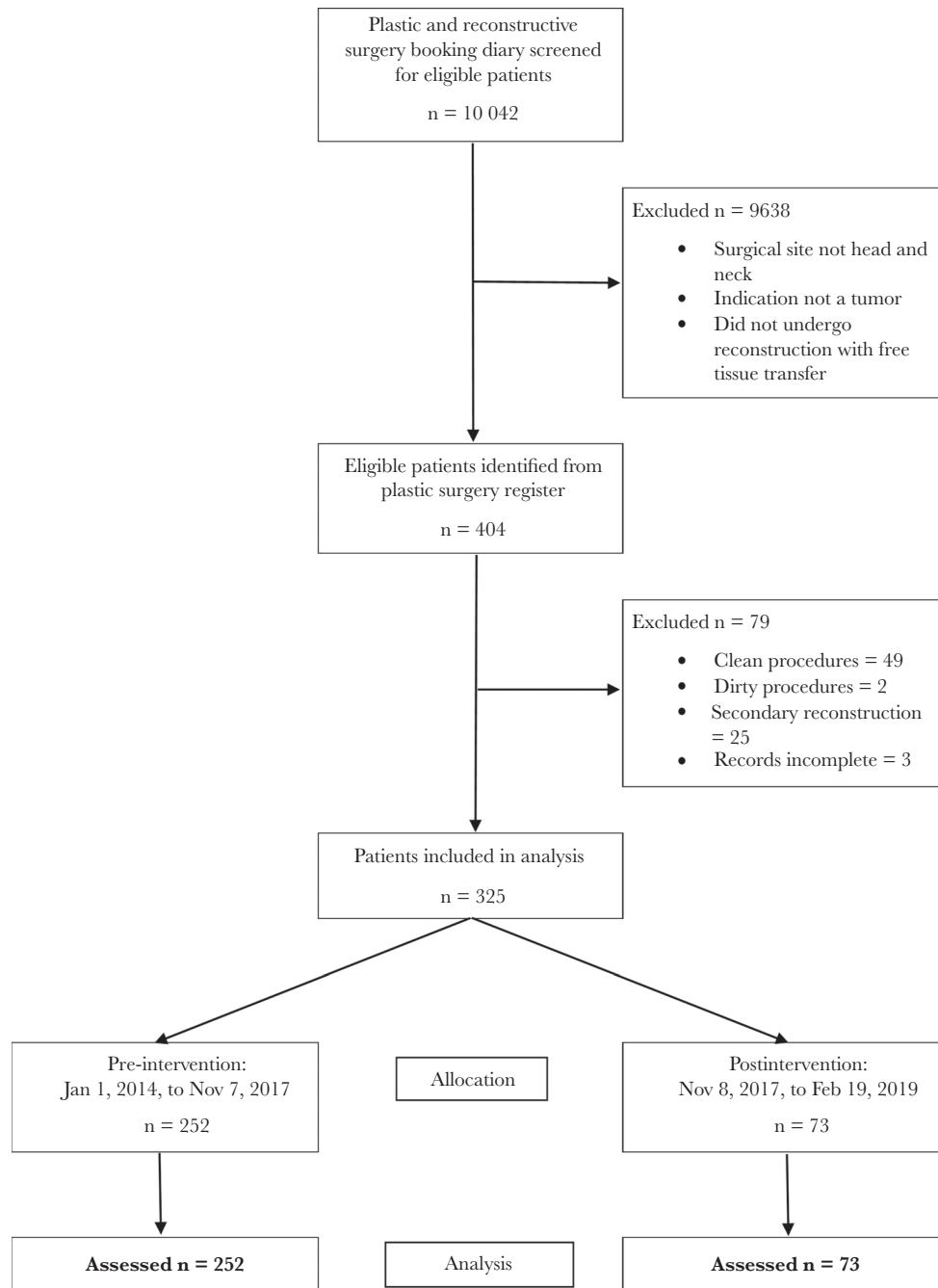
- A) purulent drainage from the deep incision;
- B) all the following:
  - I. pain or tenderness or fever  $>38^{\circ}\text{C}$ ,
  - II. spontaneous wound dehiscence or a wound deliberately opened by a surgeon, and
  - III. wound culture positive or not cultured;
- C) an abscess that involved the deep incision identified by examination, histopathology, or imaging; and
- D) diagnosis of SSI by a surgeon or physician. For example, if it was documented in a patient's discharge summary that they had a deep SSI or collection, but they did not meet criterion A, B, or C, they would still meet criterion D.

SSI was determined by 2 authors (J.D. and P.G.) independently and reviewed by all authors. In case of queries, cases were discussed between all authors and consensus achieved to determine classification. All data fields were collected for each patient; however, only the first CDC criterion for infection that the patient met was noted; for example, if a patient met criterion A, it was not noted whether they met the other criteria. Criteria in the progress notes, medication chart, or discharge summary that indicated non-surgical site infections included "*C. difficile* infection," "pneumonia," "UTI," and "sepsis." Free flap failure was defined as complete necrosis of the flap noted either on operation notes or the discharge summary. The primary end point was recipient SSI.

Binary and categorical variables, presented as frequency (%), were compared using the chi-square test of association between the 2 groups. Continuous variables with unequal variance, presented as median (interquartile range [IQR]), were compared using the Mann-Whitney *U* test. Continuous variables, presented as mean (SD), were compared using the Student *t* test. Correlations were analyzed using the Pearson *r* test. An alpha error of <.05 was taken to denote statistical significance. Statistical analyses and figures were generated using Jamovi, version 0.9 [9].

## RESULTS

A total of 10 042 operations were recorded in the RMH plastics unit theater bookings diary from January 1, 2013, to February 19, 2019, of which 404 were for resection of a head and neck tumor and reconstruction with free tissue transfer (Figure 1). Of these, 79 procedures were excluded because the operative sites were considered clean (*n* = 49) or contaminated (*n* = 2), the patient underwent secondary reconstruction (*n* = 25), or there were incomplete medical records (*n* = 3). In total, 325



**Figure 1.** Flowchart of patient selection showing total number of patient charts screened, number of patients excluded at different stages of the selection process, and final number of patients included in the analysis.

patients who underwent clean-contaminated procedures were included in the statistical analyses.

Demographic and disease characteristics for included patients are described in Table 1. As there were missing data, the total number of data entries for each variable is provided. Intraoperative and postoperative characteristics are presented in Table 2.

Surgical outcomes are described in Table 3. The overall rate of recipient SSI was 20.4% (n = 66/324), and the rate of donor SSI was 2.5% (n = 8/324).

Of the 66 patients diagnosed with a recipient SSI, 63 (95.5%) had swabs taken from the infected site for culture (Supplementary Table 1). Swab labels included “deep wound,”

“wound,” “pus,” “discharge,” “sterile fluid,” “aspirate,” “fluid drained,” “neck collection,” “abscess,” “oral,” “neck,” and “neck biopsy.” The most common organisms isolated were gram-positive aerobes, including *Streptococcus* spp. (n = 22, 33.3%), coagulase-negative *Staphylococcus* (n = 14, 21.2), methicillin-sensitive *Staphylococcus aureus* (MSSA; n = 6, 9.1), methicillin-resistant *Staphylococcus aureus* (MRSA; n = 3, 5.7%), and other gram-positive aerobes (n = 13, 19.7%). Gram-negative aerobes isolated included *Enterobacter* spp. (n = 7, 10.6%), *Enterococcus faecalis* (n = 6, 9.1%), *Proteus* spp. (n = 2, 3%), *Pseudomonas aeruginosa* (n = 2, 3%), and other gram-negative aerobes (n = 12, 18.2%). Other organisms isolated included *Candida albicans* (n = 7, 10.6%), anaerobes (n = 6, 9.1%), and mixed

**Table 1. Demographic and Disease Characteristics**

Characteristic	Overall	Pre-intervention	Postintervention	P
	No./Total (%)	No./Total (%)	No./Total (%)	
<b>Gender</b>				<b>.420</b>
Male	196/325 (60.3)	149/252 (59.1)	47/73 (64.4)	
Female	129/325 (39.7)	103/252 (40.9)	26/73 (35.6)	
<b>ASA class</b>				<b>.940</b>
1	30/302 (9.9)	23/235 (9.8)	7/67 (10.4)	
2	127/302 (42.1)	100/235 (42.6)	27/67 (40.3)	
3	140/302 (46.4)	108/235 (46.0)	32/67 (47.8)	
4	5/302 (1.7)	4/235 (1.7)	1/67 (1.5)	
5	0/302 (0)	0/235 (0)	0/67 (0)	
<b>Tobacco use</b>				<b>.887</b>
Never	156/315 (49.5)	119/244 (48.8)	37/71 (52.1)	
Former	98/315 (31.1)	75/244 (30.7)	23/71 (32.4)	
Current	61/315 (19.4)	50/244 (20.5)	11/71 (15.5)	
<b>Diabetes</b>	40/325 (12.3)	33/252 (13.1)	7/73 (9.6)	<b>.424</b>
<b>Other cardiovascular risk factors</b>				<b>.537</b>
Hypertension	58/325 (17.8)	44/252 (17.4)	14/73 (19.2)	
Hypercholesterolemia	19/325 (5.8)	11/252 (4.4)	8/73 (11.0)	
Hypertension and hypercholesterolemia	79/325 (24.3)	66/252 (26.1)	13/73 (17.8)	
<b>Prior radiotherapy to recipient site</b>	21/319 (6.6)	18/246 (7.3)	3/73 (4.1)	<b>.333</b>
<b>Disease type</b>				<b>.186</b>
SCC	275/325 (84.6)	211/252 (83.7)	64/73 (87.7)	
Adenocarcinoma	6/325 (1.8)	4/252 (1.6)	2/73 (2.7)	
Other carcinomas	17/325 (5.2)	14/252 (5.6)	3/73 (4.1)	
Sarcoma	6/325 (1.8)	4/252 (1.6)	2/73 (2.7)	
Melanoma	3/325 (0.9)	2/252 (0.8)	1/73 (1.4)	
Benign	18/325 (5.5)	17/252 (6.7)	1/73 (1.4)	
<b>Tumor stage</b>				<b>.003</b>
I	42/229 (18.3)	39/178 (21.9)	3/51 (5.9)	
II	64/229 (27.9)	54/178 (30.3)	10/51 (19.6)	
III	24/229 (10.5)	13/178 (7.3)	11/51 (21.6)	
IV	99/229 (43.2)	72/178 (40.4)	27/51 (52.9)	
	No. (Mean [SD])	No. (Mean [SD])	No. (Mean [SD])	P
<b>Age at surgery, y</b>	325 (60.4 [14.6])	252 (59.9 [15.0])	73 (62.0 [13.2])	<b>.269</b>
<b>Body mass index, kg/m<sup>2</sup></b>	324 (27.1 [6.00])	251 (27.2 [5.9])	73 (26.6 [6.45])	<b>.476</b>
<b>Pre-op albumin</b>	212 (37.9 [5.46])	162 (37.8 [4.87])	50 (38.0 [7.13])	<b>.888</b>

Bold formatting indicates statistical significance.

Abbreviations: ASA, American Society of Anesthesiologists; SCC, squamous cell carcinoma.

**Table 2. Intraoperative and Postoperative Features**

Characteristic	Overall	Pre-intervention	Postintervention	P
	No./Total (%)	No./Total (%)	No./Total (%)	
Mucosal incision				.910
Oral cavity	305/325 (93.8)	237/252 (94.0)	68/73 (93.2)	
Larynx or pharynx	38/325 (11.7)	30/252 (11.9)	8/73 (11.0)	
Nasal or sinus	9/325 (2.8)	7/252 (2.8)	2/73 (2.7)	
Bony resection				.159
Nil	82/325 (25.2)	68/252 (27.0)	14/73 (19.2)	
Mandible	144/325 (44.3)	110/252 (43.7)	34/73 (46.6)	
Maxilla	33/325 (10.2)	25/252 (9.9)	8/73 (11.0)	
Mandible and maxilla	55/325 (16.9)	43/252 (17.1)	12/73 (16.4)	
Other	11/325 (3.4)	6/252 (2.4)	5/73 (6.8)	
Neck dissection				.156
Nil	42/325 (12.9)	38/252 (15.1)	4/73 (5.5)	
Unilateral	223/325 (68.6)	168/252 (66.7)	55/73 (75.3)	
Bilateral	60/325 (18.5)	46/252 (18.3)	14/73 (19.2)	
Flap type				.131
Fasciocutaneous flap	228/325 (70.2)	182/252 (72.2)	46/73 (63.0)	
Osseocutaneous flap	97/325 (29.8)	70/252 (27.8)	27/73 (37.0)	
Metalware insertion	115/325 (35.4)	82/252 (32.5)	33/72 (45.8)	<b>.038</b>
Chloramphenicol ointment use	55/324 (17.0)	55/251 (21.9)	0/73 (0)	<b>&lt;.001</b>
Nystatin use	101/324 (31.2)	92/251 (36.7)	9/73 (12.3)	<b>&lt;.001</b>
Intraoperative antibiotic choice (from anesthetic chart)				.114
Cefazolin monotherapy	147/322 (45.7)	119/249 (47.8)	28/73 (38.4)	
Cefazolin-metronidazole	163/322 (50.6)	120/249 (48.2)	43/73 (58.9)	
Other	12/322 (4.0)	10/249 (4.0)	2/73 (2.7)	
Postoperative antibiotic choice (from medication chart)				<b>&lt;.001</b>
Cefazolin	151/320 (47.2)	141/247 (57.1)	10/73 (13.7)	
Cefazolin-metronidazole	145/320 (45.3)	84/247 (34.0)	61/73 (83.6)	
Other	24/320 (7.5)	22/247 (8.9)	2/73 (2.7)	
	No. (Mean [SD])	No. (Mean [SD])	No. (Mean [SD])	P
Operation duration, min	321 (624 [121])	248 (625 [117])	73 (620 [135])	.759
Days with tracheostomy in situ	295 (11.8 [5.64])	229 (11.9 [5.58])	66 (11.5 [5.89])	.630
Days nil by mouth	288 (13.6 [7.99])	235 (13.6 [7.29])	53 (13.8 [10.7])	.865
Days with recipient drain tube in situ	301 (12.7 [5.48])	237 (12.5 [5.31])	64 (13.5 [6.04])	.163
	No. (Median [IQR])	No. (Median [IQR])	No. (Median [IQR])	P
Duration of antibiotic prophylaxis, d	322 (7 [9])	250 (9 [8])	72 (1 [1])	<b>&lt;.001</b>

Bold formatting indicates statistical significance.

Abbreviation: IQR, interquartile range.

upper respiratory tract flora (n = 4, 6.1%). Swabs were culture negative in 4 patients.

Of patients with a recipient SSL, 45 of 66 (65.2%) had either an ultrasound or computed tomography (CT) scan of the recipient site, and 50 patients (72.5%) had a return to theater for infection within 30 days.

#### Antibiotic Prescribing—Characteristics and Changes Over Time

Data on antimicrobial use were obtained in 324 of the 325 included cases. There was a wide range of 0–28 days in the duration of antibiotic prophylaxis. The mean duration of antibiotic prophylaxis over the course of the study (SD) was 7.6 (5.8) days. We mapped the duration of prescribing over time (Figure 2B).

Based on the education campaign starting dates and the observed trend in prescribing, we divided the cohort into 2 groups: a pre-intervention group, which consisted of those before the education program (January 1, 2013, to November 7, 2017), and a postintervention group of those after (November 8, 2017, to February 19, 2019). The cutoff date was chosen to account for an expected delay in the impact of the education program, as well as because of a visible change in the duration of antibiotics around this date (Figure 2B). This encompassed 252 patients pre-intervention and 73 postintervention.

Thirty-eight patients had an allergy to first-line antibiotics recorded in their medication or anesthetic chart; of these, 33 (10.2%) were allergic to penicillin. The type of reaction and antibiotics prescribed are listed in Supplementary Table 2.

**Table 3. Surgical Outcomes**

Characteristic	Overall	Pre-intervention	Postintervention	P
	No./Total (%)	No./Total (%)	No./Total (%)	
Recipient SSI	66/324 (20.4)	41/252 (16.3)	25/72 (36.1)	<b>&lt;.001</b>
CDC criterion A	10/324 (3.1)	6/252 (2.4)	4/72 (5.6)	
CDC criterion B	16/324 (4.9)	13/252 (5.2)	3/72 (4.2)	
CDC criterion C	23/324 (7.1)	15/252 (6.0)	8/72 (11.1)	
CDC criterion D	17/324 (5.2)	7/252 (2.8)	10/72 (13.9)	
Donor SSI	8/324 (2.5)	3/252 (1.19)	5/72 (6.94)	<b>.006</b>
CDC criterion A	2/324 (0.6)	0/252 (0)	2/72 (2.8)	
CDC criterion B	4/324 (1.2)	2/252 (0.8)	2/72 (2.8)	
CDC criterion C	0/324 (0)	0/252 (0)	0/72 (0)	
CDC criterion D	1/324 (0.3)	1/252 (0.4)	1/72 (1.4)	
Other infections (≤30 d)				
UTI	8/324 (2.5)	5/252 (2.0)	3/72 (4.2)	.312
<i>C. difficile</i>	5/324 (1.5)	5/252 (2.0)	0/72 (0)	.294
Sepsis	10/324 (3.1)	6/252 (2.4)	4/72 (5.6)	.171
Pneumonia	90/323 (27.9)	77/251 (30.6)	13/72 (18.1)	<b>.035</b>
Total with other infection	113/324 (34.9)	84/252 (33.3)	18/74 (24.3)	<b>.070</b>
RTT for infection (≤30 d)	58/324 (17.9)	36/252 (14.4)	22/72 (30.6)	<b>.001</b>
RTT for other reason (≤30 d)	82/324 (25.3)	69/252 (27.4)	13/72 (18.1)	.109
Mortality (≤30 d)	1/324 (0.3)	1/252 (0.4)	0/72 (0)	.594
	No. (Mean [SD])	No. (Mean [SD])	No. (Mean [SD])	P
Hospital LOS, d	324 (17.0 [1.0])	252 (17.0 [1.0])	72 (17.5 [12.00])	.607

Bold formatting indicates statistical significance.

Abbreviations: *C. difficile*, *Clostridium difficile*; CDC, Centers for Disease Control and Prevention; LOS, length of stay; RTT, return to theater; SSI, surgical site infection; UTI, urinary tract infection.

### Pre- and Postintervention

The 2 groups were similar in demographic and disease characteristics; however, patients postintervention had significantly more advanced tumor stages (T-stages) (Table 3).

The 2 groups had similar mean operation durations, donor and recipient sites, tracheostomy duration, and nil by mouth and recipient drain tube duration; however, patients postintervention had more metalware insertion (n = 82/252, 32.5%, vs n = 33/72, 45.8%; P = .038).

There was a difference in antibiotic prophylaxis between the 2 groups, with cefazolin monotherapy being the most common regimen pre-intervention (n = 141/247, 57.1%), while cefazolin-metronidazole was most commonly used postintervention (n = 61/73, 83.6%; P < .001).

Pre-intervention, most patients received prolonged antibiotic regimens (median [IQR], 9 [8] days) (Figure 2A). Antibiotics were often continued for a period of 7 days, until all drain tubes were removed, hospital discharge, or first follow-up appointment. There was a delay between when the education campaign began (September 2017) and when an observed change in antibiotics prescribing occurred (November 7, 2017) (Figure 2B). Patients postintervention had significantly shorter courses of prophylactic antibiotics (median [IQR], 1 [1] day).

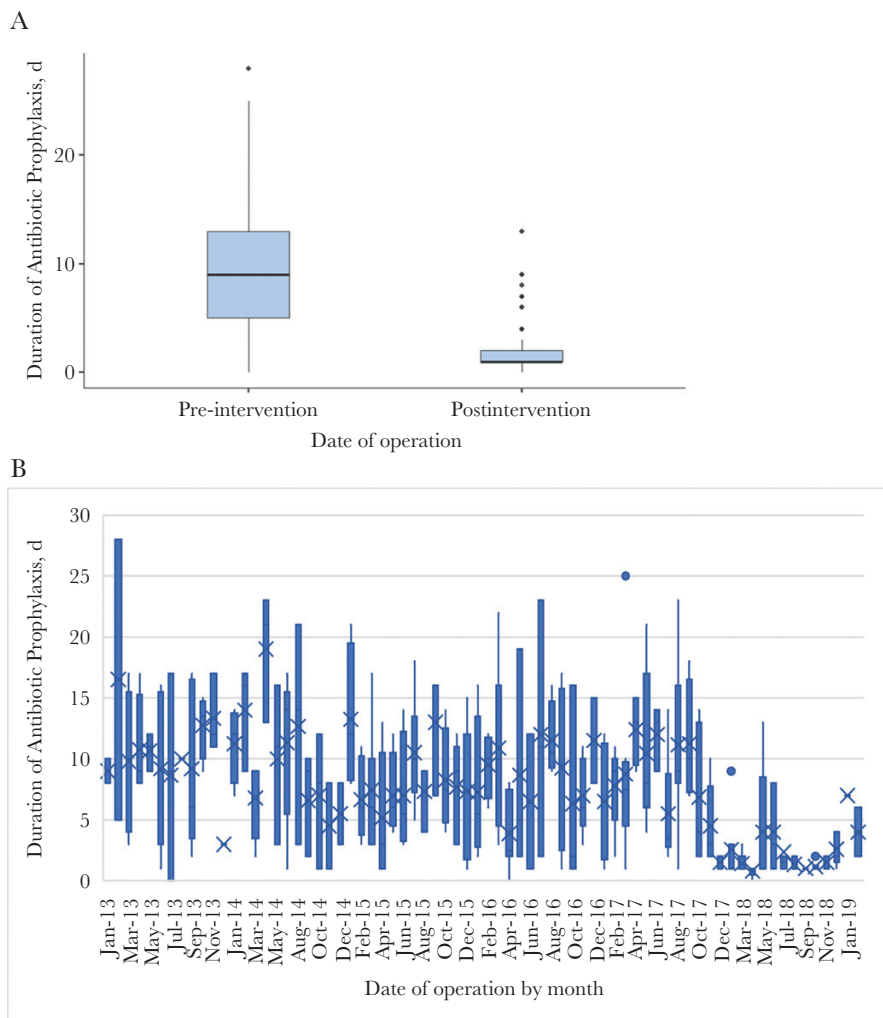
Before the education campaign, 21.9% of patients received topical chloramphenicol ointment, often administered to improve wound moisture and enhance healing. As part of

the education campaign, the plastics unit was encouraged to use an alternative moisturizer, such as liquid paraffin, except for incisions close to the eye. Subsequently, no patients postintervention received topical chloramphenicol. There was also less use of oral nystatin drops (n = 92/251, 36.7%, vs n = 9/73, 12.3%; P < .001).

The rates of both recipient and donor SSIs were higher postintervention. For recipient SSIs, the rate was 16.3% (n = 41/252) pre-intervention and 36.1% (n = 25/72) postintervention. The CDC criterion that each patient met is listed in Table 3. While criteria A, B, and C of the CDC criteria could be objectively assessed, criterion D was more ambiguous, and several cases remained unclear despite discussions between multiple authors. Notably, more patients in postintervention met criterion D (n = 7/252, 2.8%, vs n = 10/72, 13.9%). For donor SSI, the rate was 1.19% (n = 3/252) pre-intervention and 6.94% (n = 5/72) postintervention. Return to theater for infection at <30 days was significantly higher postintervention (n = 36/252, 14.4%, vs n = 22/72, 30.6%; P = .001). There was no statistically significant difference in non-surgical site infections, flap loss, hospital length of stay, or mortality (Table 3).

### DISCUSSION

Although the education campaign successfully led to more patients receiving the recommended regimen of cefazolin and



**Figure 2.** A, A box plot comparing the medians between patients from pre- and postintervention. Boxes signify interquartile ranges (IQRs), whiskers signify data within 1.5 IQRs of the nearest quartile, and individual points are outliers. B, A box plot showing the duration of prophylactic antibiotics (days) over time (month).

metronidazole, shorter courses of antibiotics, and less use of topical antimicrobials, there was an unexpected increase in the rate of recipient SSIs.

The intervention undertaken to change prescribing was remarkably successful in engaging local providers. Difficulties in changing surgical antibiotic prescribing practice have been explored, including lack of surgeon engagement, lack of accountability, and social factors such as professional hierarchy and varied perceptions of risks and fears [10]. A key strength of our study was the ongoing nature of the intervention, with joint ward rounds undertaken throughout the year, as well as the depth of engagement with the unit at all levels that was undertaken.

A key finding from our study is the importance of auditing outcomes when changing practice. It is critical to demonstrate that a change in practice is safe and effective in the local context. While the recipient SSI rate of the total cohort (20.4%) was comparable to other studies [6], it significantly increased after

the education campaign. There are several possible reasons for this.

First, patients postintervention were undergoing surgery for more advanced tumors (T-stage), possibly as a result of improved surgical techniques that enabled more advanced cases to be managed surgically. They also had more metalware insertion—a risk factor for infection [11].

Second, cases involving reconstruction of the head and neck are lengthy, with multiple surgical teams involved and numerous opportunities for sterile barriers to be compromised. There may have been changes in the maintenance of intraoperative sterile barriers between the 2 groups. For example, the widespread use of Skinman Alcohol Surgical Rub as an alternative to the traditional 3-minute Betadine Surgical Scrub occurred at a similar time as the education campaign.

Finally, it may be that extended courses of prophylactic antibiotics are indeed protective against SSI. The Australian Therapeutic Guidelines [7] state that a single preoperative dose

is likely sufficient for head and neck cancer resection, reconstruction, and extensive neck dissection. This guideline also notes that antibiotics may be considered for up to 24 hours postoperation, but should not be continued because of the presence of a drain tube. Other guidelines, including the American Society of Health-Systems Pharmacists (ASHP) [12], the World Health Organization [13], the CDC [5], and the Scottish Intercollegiate Guidelines Network (SIGN) [14], also all recommend against continuing antibiotic prophylaxis after wound closure in clean-contaminated surgery of the head and neck, even in the presence of a drain.

Given the higher risk of SSIs in complex head and neck surgery with microvascular reconstruction [6], it has been suggested that guidelines fail to account for the complexity of microvascular reconstruction relative to other head and neck procedures [15]. Most other studies have confirmed that there is no clear benefit of extended antibiotic prophylaxis in head and neck surgery [16–24]. A recent meta-analysis by Haidar [4] of 5 articles, with a total of 861 patients undergoing pedicle and free flap reconstruction for head and neck tumor defects, revealed that >24 hours of antibiotic administration may be more protective against recipient site infection.

The potential benefits of extended antibiotic prophylaxis must be weighed against the risk of side effects and of contributing to antimicrobial resistance [25, 26]. In addition to eradicating the bacteria causing SSIs, antibiotics may eliminate normal flora, thereby facilitating overgrowth of drug-resistant bacteria [2]. Infections with multidrug-resistant organisms may increase morbidity and mortality, as well as contribute to an increased length of hospital stay and health care costs [27]. We found that multidrug-resistant organisms accounted for only a small proportion of recipient SSIs, comparable to other studies [28, 29]. We therefore did not analyze the change in the incidence of multidrug-resistant organisms pre- and postintervention.

Interestingly, while the drop in patients receiving oral nystatin postintervention may have been a result of the education campaign, it may also have been as a result of the higher rate of oral candidiasis in the pre-intervention group due to the longer antibiotic courses altering the oral microbiome and facilitating overgrowth of *Candida* [30]. The poor documentation of whether nystatin drops were given prophylactically or as treatment makes it hard to evaluate this.

It is unlikely that antibiotic choice played any role in contributing to the increased rate of SSIs postintervention. Cefazolin, which covers predominantly gram-positive aerobes [31], has been shown to be more effective when combined with metronidazole, which provides additional anaerobic coverage (rate of recipient SSI 9.5% for cefazolin and metronidazole vs 18.6% for cefazolin monotherapy) [32]. However, the type of antibiotic used to prevent SSI in head and neck oncological surgery differs according to local guidelines and practices. For example, the ASHP [12] recommends broad-spectrum antibiotic

prophylaxis with cefazolin or ampicillin-sulbactam. Similarly, the SIGN [14] recommends broad-spectrum antimicrobial cover for aerobic and anaerobic organisms, for example, with ampicillin-sulbactam.

### Limitations

We found that the use of antimicrobials was poorly documented. This made it difficult to evaluate if they were being given prophylactically or as treatment. We therefore had to employ a consistent method for determining the length of prophylactic antibiotics retrospectively. Despite this, we noticed a wide range of prophylactic antibiotics of 0–28 days. On discussion with an experienced plastic surgeon (A.R.), it was noted that it would be very unusual for antibiotics to be continued beyond 7–10 days once a drain tube had been removed. Instead, they would have been continued for suspected infection.

Another limitation of the study is that we had to rely on accurate reporting of SSIs in patients' charts. While criteria A to C for deep SSI could be objectively assessed, criterion D was more subjective. The education campaign may have led to doctors being more aware of infections and better documentation of SSIs, thus explaining the higher number of patients who met criterion D postintervention.

Finally, the retrospective nature of our study meant we were unable to account for potential confounders, in particular, the more advanced tumor stages (T-stages) and metalware insertion in patients postintervention. Another potential confounder was a possible change in timing of intra-operative surgical antimicrobial prophylaxis. Although we did not collect any data on this, the timing of intra-operative prescription of antibiotics is run by the anesthetic department, which was not targeted by the intervention, and Surgical National Antimicrobial Prescribing Surveys suggest high rates of compliance with national guidelines [33]. It is therefore unlikely that this could have had an impact on increased SSIs postintervention.

### CONCLUSIONS

The education campaign on prophylactic antibiotic prescribing in the plastic and reconstructive surgery department, RMH, in 2017 led to shortening of courses of prophylactic antibiotic, more treatment with the recommended cefazolin and metronidazole regimen, and less use of topical antimicrobials. However, there was also a higher rate of SSIs. Given the discrepancy between guidelines and clinical practice, as well as limited evidence for single-dose regimens in complex head and neck surgery with free flap reconstruction, a prospective trial is needed to assess the efficacy of intraoperative-only compared with prolonged regimens.

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**Patient consent.** The procedures followed were in accordance with the ethical standards of the Helsinki Declaration (1964, amended most recently in 2008) of the World Medical Association. The study was approved by the Human Research Ethics Committee at Melbourne Health (QA2019019). Our study did not include factors necessitating patient consent.

**Availability of data.** Data are available upon request.

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