Antibiotic Prophylaxis for Preventing Surgical-Site Infection in Plastic Surgery: An Evidence-Based Consensus Conference Statement from the American Association of Plastic Surgeons

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Background: There is a growing concern for microbial resistance as a result of overuse of antibiotics. Although guidelines have focused on the use of antibiotics for surgery in general, few have addressed plastic surgery specifically. The objective of this expert consensus conference was to evaluate the evidence for efficacy and safety of antibiotic prophylaxis in plastic surgical procedures.
Methods: The authors searched for existing high-quality systematic reviews for antibiotic prophylaxis in the literature from the MEDLINE, Cochrane Library, and Embase databases. All synonyms for antibiotics were combined with terms for relevant plastic surgery procedures. The searches were not limited by language, and included all study designs. In addition, supplemental hand searches were performed of bibliographies of relevant articles, and extensive "related articles." Meta-analyses were performed and reviewed by experts selected by the American Association of Plastic Surgeons to reach consensus recommendations.
Results: Database searches identified 4300 articles, from which 2042 full-text articles were identified for eligibility. De novo meta-analyses were performed for each plastic surgical category. In total, 67 studies met the inclusion criteria, including nine for breast surgery, 17 for head and neck surgery, 10 for orthognathic surgery, seven for rhinoplasty/septoplasty, 19 for hand surgery, five for skin surgery, and two for abdominoplasty.
Conclusions: Systemic antibiotic prophylaxis is recommended for clean breast surgery and for contaminated surgery of the hand or the head and neck. It is not recommended to reduce infection in clean surgical cases of the hand, skin, head and neck, or abdominoplasty. (*Plast. Reconstr. Surg.* 135: 1723, 2015.)

In this era of overuse of antibiotics, microbial resistance is a growing concern. The benefit of antibiotic prophylaxis in preventing clinically

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relevant surgical-site infections must be balanced with the inherent risks of antibiotics.

Studies have demonstrated the relationship between antibiotic overuse and resistance.[1,2] The risks of antibiotic prophylaxis, both to the individual patient (e.g., gastrointestinal adverse events, *Clostridium difficile* risk, allergic reactions) and to the institution or region (e.g., increased resistance, reduced global efficacy of antibiotics) suggest that this question should not be considered lightly.

Existing surgical antibiotic prophylaxis guidelines[3,4] have focused on the use of antibiotics for surgery in general, but few have addressed plastic surgery specifically. Concern regarding the unnecessary use of antibiotics in the specialty of plastic surgery dates back to studies performed by Krizek, Koss, and Robson.[5–7] In their first survey of American Society of Plastic Surgeons members, a minority of surgeons reported using routine antibiotic prophylaxis.[5] When the survey was reported in 1985,[6] and again in 2003,[7] they found that the proportion of respondents using antibiotic prophylaxis increased dramatically with each passing decade (Fig. 1). They concluded that "Prophylactic antibiotics by plastic surgeons has increased by 100% to 200% ... without scientific evidence of increased incidence of infection, or efficacy."[7]

The Surgical Care Improvement Project of the Centers for Medicare and Medicaid Services includes surgical-site infection in its list of core quality performance indicators. The Surgical Care Improvement Project identifies six operative procedures that should be treated with prophylactic antibiotics: coronary artery bypass graft, other cardiac surgery, vascular surgery, total hip/knee arthroplasty, colon surgery, and hysterectomy. To be considered compliant, surgeons are expected to provide antibiotic prophylaxis for all patients undergoing these operations using the appropriate antibiotic, administered through the proper route, with the proper timing (within 1 hour of the incision), and discontinuing the antibiotics within the appropriate time (usually within 24 hours).

Preoperative antibiotics have historically been proposed for two main purposes: (1) to prevent surgical-site infections, and (2) to prevent bacteremia-induced joint prosthesis infection or infective endocarditis in high-risk patients. The updated guidelines from the American Heart Association[8] now recommend against routine antibiotic prophylaxis for preventing joint prosthesis infection or infective endocarditis in dental procedures, except for patients with artificial cardiac valve or certain congenital heart diseases, cardiac transplantation recipients who develop cardiac valve problems, patients who have received an artificial patch to repair a congenital heart defect within the past 6 months, and patients who have had previous infective endocarditis. Similarly, in the recent American Academy of Orthopaedic Surgeons and American Dental Association Clinical Practice Guidelines,[9] antibiotic prophylaxis is not recommended for most dental patients with total joint prostheses. The risk of antibiotic-associated adverse outcomes, including development of drug-resistant microorganisms, or anaphylaxis, exceeds the small benefit of prophylaxis, except in the select few patient groups at greatest risk listed above.

Because of the lack of randomized trials addressing antibiotic prophylaxis for plastic surgery, the general guidelines for surgical antibiotic prophylaxis do not specifically address plastic surgical procedures.[3,4] The silence regarding plastic surgery has further contributed to confusion, because "lack of evidence" is often confused with "evidence of lack" (of benefit). Attempts to provide guidelines for subsets of procedures related to plastic surgery have been published. In particular, Wright et al. and Maragh et al. published guidelines for dermatologic surgery in 2008,[10,11] and Bae-Harboe and Liang provided a recommended update in 2012.[12] Guidelines for other plastic surgical procedures are lacking, and as a result there is lack of consensus. Given the pressure to take an evidence-informed approach to antibiotic prophylaxis in plastic surgery, coupled with recent advances in understanding regarding global and patient-level antibiotic risks, we sought to develop evidence-based recommendations to guide appropriate use of antibiotic prophylaxis for common plastic surgical procedures.

OBJECTIVES

The objectives of this consensus statement were to evaluate the evidence for effectiveness and safety of antibiotics to prevent surgical-site infection in patients undergoing plastic surgery, and to develop evidence-based recommendations for the use of antibiotic prophylaxis across different types of plastic surgery.

METHODS

The methodology for evidence identification, retrieval, synthesis, and interpretation for this consensus statement was similar to previous published

PROCEDURE	1975	1985	2003
Blepharoplasty	7	11	47
Rhytidectomy	16	22	73
Brow Lift	-	-	67
Chemical Peel	-	17	49
Laser Resurfacing	-	-	74
Dermabrasion	-	-	60
Malar/Chin Implant	-	64	93
Rhinoplasty	25	24	78
Rhinoplasty (septum)	-	31	80
Rhinoplasty (cartilage grafts)	-	50	88
Rhinoplasty(alloplastic implants)	50	74	93
Abdominoplasty	31	43	88
Thigh Lift	-	41	88
Buttock Lift	-	41	87
Arm Contouring	-	24	81
Suction-Assisted Lipectomy	-	33	79
Ultrasound-Assisted Lipectomy	-	-	81
Breast Augmentation	43	59	94
Breast Reduction	30	44	88

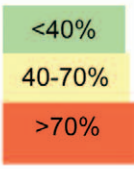

Fig. 1. Frequency of use of prophylactic antibiotics. (Data from Krizek TJ, Koss N, Robson MC. The current use of prophylactic antibiotics in plastic and reconstructive surgery. *Plast Reconstr Surg*. 1975;55:21–32; Krizek TJ, Gottlieb LJ, Koss N, Robson MC. The use of prophylactic antibacterials in plastic surgery: A 1980s update. *Plast Reconstr Surg*. 1985;76:953–963; and Lyle WG, Outlaw K, Krizek TJ, Koss N, Payne WG, Robson MC. Prophylactic antibiotics in plastic surgery: Trends of use over 25 years of an evolving specialty. *Aesthet Surg J*. 2003;23:177–183.)

consensus conferences in the field of surgery.[13–15] Specifically selected members of the American Association of Plastic Surgeons were invited to participate in the consensus panel based on their clinical expertise in selected plastic surgical procedures. Additional consensus conference panelists were invited to provide expertise in infectious diseases, clinical epidemiology, evidence-based medicine, and guidelines development. Panelists short-listed potential types of plastic surgery for inclusion in the review based on the need to prioritize and to focus on areas of highest importance to plastic surgeons.

Systematic reviews with meta-analysis of randomized trials were considered preferentially to inform the evidence-based statements. Because randomized controlled trials are often underpowered for uncommon events, or of insufficient duration to assess longer term effects, we also included evidence from quasi-randomized

Table 1. Surgical Wound Classification*

Class	Type	Definition
I	Clean	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. Clean wounds are closed primarily, and if necessary, drained with closed drainage.
II	Clean-contaminated	Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions, and without unusual contamination.
III	Contaminated	Open, fresh, accidental wounds, or incisions in which acute, nonpurulent inflammation is encountered; or, operations with major breaks in sterile technique or gross spillage from the GI tract.
IV	Dirty or infected	Wounds with existing clinical infection or perforated viscera, and old traumatic wounds with retained devitalized tissues. This category presumes that the organisms causing postoperative infection were present in the operative field before the operation.

GI, gastrointestinal.
*From http://www.cdc.gov, January of 2013.

(patient allocation by chart number or alternating days), and observational studies in secondary meta-analyses.

After consideration of the existing evidence, recommendations were made regarding the use of antibiotic prophylaxis. The Grading of Recommendations, Assessment, Development and Evaluation framework was used to assess the level of evidence and to label the class of recommendation.[16] The Grading of Recommendations, Assessment, Development and Evaluation is a system developed to grade evidence and recommendations, increasingly being adopted by organizations worldwide, which has many advantages over previous methods including an explicit set of criteria for downgrading and upgrading evidence quality, and provision of explicit interpretations of strong versus weak recommendations.

Search Strategy and Evidence Retrieval

The searches were not limited by language, and included all study designs, to be maximally sensitive. Gray literature was searched, including guidelines Web sites, health technology assessment sources, and clinical trial registries. In addition, supplemental hand searches were performed of bibliographies of relevant articles, and extensive "related articles" searches were performed electronically. All synonyms for antibiotics were combined with terms for relevant plastic surgery procedures.

For each subtype of plastic surgery, we searched for existing high-quality systematic reviews or meta-analyses of antibiotic prophylaxis. Because high-quality recent reviews were not found, de novo systematic reviews and meta-analyses were performed by a subset of members of the group for subsequent publication and are reported in detail elsewhere.[17] These reviews were performed and reported in accordance with recent guidelines for evidence synthesis.[18,19] MEDLINE, Cochrane Library, and Embase databases were searched from their date of inception to February of 2013, and were supplemented with updates of PubMed to January of 2014.

Data Extraction and Data Analysis

Data were extracted in duplicate and double-checked by a team of independent systematic reviewers and compared. Descriptive information was also extracted, including study design, type of surgical procedure, antibiotic regimen, timing and duration of antibiotic administration, classification of surgery (clean, clean-contaminated, contaminated, or dirty) (Table 1), and definition of surgical-site infection (Table 2).

Statistical synthesis through meta-analysis was performed using the random effects model. Because random effects and fixed effects models provide identical results when the heterogeneity is low or absent, the Cochrane Collaboration and other meta-analysis methodologists recommend the use of random effects for all outcomes. Odds ratios and 95 percent confidence intervals were reported for the primary outcome of surgical-site infection for each type of surgery, and for each class (i.e., clean, clean-contaminated, contaminated, and dirty). Heterogeneity across studies was estimated using the I^2 statistic, whereby an I^2 value below 50 percent was considered low heterogeneity, I^2 exceeding 50 percent was considered moderately heterogeneous, and I^2 exceeding 75 percent was considered highly heterogeneous.

Levels of Evidence and Grade of Recommendations

The method of Grading of Recommendations, Assessment, Development and Evaluation was used to appraise the quality of evidence and provide the grade of recommendation.[16] Summary-of-findings tables were created to guide

Table 2. Surgical-Site Infection Types and Definitions

SSI Type	Definition
Superficial	Infection occurs within 30 days after surgery and involves only skin and subcutaneous tissue of the incision and patient has at least one of the following: 1. Purulent drainage from the superficial incision. 2. Organisms isolate from an aseptically obtained culture of fluid or tissue from the superficial incision. 3. Superficial incision that is deliberately opened by a surgeon and is culture-positive or not cultured and patient has at least one of the following signs or symptoms: pain or tenderness, localized swelling, redness, or heat. A culture-negative finding does not meet this criterion. 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.
Deep incisional	Infection occurs within 30 or 90 days after the operation and involves deep soft tissues of the incision (i.e., fascial and muscle layers) and the patient has at least one of the following: 1. Purulent drainage from the deep incision. 2. A deep incision that spontaneously dehisces or is deliberately opened by the surgeon and is culture-positive or not cultured, and patient has at least one of the following: fever (>38°C), localized pain, or tenderness. A culture-negative finding does not meet this criterion. 3. An abscess or other evidence of infection involving the deep incision that is found on direct examination, during an invasive procedure, or by histopathologic examination or imaging test. 4. Diagnosis of deep incisional SSI by a surgeon or attending physician.
Organ/space	Infection occurring within 30 or 90 days after the operation and infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure and the patient has at least one of the following: 1. Purulent drainage from a drain that is placed into the organ/space. 2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space. 3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during invasive procedure, or by histopathologic examination or imaging test. 4. Diagnosis of an organ/space SSI by a surgeon or attending physician. 5. Meets at least one criterion for a specific organ/space infection site (e.g., bone, breast abscess or mastitis, ear, mastoid, oral cavity, sinusitis).

SSI, surgical-site infection.

the progression from systematic review results to making clear recommendations (see www.armg.cochrane.org for more information on summary-of-findings and Grading of Recommendations, Assessment, Development and Evaluation methodology). For each evidence statement, the rationale for the determination of level of evidence (Grade of Recommendation) is provided in the summary-of-findings tables (Table 3 and 4) to provide the basis for labeling the recommendations as strong or weak.[16,18,19]

RESULTS

Database searches identified over 4300 articles, with 2042 full-text articles assessed for eligibility (Fig. 2). Because no systematic reviews or meta-analyses of adequate quality met the inclusion criteria for the plastic surgery procedures of interest, we compared de novo meta-analyses for each procedure of interest. In total, 67 studies met the inclusion criteria,[20–85] including nine for breast surgery, 17 for head and neck surgery, 10 for orthognathic surgery, seven for rhinoplasty/septoplasty, 19 for hand surgery, five for skin surgery, and two for abdominoplasty. Most studies used a single dose or up to 24 hours of antibiotic prophylaxis; however, some studies provided longer term administration, for days or even weeks. Most studies reported giving the antibiotic before surgical incision; however, a substantial number reported initiating the antibiotic "perioperatively," and many did not report how long before incision the antibiotic was given. The class of antibiotic and doses given were sufficiently variable for each type of surgery that we did not attempt to assess efficacy by type of antibiotic.

The results of this consensus conference are outlined below by each category of surgery, with further information given for the relevant evidence that formed the basis for the statements and recommendations. Readers are referred to Table 5 for a summary of the meta-analysis results, and to Tables 3 and 4 for the summary of findings and Grading of Recommendations, Assessment, Development and Evaluation tables.

FOCUS ON INDIVIDUAL OPERATIONS

Breast Surgery

Clean Cases

Primary analysis (randomized controlled trials only): Meta-analysis of three randomized trials[20–22] showed a significant reduction in risk of surgical-site infection with antibiotic prophylaxis versus control (2.5 percent versus 11.4 percent; OR, 0.16; 95 percent CI, 0.04 to 0.61; $p = 0.01$) for patients undergoing cosmetic breast surgery (Table 5). Studies failed to

Table 3. Summary of Findings and Grade of Evidence Rating for Clean (i.e., Class I) Plastic Surgery

		Quality Assessment						No. of Patients		Effect		
Type of Surgery	No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Routine Antibiotic Prophylaxis (%)	No Antibiotic Prophylaxis (%)	Relative (95% CI)	Absolute	Quality of Evidence[a]
Breast (clean)	3	Randomized trials	Very serious[b–e]	No serious inconsistency[f]	Serious[g,h]	No serious imprecision	Strong association[i]	2.5	11.4	OR, 0.16 (0.04–0.61)	94 fewer per 1000 (from 41 fewer to 109 fewer)[j]	Low
Hand (clean)	1	Randomized trials	Serious[k]	No serious inconsistency[f]	No serious indirectness	Serious[l]	None[m]	8.8	14.5	OR, 0.57 (0.21–1.57)	57 fewer per 1000 (from 111 fewer to 65 more)	Low
Head and neck (clean)	4	Randomized trials	Very serious[e,n–p]	No serious inconsistency	No serious indirectness[q]	Serious[l]	None[m]	1	1	OR, 0.77 (0.13–4.65)	2 fewer per 1000 (from 9 fewer to 36 more)	Very low
Skin (clean)	4	Randomized trials	Serious[e,n,o]	Serious[r]	Serious[q,s]	Serious[l]	None[m]	1.3	4.5	OR, 0.55 (0.13–2.38)	20 fewer per 1000 (from 39 fewer to 56 more)	Very low

SSI, surgical-site infection.

[a]Grading of Recommendations, Assessment, Development and Evaluation Working Group grades of evidence. High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate.

[b]Loss to follow-up in Amland (1983) (more patients lost to follow-up than had an SSI, suggesting that if all patients had been followed up, the conclusions might have differed significantly).

[c]Gylbert was the largest study, and reported zero events (and thus does not contribute to pooled estimate of risk).

[d]Platt (1990) did not describe loss to follow-up.

[e]A number of these were small subgroups reported within a larger study [i.e., Amland (1995), Eschelman (1971)].

[f]No statistical heterogeneity across randomized controlled trials.

[g]Gylbert did not provide definition for infection.

[h]Platt and Gylbert recruited patients in the 1980s, and Amland recruited patients in the early 1990s, which may not reflect contemporary practice.

[i]80% reduction in odds of infection (35% to 95%).

[j]Absolute risk given for ease of interpretation, although OR is more reliable statistically for this meta-analysis.

[k]In Whittaker (2005), 13 patients were excluded and five were lost to follow-up for unknown reasons.

[l]Large 95% CI, ranging from important reduction in SSI risk to important increase in SSI risk.

[m]Low power to detect publication bias.

[n]Eschelman (1971) discontinued early, because of large difference between groups (i.e., stopped early, when only nine patients in the head and neck surgery subgroup).

[o]Amland (1995) excluded 25 patients (because they received antibiotics off-protocol). This exclusion supersedes the small number of outcomes reported, and introduces a large risk of bias.

[p]Mailler-Savage (2008) did not describe randomization process, and a few patients were lost to follow-up.

[q]In Eschelman (1971), patients recruited in 1960s, and may not reflect contemporary practice.

[r]Different magnitude and direction of effect size (high heterogeneity across studies).

[s]Bencini (1991) and Ma (1989) recruited patients in the 1980s, and may not reflect contemporary practice.

Table 4. Summary of Findings and Grade of Evidence Rating for Contaminated (i.e., Class II, III, or IV) Plastic Surgery

		Quality Assessment						No. of Patients		Effect		
Type of Surgery	No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Routine Antibiotic Prophylaxis	No Antibiotic Prophylaxis	Relative (95% CI)	Absolute	Quality [a]
Head and neck (nonclean)	8	Randomized trials	Very serious[b–e]	No serious inconsistency	Serious[f]	No serious imprecision	Strong association[g]	16.4%	41.9%	OR, 0.23 (0.11–0.46)	277 fewer per 1000 (from 170 fewer to 346 fewer)	Low
Hand (nonclean)	6	Randomized trials	Very serious[f,h–o]	No serious inconsistency	Serious[f]	Serious[p]	None[q]	5.1%	7.7%	OR, 0.254 (0.30–0.96)	56 fewer per 1000 (from 3 fewer to 53 fewer)	Very low
Orthognathic/mandibular (nonclean)	6	Randomized trials	Very serious[e,k,n,r,s]	No serious inconsistency	Serious[f]	No serious imprecision	Strong association [g]	6.5%	31.8%	OR, 0.17 (0.10–0.31)	245 fewer per 1000 (from 192 fewer to 274 fewer)	Low
Septoplasty/rhinoplasty (nonclean)	4	Randomized trials	Very serious[e,k,r,t]	No serious inconsistency	Serious[f]	No serious imprecision	Strong association[g]	16/327 (4.9%)	33/292 (11.3%)	OR, 0.45 (0.24–0.86)	59 fewer per 1000 (from 14 fewer to 83 fewer)	Low

SSI, surgical-site infection.

[a]Grading of Recommendations, Assessment, Development and Evaluation Working Group grades of evidence. High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate.

[b]Loss to follow-up in Amland (1983) (more patients lost to follow-up than had an SSI, suggesting that if all patients had been followed up, the conclusions might have differed significantly).

[c]Becker excluded four patients because of death.

[d]Ketcham (1962), Eschelman (1971), and Johnson (1984) were discontinued early because of perceived "large difference" between groups (although early stopping rules were not clearly defined).

[e]A number of these were small subgroups reported within a larger study [i.e., Amland (1995), Eschelman (1971)].

[f]A number of the studies recruited patients in the 1960s, 1970s, 1980s, and may not reflect contemporary practice.

[g]Large effect size, adds strength to the suggestion that antibiotics may reduce risk of infection; albeit this needs to be interpreted in light of the caveats because of the significant risk of bias in these studies.

[h]Length of follow-up was not described in many studies, and ranged from 3 days to 3 months.

[i]In Altergott (2008), 11 patients were withdrawn or lost to follow-up.

[j]Altergott (2008) was discontinued early, because of staffing issues.

[k]Definition of infection was unclear or undefined in a number of studies.

[l]Randomization process not described in Roberts (1977).

[m]Sloan (1987) was stopped early for unclear reasons.

[n]Most trials were not blinded.

[o]In Stevenson (2003), six patients were lost to follow-up.

[p]Effect size estimate ranges from clinically important to clinically negligible.

[q]The small number of studies, together with the small range of sample sizes, means this meta-analysis is underpowered to detect publication bias.

[r]Eschelman (1971) discontinued early, because of large difference between groups (i.e., stopped early, when only nine patients were in the head and neck surgery subgroup).

[s]Zallen (1971) did not provide details of randomization or definitions of infection.

[t]In Lilja (2010), the randomization process was not clearly described.

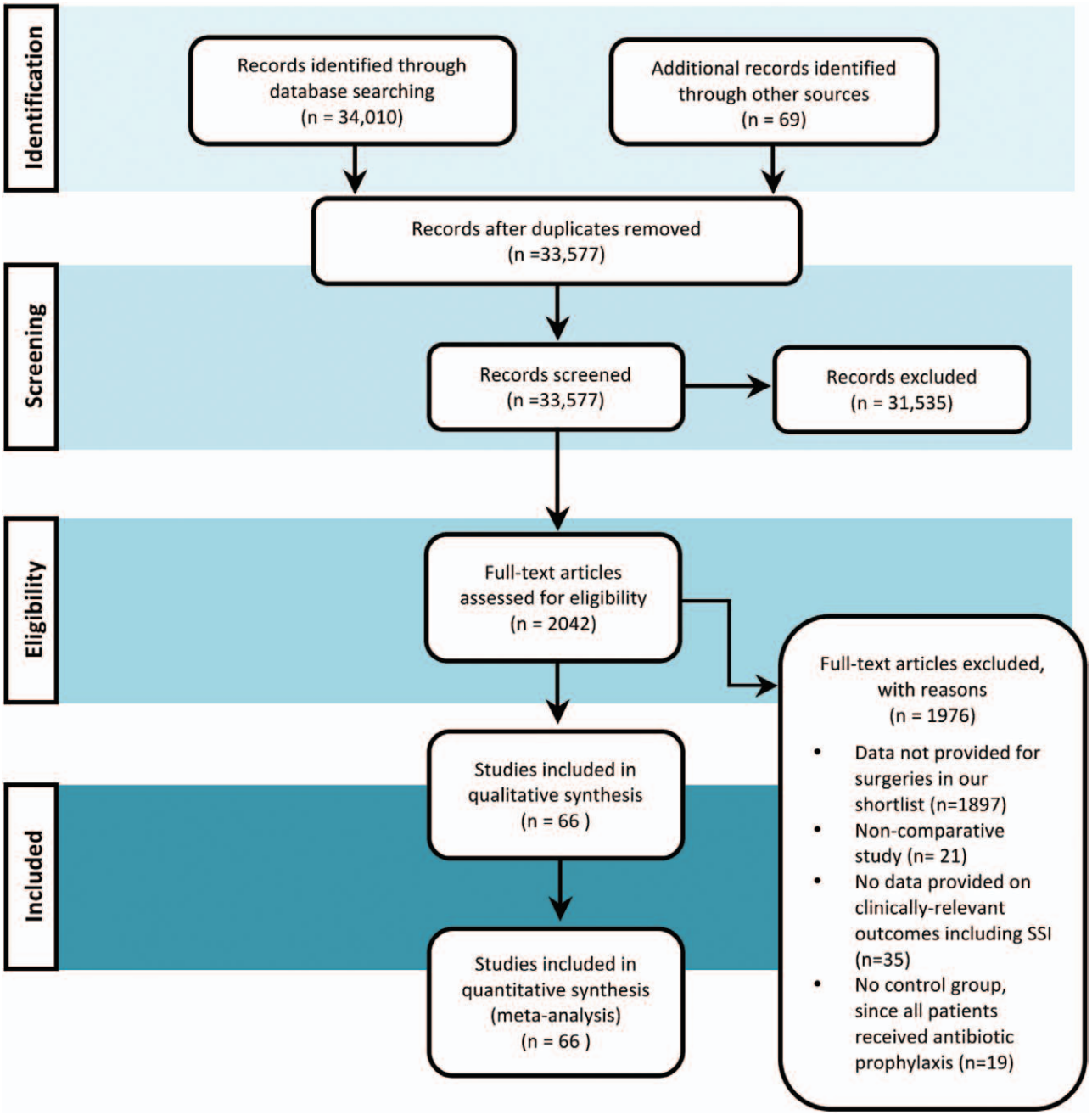

Fig. 2. PRISMA Study inclusion flowchart. *SSI*, surgical-site infection.

report on adverse events or development of antibiotic resistance. There were insufficient data from randomized controlled trials for subanalysis of efficacy by implant versus no implant.

Secondary analysis (randomized controlled trials plus nonrandomized controlled trial combined): When randomized, pseudorandomized, and nonrandomized studies were considered together,[20–28] the risk of surgical-site infection remained significantly reduced, but the results were lesser in magnitude than in randomized controlled trials alone (3.8 percent versus 6.7 percent; OR, 0.50; 95 percent CI, 0.26 to 0.94; $p = 0.03$).

Subgroup analysis for breast augmentation (with implant) versus breast reduction did not show a significantly greater effect for patients receiving implants. However, this subanalysis was underpowered because only two studies reported on breast augmentation.[21,25] Similarly, only one study provided results by presence or absence of drain, and this was underpowered to find differences between groups.[25] One nonrandomized controlled trial

Table 5. Summary Results of Meta-Analysis of Studies Comparing Antibiotic Prophylaxis versus Control in Plastic Surgery

	SSI Event Rate (Unweighted)			
	Abx Px Group (%)	Control Group (%)	OR (95%CI) (Weighted)	*p*
Breast surgery (clean surgery)				
RCTs (3 RCTs, 224 patients)	2.5	11.4	0.16 (0.04–0.61)	0.01
RCTs plus non-RCTs combined (9 studies; 1194 patients)	3.8	6.7	0.50 (0.27–0.92)	0.03
Hand surgery (clean)				
RCTs (1 RCT; 157 patients)	8.8	14.5	0.57 (0.21–1.57)	0.28
RCTs and non-RCTs combined (5 studies; 11,936 patients)	0.9	0.6	0.81 (0.40–1.66)	0.56
Hand surgery (contaminated)				
RCTs (6 RCTs; 1435 patients)	5.1	7.7	0.54 (0.30–0.96)	0.04
RCTs and non-RCTs combined (15 studies; 3715 patients)	4.9	5.7	0.76 (0.49–1.17)	0.13
Head and neck surgery (clean)				
RCTs (4 RCTs; 591 patients)	1.0	1.0	0.77 (0.13–4.65)	0.77
RCTs and non-RCTs combined (8 studies; 1423 patients)	2.4	3.7	0.49 (0.19–1.23)	0.13
Head and neck surgery (contaminated)				
RCTs (8 RCTs; 416 patients)	16.4	41.9	0.23 (0.11–0.46)	<0.0001
RCTs and non-RCTs combined (10 studies; 836 patients)	12.2	25.7	0.26 (0.12–0.54)	<0.0001
Orthognathic/mandibular surgery (clean)				
RCTs (no RCTs)	—	—	—	—
RCTs and non-RCTs combined (1 study; 74 patients)	0	2.2	0.56 (0.02–14.3)	0.73
Orthognathic/mandibular surgery (contaminated)				
RCTs (6 RCTs; 480 patients)	6.5	31.8	0.17 (0.10–0.31)	<0.0001
RCTs and non-RCTs combined (10 studies; 1201 patients)	5.0	15.5	0.34 (0.14–0.80)	0.01
Septoplasty/rhinoplasty (clean)				
RCTs (0 RCTs)	—	—	—	—
RCTs and non-RCTs combined (0 studies)	—	—	—	—
Septoplasty/rhinoplasty (contaminated)				
RCTs (4 RCTs; 619 patients)	4.9	11.3	0.45 (0.24–0.86)	0.02
RCTs and non-RCTs combined (7 studies; 928 patients)	5.2	9.5	0.60 (0.35–1.03)	0.06
Skin surgery (clean)				
RCTs (5 RCTs; 1782 patients)	1.3	4.5	0.55 (0.13–2.38)	0.42
RCTs and non-RCTs combined (6 studies; 2158 patients)	1.9	5.2	0.54 (0.21–1.42)	0.21
Skin surgery (contaminated)				
RCTs (0)	—	—	—	—
RCTs and non-RCTs combined (2 studies; 111 patients)	21.4	44.4	0.34 (0.05–2.16)	0.25
Abdominoplasty				
RCTs	—	—	—	—
RCTs and non-RCTs combined (1 study; 207 patients)	6.5	13.0	0.47 (0.18–1.23)	0.12

SSI, surgical-site infection; Abx, antibiotic; Px, prophylaxis; RCT, randomized controlled trial.

reported delayed wound healing and found a significant reduction with antibiotic prophylaxis.[23] One nonrandomized controlled trial[21] measured capsular contracture, and showed no reduction with antibiotic prophylaxis (53 percent with antibiotics versus 47 percent in controls).

Discussion

Meta-analysis of randomized controlled trials suggests that patients undergoing clean cosmetic/aesthetic breast surgery benefit from routine antibiotic prophylaxis. Although it has been proposed that individuals receiving tissue expanders and breast implants would benefit most from antibiotic prophylaxis, because infection in the presence of implants generally necessitates removal of the involved device, randomized controlled trials and nonrandomized controlled trials have not adequately addressed this important area. Subgroup analyses of patients undergoing breast reduction versus augmentation (implants)

suggests that both groups receive benefit from antibiotic prophylaxis.

Because of the heterogeneity of types and doses of antibiotic provided, conclusions were not possible about the best antibiotic and optimal dose. All of the studies provided a single dose of antibiotic preoperatively, and conclusions about optimal duration of antibiotics are not possible given the lack of evidence exploring duration. Because of the risk of bias in existing randomized controlled trials, the grade of recommendation is labeled as weak.

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis significantly reduced the risk of surgical-site infection in patients undergoing cosmetic breast surgery (2.5 percent versus 11.4 percent; OR, 0.16; 95 percent CI, 0.04 to 0.61; $p = 0.01$; $I^2 = 0$ percent; three randomized controlled trials) (**Level of Evidence: Low**).
- Recommendation: Preoperative antibiotic prophylaxis is recommended for patients undergoing clean cosmetic breast surgery (with or without implant) to reduce risk of surgical-site infection (**Level of Evidence: Low**; **Grade of Recommendation, Weak**).

Head and Neck Surgery

Clean Cases

Primary analysis (randomized controlled trials only): Four randomized controlled trials provided data for subgroups of patients undergoing clean head and neck surgery.[20,29–31] Meta-analysis of the randomized controlled trials showed no significant reduction in risk of surgical-site infection antibiotic prophylaxis (1.0 percent versus 1.0 percent; OR, 0.77; 95 percent CI, 0.13 to 4.65; $I^2 = 16$ percent; $p = 0.77$). Because antibiotic regimens ranged from a single preoperative dose to 5 days, conclusions regarding optimal dose and duration of antibiotics are not possible.

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were considered together, data from eight studies contributed to the analysis, including subpopulations from four randomized controlled trials[20,29–31] and four nonrandomized controlled trials.[32–36] Meta-analysis of these studies showed that the risk of surgical-site infection was reduced with antibiotic prophylaxis versus controls in clean head and neck surgery (but the difference was not statistically significant) (2.4 percent versus 3.7 percent; OR, 0.49; 95 percent CI, 0.19 to 1.23; $p = 0.13$). All of the studies provided one dose or a maximum of 24 hours of antibiotic prophylaxis; therefore, conclusions about duration of antibiotics are not possible.

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis did not significantly reduce the risk of surgical-site infection in patients undergoing clean head and neck surgery (**Level of Evidence: Very Low**).
- Recommendation: Antibiotic prophylaxis is not recommended for patients undergoing clean head and neck surgery (**Level of Evidence: Very Low; Grade of Recommendation: Weak**).

Contaminated Cases

Primary analysis (randomized controlled trials only): Eight randomized controlled trials[20,30,37–42] contributed to the meta-analysis of contaminated head and neck surgery, which showed an overall significant reduction in risk of surgical-site infection with antibiotic prophylaxis versus control (16.4 percent versus 41.9 percent; OR, 0.23; 95 percent CI, 0.11 to 0.46; $p < 0.0001$).

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were considered, 10 studies contributed to the meta-analysis of contaminated head and neck surgery,[20,30,37–44] which showed an overall significant reduction in risk of surgical-site infection with antibiotic prophylaxis versus control (12.2 percent versus 25.7 percent; OR, 0.26; 95 percent CI, 0.12 to 0.54; $p < 0.0001$).

Discussion

The studies date back to the decades wherein patients were treated with large doses of radiation therapy before definitive surgery, or had surgery because of recurrence of cancer after definitive full-course radiation therapy. This is consistent with research that has shown that irradiated tissue cannot tolerate bacterial contamination. However, at the present time, patients are treated with postoperative radiation therapy. In addition, clinical significance of surgical-site infection, need for reintervention, adverse events, and balance of benefit/risks were not addressed.

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis significantly reduces the risk of surgical-site

infection in patients undergoing contaminated head and neck surgery (**Level of Evidence: Low**).
- Recommendation: Antibiotic prophylaxis is recommended for patients undergoing contaminated head and neck surgery to reduce the risk of surgical-site infection (**Level of Evidence: Low; Grade of Recommendation: Weak**).

Orthognathic/Mandibular Surgery: Clean

Randomized trials (randomized controlled trials): None.

All study designs combined (randomized controlled trials plus nonrandomized controlled trial): There was only 1 study for clean orthognathic surgery, which was a small nonrandomized controlled trial of 74 patients undergoing surgery for prognathism.[45] There was only one surgical-site infection reported, and it occurred in the control group; therefore, no significant difference was found between groups (0 versus 2.2 percent; OR, 0.56; 95 percent CI, 0.02 to 14.3; $p = 0.73$).

Because only this one small study was identified for clean orthognathic surgery, no conclusions are possible regarding the role of antibiotics; and because the evidence base is small, the grade of recommendation remains weak.

- Evidence statement (randomized controlled trials): No evidence-based statement can be provided since no randomized trials of antibiotic prophylaxis for clean orthognathic/mandibular surgery have been performed.
- Recommendation: Preoperative single dose antibiotic prophylaxis is not recommended for patients undergoing clean orthognathic/mandibular surgery (**Level of Evidence: Very Low; Grade of Recommendation: Weak**).

Orthognathic/Mandibular Surgery: Contaminated

Randomized trials (randomized controlled trials only): Six randomized studies[30,46–50] contributed to the meta-analysis of contaminated (clean-contaminated or contaminated) orthognathic/mandibular surgery, which showed a significant reduction in risk of surgical-site infection with antibiotic prophylaxis versus control (6.5 percent versus 31.8 percent; OR, 0.17; 95 percent CI, 0.10 to 0.31; $p < 0.0001$).

All study designs combined (randomized controlled trials plus nonrandomized controlled trial): When all study designs were considered, ten studies[30,46–54] contributed to the meta-analysis of contaminated orthognathic/mandibular surgery, and showed a significant reduction in risk of surgical-site infection (5.0 percent versus 15.5 percent; OR, 0.34; 95 percent CI, 0.12 to 0.80; $p = 0.01$).

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis significantly reduced the risk of surgical-site infection in patients undergoing contaminated orthognathic/mandibular surgery (**Level of Evidence: Low**).
- Recommendation: Antibiotic prophylaxis is recommended for patients undergoing contaminated orthognathic/mandibular surgery (**Level of Evidence: Low; Grade of Recommendation: Weak**).

Septoplasty/Rhinoplasty Surgery: Contaminated

Understandably, because of the nature of this operation, which transgresses the aero-mucous membranes, no studies of clean rhinoplasty/septoplasty were identified

Primary analysis (randomized controlled trials only): Four randomized studies[30,55–57] contributed to the meta-analysis of contaminated septoplasty/rhinoplasty surgery, which showed an overall significant reduction in risk of surgical-site infection with antibiotic prophylaxis versus control (4.9 percent versus 11.3 percent; OR, 0.45; 95 percent CI, 0.24 to 0.86; $p = 0.02$).

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were considered, seven studies[30,55–60] contributed to the meta-analysis of contaminated septoplasty/rhinoplasty surgery, and the reduction in surgical-site infection did not reach conventional statistical significance (5.2 percent versus 9.5 percent; OR, 0.60; 95 percent CI, 0.35 to 1.03; $p = 0.06$).

These studies included a variety of septoplasty or rhinoplasty procedures, with or without turbinectomy. In most of the studies, the antibiotic arm received repeated doses of antibiotics for a course of a few days or up to 3 weeks, and it was not always clear whether the antibiotics were initiated preoperatively. Infection may be particularly difficult to diagnose in septoplasty/rhinoplasty surgery (i.e., nasal discharge, swelling, redness), and as a result, the definition of infection and rigor of follow-up for infection varied considerably in these studies.

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis significantly reduces the risk of surgical-site infection in patients undergoing contaminated septoplasty/rhinoplasty (**Level of Evidence: Low**).
- Recommendation: Antibiotic prophylaxis is recommended for patients undergoing contaminated septoplasty/rhinoplasty (**Level of Evidence: Low; Grade of Recommendation: Weak**).

Hand and Limb Surgery

Clean

Primary analysis (randomized controlled trials only): There was only one small study of clean hand surgery[61] eligible for analysis, which showed that antibiotic prophylaxis did not significantly reduce the risk of surgical-site infection (8.8 percent versus 14.5 percent; OR, 0.57; 95 percent CI, 0.21 to 1.57; $p = 0.28$).

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were included[61–65] in the meta-analysis, antibiotic prophylaxis did not reduce the risk of infection (0.9 percent versus 0.6 percent; OR, 0.81; 95 percent CI, 0.40 to 1.66; $p = 0.56$).

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis did not significantly reduce the risk of surgical-site infection in patients undergoing clean hand surgery (**Level of Evidence: Low**).
- Recommendation: Antibiotic prophylaxis is not recommended for patients undergoing clean hand surgery (**Level of Evidence: Low; Grade of Recommendation: Weak**).

Contaminated

The majority of studies included hand only, but at least one study provided the results of hand and foot surgery in aggregate. Because the number of patients undergoing foot surgery was small (<5 percent), these data largely reflect the results of antibiotic prophylaxis in hand surgery.

Primary analysis (randomized controlled trials only): Data from six studies contributed to meta-analysis for the primary analysis of randomized controlled trials only,[66–71] and showed that antibiotic prophylaxis significantly reduced the risk of surgical-site infection (5.1 percent versus 7.7 percent; OR, 0.54; 95 percent CI, 0.30 to 0.96; $p = 0.04$).

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were included,[62,65–79] the reduction in surgical-site infection with antibiotic prophylaxis was not statistically significant (4.9 percent versus 5.7 percent; OR, 0.76; 95 percent CI, 0.49 to 1.17; $p = 0.13$).

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis significantly reduced the risk of surgical-site infection for contaminated hand surgery (**Level of Evidence: Very Low**).
- Recommendation: Antibiotic prophylaxis is recommended for patients undergoing contaminated hand surgery (**Level of Evidence: Low; Grade of Recommendation: Weak**).

Skin Surgery

Clean

Primary analysis (randomized controlled trials only): For clean surgery of the skin, there were four randomized controlled trials that contributed data to the meta-analysis.[20,30,80,81] Overall, the reduction in surgical-site infection was not significant with antibiotic prophylaxis in these clean surgery trials (1.3 percent versus 4.5 percent; OR, 0.55; 95 percent CI, 0.13 to 2.38; $p = 0.42$).

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were considered, six studies contributed data to the meta-analysis,[20,30,78,80–82] and showed that there was no overall reduction in surgical-site infection with antibiotic prophylaxis in clean surgery (1.9 percent versus 5.2 percent; OR, 0.54; 95 percent CI, 0.21 to 1.42; $p = 0.21$). These studies included a variety of skin surgical procedures, in various settings, including the operating room, outpatient clinic, and emergency department.

- Evidence statement (randomized controlled trials): Antibiotic prophylaxis did not significantly reduce the the risk of surgical-site infection in patients undergoing clean skin surgery (**Level of Evidence: Low**).
- Recommendation: Antibiotic prophylaxis is not recommended for patients undergoing clean skin surgery (**Level of Evidence: Low; Grade of Recommendation: Weak**).

Contaminated

Primary analysis (randomized controlled trials only): None.

Secondary analysis (randomized controlled trials and nonrandomized controlled trials combined): When all study designs were considered, subgroup data from two observational studies contributed to the meta-analysis.[78,82] The difference in surgical-site infection was not significant with antibiotic prophylaxis (21.4 percent versus 44.4 percent; OR, 0.34; 95 percent CI, 0.05 to 2.16; $p = 0.25$); however, the evidence was significantly at risk of bias and was extremely underpowered ($n = 111$ patients in total). When one further study that included a mixed population of clean and contaminated skin surgery ($n = 180$)[83] was added in a sensitivity analysis, the results remained nonsignificant. Given the paucity of evidence, it is difficult to be guided by evidence directly from contaminated skin surgery trials.

- Evidence statement (randomized controlled trials): No evidence-based statement can be provided because no randomized trials of antibiotic prophylaxis have been performed (and even the available observational studies addressing this population were extremely small and underpowered).
- Recommendation: It is not known whether antibiotic prophylaxis reduces the risk of surgical-site infection in contaminated skin operations (**Level of Evidence, Very Low; Grade of Recommendation, Weak**).

Abdominoplasty: Clean

Primary analysis (randomized controlled trials only): None.

Secondary analysis (nonrandomized controlled trials): One pseudorandomized study[84] of patients receiving antibiotic prophylaxis versus control was identified for patients undergoing abdominoplasty. In this study, antibiotic prophylaxis did not result in a significant reduction in surgical-site infection (6.5 percent versus 13.0 percent; OR, 0.47; 95 percent CI, 0.18 to 1.23; $p = 0.12$). When sensitivity analysis was performed to include other studies of miscellaneous plastic surgery (including some abdominoplasties, but for which data was not provided separately for abdominoplasty), the results did not materially change.[43,85]

- Evidence statement (randomized controlled trials): No evidence-based statement can be provided because no randomized trials of antibiotic prophylaxis of abdominoplasty have been performed (and even the only available pseudorandomized study addressing this population was underpowered).
- Recommendation: Antibiotic prophylaxis is not recommended for clean abdominoplasty (**Level of Evidence, Very Low; Grade of Recommendation, Weak**).

DISCUSSION

To our knowledge, this represents the first consensus statement for antibiotic prophylaxis in plastic surgery that is based on comprehensive systematic review of the evidence. Focusing on the highest level of evidence from randomized trials, the systematic review suggests that, in general, for:

1. Clean surgery: With the exception of cosmetic breast surgery, clean operations have not been shown to benefit from routine antibiotic prophylaxis.
2. Contaminated (class II, III, and IV) surgery: Contaminated plastic surgical procedures benefit from the use of antibiotic prophylaxis. It is important to note that most of the operations in the contaminated subgroup were class II (clean-contaminated). Unfortunately, contaminated/dirty skin surgery was rarely represented separately within any of the studies, and as a result definitive conclusions are difficult for class III and IV based on current evidence.
3. Duration of antibiotic use: The duration of antibiotic use should generally be limited to a single preoperative dose because studies have generally showed no benefit for longer term antibiotic prophylaxis.[35,59,61,80,84] In fact, in some studies, there was a trend toward significantly reduced benefit for patients receiving prolonged antibiotic prophylaxis beyond 24 hours, although this was largely from nonrandomized evidence and is subject to bias.
4. Evidence quality for individual studies was low: Perhaps one of the most notable aspects was the relative lack of adequately designed randomized trials to determine the appropriate role of antibiotic prophylaxis for plastic surgery.

Areas Not Addressed

A number of important aspects were not addressed during this consensus statement,

recognizing that future consensus processes may address these areas, including the following.

Which Antibiotic Is Best?

The type of surgery, length of surgery, and patient demographics considered together with the local resistance patterns and antibiotic availability will be important factors driving the consideration of which antibiotic is best. The most commonly encountered microorganisms associated with postoperative infections in plastic surgery include *Staphylococcus aureus* and various streptococci.[86] As a general principle, the antibiotic should have activity against the most frequently encountered microorganisms in postoperative surgical-site infections. Cefazolin as a single dose preoperatively is the most commonly recommended agent and would be considered appropriate in most cases.[86] In the event of allergy or intolerance, clindamycin or vancomycin may be appropriate alternatives.

Appropriate Prophylaxis for Inserts and Prostheses

Antibiotic prophylaxis for patients undergoing plastic surgery involving insertion of a prosthesis or implant remains understudied. In this systematic review, we identified only one study[25] involving implants for breast augmentation. Therefore, evidence was insufficient to determine whether the role of antibiotics should differ from patients undergoing procedures without implants.

Appropriate Prophylaxis for Infected or Dirty Wounds

Even though we retrieved all identifiable evidence for a systematic review of plastic surgery and the role of antibiotics, there were no studies that addressed the appropriate use of antibiotics for patients undergoing revision for infected wounds or patients with infected prostheses. Given the evidence from other surgical areas,[86] antibiotic prophylaxis is recommended for contaminated surgery. However, further active-controlled studies should evaluate type of antibiotic, and dosing schedules.

Cost-Effectiveness, Availability, and Local Contextual Considerations

This consensus statement did not specifically address issues of cost-effectiveness, and this should not be interpreted to suggest that costs and resource considerations are not important. Antibiotic prophylaxis may induce additional drug costs for the system (or for the patient); however, by preventing infections, they may potentially reduce overall cost of care because of reduced morbidity, surgical reintervention, readmissions, and physician visits. Nonetheless, this is an area where devoted research should be undertaken, to better define which drug, at what dose, and for what duration will optimize outcomes (reduce infection, but not induce undue risk of *Clostridium difficile* or resistant bacteria). Finally, we need to determine whether antibiotic prophylaxis in these various procedures reduces the risk of clinically relevant infections sufficiently to warrant the risk of adverse events compared with a "wait-and-treat" approach.

In a nutshell, because antibiotics can cause harm, and because it is clear that there is not a "large" effect from antibiotics in clean surgery (if any at all), and because there is increasing concern that overuse is reducing the future efficacy of antibiotics by driving up resistance unnecessarily, the emerging global consensus is that antibiotics should not be used routinely for clean surgery. This is consistent with studies and recommendations from areas other than plastic surgery.

What is somewhat surprising is that for clean breast surgery, a significant benefit was found in our meta-analysis; thus, given the evidence base sufficient to unseat the default of no prophylaxis in this case, antibiotics are recommended for clean breast surgery in our consensus statement. For all other clean plastic surgery, we need adequate randomized studies to determine whether routine prophylaxis is helping or harming patients. There is no longer a good excuse for our profession to fail to perform such studies, given the potential importance of the resulting knowledge. There is no good reason to think that we already "know" the answer without conducting the studies, because the results could equally go either way.

CONCLUSIONS

Systemic antibiotic prophylaxis is recommended for nonclean (clean-contaminated, contaminated, or dirty) plastic surgery of the head and neck, orthognathic/mandibular, septoplasty/rhinoplasty, hand and upper limb, and skin. Antibiotic prophylaxis is also recommended to reduce surgical-site infection for clean plastic surgery of the breast. However, antibiotic prophylaxis is not recommended to reduce surgical-site infection in clean surgical cases of the head and neck, orthognathic/mandibular area, hand and upper limb, skin, and abdominoplasty. Further research is encouraged to determine the appropriate dose, duration, and class of antibiotic in plastic surgical operations of all types.

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