

## Antibiotic Prophylaxis in Anterior Skull Base Surgery: A Survey of the North American Skull Base Society

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**ABSTRACT**

**Introduction:** There is a paucity of data evaluating antibiotic use in anterior skull base surgery (ASBS). The goal of this study was to determine antibiotic prescribing patterns and factors that influence antibiotic use in ASBS.

**Methods:** An online-based survey was distributed to the membership of the North American Skull Base Society in 2018. Outcomes included practitioner preference regarding intra- and postoperative antibiotic use, practice location and environment, surgeon experience, and patient factors influencing antibiotic use.

**Results:** There was a total of 208 respondents (25.6% response rate) of which 182 (87.5%) performed ASBS. 60.4% were in academic institutions. Respondents were neurosurgeons (59.3%) or otolaryngologists (40.7%), and 75.3% were fellowship-trained in ASBS. Most surgeons (95.0%) gave intraoperative antibiotics. Academic surgeons were 4 times more likely to prescribe intraoperative antibiotics than private practitioners (OR 3.98 [95% CI 1.53-10.36],  $p=0.005$ ). Among surgeons who did not routinely prescribe intraoperative antibiotics, regression analysis indicated that the presence of actively infected sinuses, transplantation, diabetes, HIV/AIDS, and pulmonary disease influenced decision-making ( $p<0.03$ ). Postoperative antibiotics were prescribed by 73.6% of respondents. European surgeons were 3 times less likely to prescribe postoperative antibiotics (OR 0.34 [95% CI 0.15-0.80],  $p=0.01$ ). Regression modeling indicated that HIV/AIDS, cystic fibrosis, diabetes, transplantation, and pulmonary disease, as well as the use of absorbable packing influenced the decision to use postoperative antibiotics ( $p<0.003$ ).

**Conclusion:** This study demonstrates the significant variation in intra- and postoperative antibiotic use among surgeons performing ASBS. Prospective randomized studies are necessary to establish evidence-based practice guidelines for perioperative antibiotic use in ASBS.

## INTRODUCTION

Skull base surgery (SBS) can be classified as clean or clean-contaminated depending on whether sinonasal mucosa is violated. In many cases, there is a direct connection between the sinonasal mucosa and intracranial space. Furthermore, endoscopic cases involve transnasal passage of instruments and graft materials. These two factors create a theoretical risk for contamination of the sterile intracranial space with sinonasal flora. A systematic review of 2,005 patients who underwent

endoscopic expanded endonasal approaches for SBS showed an overall postoperative rate of meningitis of 1.8% with higher rates in cases of postoperative cerebrospinal fluid (CSF) leak.<sup>1</sup> Given the severe consequences of an intracranial infection, perioperative antibiotics are routinely used in anterior skull base surgery (ASBS).

To date, there have been no randomized controlled trials evaluating the use of prophylactic antibiotics for clean-contaminated ASBS. A recent evidence-based review by Patel et al. recommended intra- and postoperative antibiotic use for less than 24 hours.<sup>2</sup> The exception being cases where the use of nasal packing or splints is anticipated to exceed 48 hours, though there is a paucity of evidence for this recommendation. The theoretical benefits of antibiotic use in ASBS include a reduction in infection risk by sterilizing CSF that is seeded by sinonasal flora during surgical extirpation of the lesion. However, the prophylactic use of antibiotics should be weighed against the costs and potential side effects, including allergic reactions, *Clostridium difficile* enterocolitis, and spread of antimicrobial resistance.<sup>3</sup>

Given the lack of high-level evidence supporting the use of perioperative antibiotics in ASBS, we sought to survey the members of the North American Skull Base Society (NASBS) to determine current practice patterns pertaining to perioperative antibiotic use and to identify factors that influence the use of antibiotics.

## **MATERIALS AND METHODS**

A 22-item online-based survey was designed using SurveyMonkey (San Mateo, CA). This study was electronically distributed to the general NASBS membership. Three e-mail notifications were sent over a period of eight weeks. The survey remained open online for a period of 4 weeks after the final notification and participation was voluntary. Responses were recorded anonymously, and no identifying information was collected.

Demographic characteristics of the respondents were collected, including type of clinical practice (full-time academic, private practice with academic affiliation, independent private practice, government facility), geographic location of the practice, duration of practice in years, neurosurgical or otolaryngology training, and completion of a fellowship. Practice volume was assessed by number of ASBS cases performed per year. Intraoperative and postoperative antibiotic practice patterns were assessed. Frequency of antibiotic use in each of these categories was stratified as “Always (100% of the time)”, “Often (>70% of the time)”, “Sometimes (30-70% of the time)”, or “Infrequent (<30% of the time)”. Respondents were given the opportunity to select one or more reasons as to why they prescribed perioperative antibiotics. The impact of patient comorbidities on antibiotic use was also assessed. The type and duration of antibiotic used, placement of a lumbar drain, use of intranasal packing, and information on methods used to diagnose a postoperative infection was obtained.

Only complete survey responses were included in the analysis. Percentage response rates were calculated for each item based on the number of respondents for that specific item. Responses were operationalized and entered into Excel 2016 (Microsoft, Redmond, WA) and then transferred to SPSS Statistics v21.0 (IBM, Armonk, NY) for statistical analysis. Associations between variables and antibiotic usage were evaluated using Pearson’s chi-square test with Yates continuity correction.

Any variable that differed between those using and those not using antibiotics with a p-value  $\leq 0.20$  on bivariate analysis was considered a potential independent variable and was entered a multivariate logistic regression model. Significant differences were identified at a conventional 0.05 alpha level.

## RESULTS

### Cohort Characteristics

Of the 813 NASBS members who received the survey, 208 respondents completed the survey for a response rate of 25.6%. Not every question was applicable to every respondent – for example, those who did not prescribe postoperative antibiotics were not then asked about reasons for prescribing postoperative antibiotics. Consequently, the response rate for each survey question ranged from 64.4 to 100%.

Of the 208 respondents, 182 perform ASBS (**Table 1**). Of these 182 respondents, the majority (n=130, 71%) were in a full-time academic or government-funded position. Twenty-nine percent (n=52) were in private practice, of whom 79% (n=41) were academically affiliated and 21% (n=11) were in independent practice. Over half of the respondents were neurosurgeons (n=108, 59.3%) and the remainder (n=74, 40.7%) were otolaryngologists. Most respondents had undergone fellowship training in SBS (n=137, 75.3%). Geographic practice location was provided by 178 respondents. Over half (61.5%) were from North America, 15.2% from Europe, 12.9% were from Australia or Asia, 6.7% from South and Central America, and 1.7% from Africa.

There was a wide range of experience among respondents (**Table 1**). Forty-two respondents (23.1%) had over 20 years of experience, but nearly one-third (n=57, 31.3%) had been in practice for less than 5 years. Many respondents (n=126, 69.2%) perform open and endoscopic SBS, whereas a smaller percentage perform only endoscopic (n=37, 20.3%) or only open SBS (n=19, 10.4%).

### **Intraoperative antibiotic use patterns**

Most respondents who performed ASBS used intraoperative antibiotics (n=173, 95.1%) with 85.0% (n=155) indicating that they gave intraoperative antibiotics 100% of the time (**Table 2**). In a multivariable logistic regression model controlling for surgeon volume, years of experience, and type of SBS (open, endoscopic, or both), being a full-time academic surgeon (including those in government practice) was associated with prescribing more intraoperative antibiotics (OR 6.67 [95% CI 1.34-33.12], p=0.02). Given that most prescribers of intraoperative antibiotics prescribed these “100% of the time”, we restratified intraoperative antibiotic use into “never”, “sometimes (<100%)” and “always (100% of the time)”. In a multivariate cumulative logit model controlling for surgeon volume, years of experience, and type of skull base surgery, academic surgeons were found to prescribe intraoperative antibiotics 4 times more frequently than private practitioners (OR 3.98 [95% CI 1.53-10.36], p=0.005). The most commonly used intraoperative antibiotics were 1<sup>st</sup>-2<sup>nd</sup> generation cephalosporins (n=96, 55.5%) and 3<sup>rd</sup>-5<sup>th</sup> generation cephalosporins (n=75, 43.4%) (**Table 2**).

Of the 173 respondents who gave intraoperative antibiotics, the most common reason was to reduce the risk of postoperative infection (n=157, 90.8%) (**Table 3**). By using logistic regression modelling, we analyzed factors associated with use of intraoperative antibiotics less than 100% of the time as these factors may influence prescribing practices in those surgeons who do not routinely

give intraoperative antibiotics. Surgeons who reported “actively infected sinuses” as one of the reasons to prescribe intraoperative antibiotics were less likely to prescribe intraoperative antibiotics 100% of the time (OR 0.3 [95% CI 0.1-0.8],  $p=0.027$ ). Most respondents ( $n=148$ , 85.5%) stated that they would not change their intraoperative antibiotic prescribing pattern based on patient comorbidities (**Table 4**). Of the minority who personalize intraoperative antibiotic use based on patient comorbidities ( $n=25$ , 14.5%), a history of transplantation, diabetes, human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), and pulmonary disease were each independently associated with a reduced likelihood of prescribing intraoperative antibiotics 100% of the time (OR 1.0 for each factor,  $p<0.02$ ) (**Table 4**). This suggests that among surgeons who did not reflexively prescribe intraoperative antibiotics, these comorbidities were the most influential factors in informing antibiotic use.

#### **Postoperative antibiotic use patterns**

Most respondents ( $n=134$ , 73.6%) gave postoperative antibiotics after ASBS (**Table 1**). Over half ( $n=112$ , 62%) gave postoperative antibiotics for every case, whereas 26% ( $n=48$ ) never gave postoperative antibiotics. A small minority of respondents ( $n=22$ , 11%) sometimes gave antibiotics postoperatively (**Table 2**). By stratifying postoperative antibiotic use as “always (100% of the time)”, “sometimes (<100%)”, and “never”, we built a multivariable cumulative logit model that controlled for surgeon volume, years of experience, and type of SBS. Our model indicated that European surgeons were nearly 3 times more likely than others to never prescribe postoperative antibiotics (OR 0.34 [95% CI 0.15-0.80],  $p=0.01$ ).

Postoperative antibiotics were generally given for 24 hours ( $n=41$ , 30.6%), 24-72 hours ( $n=40$ , 29.9%), or 1 week ( $n=36$ , 26.9%). They were less frequently given for 1-2 weeks ( $n=16$ , 11.9%). The most common postoperative antibiotics used were 1<sup>st</sup>-2<sup>nd</sup> generation cephalosporins ( $n=68$ , 50.7%)



or 3<sup>rd</sup>-5<sup>th</sup> generation cephalosporins (n=59, 44.0%) (**Table 2**). Postoperative antibiotics were most commonly given to prevent postoperative infection (82.1%), to reduce the perceived infection risk of non-absorbable packing (n=51, 38.1%), and secondary to concern for a potential CSF leak (n=31, 23.1%). Surgeons who reported “use of absorbable packing” (OR 0.2 [95% CI 0.1-0.6], p=0.003) or “that’s how I was taught” (OR 0.3 [95% CI 0.1-0.8], p=0.027) as a reason for prescribing postoperative antibiotics were less likely to prescribe postoperative antibiotics 100% of the time, suggesting that this cohort may be more discriminating in their decision to use antibiotics (**Table 3**).

Surgeons were also asked how often they give culture-directed postoperative antibiotics. Less than one-third of respondents (n=33, 24.6%) used culture-directed postoperative antibiotics on every occasion. The majority (n=41, 30.6%) of those who used culture-directed postoperative antibiotics, reported that they used cultures to inform the prescription less than 30% of the time. Of the respondents who give postoperative antibiotics, nearly three-quarters (n=100, 74.6%) reported that their decision was not influenced by patient comorbidities. Of the 34 respondents (25.4%) who reported that their decision to prescribe postoperative antibiotics was influenced by patient comorbidities, HIV/AIDS, cystic fibrosis, diabetes, history of transplant, and pulmonary disease all reduced the likelihood that the surgeon would reflexively prescribe postoperative antibiotics for ASBS (**Table 4**). These factors directly influenced decision-making, with history of transplant having the most effect on the decision to use postoperative antibiotics among surgeons who do not routinely prescribe them for every case (OR 0.1 [95% CI 0.04-0.4], p<0.0001).

Surgeons were asked how they diagnosed postoperative infection. Most respondents used systemic symptoms and signs, such as fever and increased white blood cell count (n=124, 92.5%). Visualization of purulence on postoperative endoscopic examination (n=93, 69.4%) and patient report of purulent nasal discharge (n=66, 49.3%) were also commonly used.

## DISCUSSION

Anterior skull base surgery approaches often involve passage through the microbe-rich nasal cavity to access the sterile intracranial space. The sinonasal cavities are known to be reservoirs of several bacterial species including *Staphylococcus aureus*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*.<sup>4</sup> Prophylactic antibiotics are commonly used in this setting to prevent a postoperative infection. The use of prophylactic antibiotics in surgery is commonly dictated by the nature of the procedure and patient characteristics. For example, in neurosurgery, the use of prophylactic antibiotics is supported by a prospective study of 4,578 craniotomies by Korinek et al.<sup>5</sup> The initial cohort of cases were not prescribed penicillin-based prophylaxis for scheduled, clean craniotomies of short duration whereas emergent, clean-contaminated or longer duration cases did receive antibiotic prophylaxis. The subsequent cohort of cases received antibiotic prophylaxis regardless of craniotomy characteristics. Antibiotic prophylaxis reduced postoperative infection rate from 9.7% to 5.8% across the study population primarily due to significant reductions in infection rates among low risk patients from 10.0% to 4.6%.

Despite the minimally invasive nature of endoscopic ASBS, communication between the sinonasal and intracranial cavities may represent a higher risk of postoperative infection compared to open skull base procedures. Furthermore, institutional guidelines on antibiotic prophylaxis often vary depending upon whether the dura is violated during ASBS. Given the expanding indications of endoscopic ASBS, evidence-based guidelines of perioperative antibiotic management should be established. The recent American Rhinologic Society (ARS) international consensus statement on endoscopic SBS does not make a recommendation for or against perioperative antibiotic use, deferring to surgeon discretion.<sup>6</sup> We sought to determine the practice patterns of anterior skull base surgeons, specifically regarding intra- and postoperative antibiotic use.

Web-based physician-directed surveys often have response rates below 20%.<sup>7,8</sup> Our survey response rate was 25.6%, which is comparable to the response rates in prior survey studies.<sup>9-14</sup> The majority of our respondents worked in full-time academic positions (60.4%) and had undergone fellowship training (75.3%), which speaks to the nature of ASBS cases that usually require high-level tertiary multi-specialty care. Though nearly a third of respondents (31.3%) had been in practice for less than 5 years, 23.1% had over 20 years of experience. Thus, the responses detailed in this study likely represent the opinions of a highly-trained and, in many instances, experienced cohort. Neurosurgeons represented 59.3% and otolaryngologists 40.7% of the study cohort. Our respondents were from many geographic locations, including North America (61.5%), Europe (15.2%), and Asia (8.4%). The diversity of geographic location and specialty background improves the generalizability of our results.

Most of our survey respondents (95.1%) gave intraoperative antibiotics for ASBS cases and 85.0% gave antibiotics for every case. Academic surgeons were four times more likely than private practitioners to give intraoperative prophylactic antibiotics. This could reflect the increased complexity of cases presenting to a tertiary referral academic center. The inherent risk of CSF leak, which is a known risk factor for postoperative infection in SBS, is higher in cases of greater complexity where a larger skull base defect is created.<sup>6,15-18</sup> In a retrospective chart review of 1,000 patients who underwent endoscopic SBS, both CSF leak and high level of case complexity, were associated with a higher risk of postoperative infection.<sup>15</sup> Unsurprisingly, the desire to reduce the risk of postoperative infection was the driving factor to prescribe intraoperative antibiotics in 91% of respondents. Among surgeons who did not routinely prescribe intraoperative antibiotics for every ASBS case, the presence of actively infected sinuses or patient comorbidities including transplantation, diabetes, HIV/AIDS, and pulmonary disease influenced decision-making on whether to prescribe.

Interestingly, we did not find a difference in antibiotic usage between those performing endoscopic approaches versus open approaches. The incidence of postoperative meningitis in these two groups has not been shown to vary greatly with rates ranging from <1-14% for endoscopic endonasal SBS<sup>18-22</sup> versus 1.8-11% for open craniofacial SBS.<sup>16,22,23</sup>

Of the participants who gave intraoperative antibiotics, the majority used a 1<sup>st</sup> or 2<sup>nd</sup> generation cephalosporin (55.5%) or a 3<sup>rd</sup>, 4<sup>th</sup>, or 5<sup>th</sup> generation cephalosporin (43.4%). This is similar to findings in a survey of endoscopic skull base surgeons among the membership of the ARS, in which many respondents used 1<sup>st</sup> generation (41.4%) or 3<sup>rd</sup> generation cephalosporins (35.7%).<sup>11</sup> First-generation cephalosporins, namely cefazolin, have a good safety profile, a favorable duration of action, and adequate coverage of organisms commonly involved in surgical site infections, including *Staphylococcus* species.<sup>24,25</sup> 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> generation cephalosporins may be preferred for their improved blood-brain barrier penetration. These newer medications achieve higher concentrations in the CSF that are sufficient to inhibit *Staphylococcus* and a wide spectrum of gram-positive and gram-negative bacteria.<sup>26</sup>

The use of prophylactic antibiotic coverage for ASBS was first addressed by Carrau et al. in 1991 who recommended coverage of gram-positive and gram-negative bacteria for at least 48 hours following surgery.<sup>27</sup> They noted that ideal antibiotic prophylaxis would include good CSF penetration, single agent therapy, absence of associated morbidity, and convenient dosing schedule.<sup>27</sup> To date, there are no randomized controlled trials evaluating the appropriate choice, number, and duration of antibiotics in ASBS. Indeed, a prior survey of the membership of the International Society of Pituitary Surgeons showed that 90% of respondents thought there was a lack of high-quality

evidence guiding perioperative antibiotic use in endoscopic pituitary surgery.<sup>28</sup> Studies have suggested that there is a potential benefit of broad-spectrum antibiotic coverage in ASBS. A prospective study of 211 patients undergoing open SBS compared patients who received an antibiotic regimen of ceftazidime, metronidazole, and vancomycin of varying duration to those who received non-standardized antibiotic prophylaxis.<sup>16</sup> Those who received the standardized antibiotic regimen were 2.5 times less likely to develop an infectious complication.<sup>16</sup>

Although the use of broad-spectrum prophylaxis intraoperatively appears to be beneficial, optimal postoperative antibiotic prophylaxis has yet to be established. Postoperative antibiotic prophylaxis was used by 73.6% of survey respondents, and 62% always gave postoperative antibiotics. Cephalosporins were the preferred agents. Postoperative antibiotics were given for 24 hours by approximately one-third of respondents or 24 to 72 hours by nearly 30% of respondents. Several studies have suggested that a short course of postoperative antibiotics is adequate for prophylaxis in ASBS.<sup>18,19,29-31</sup> One prior study found that the use of a single agent covering gram-positive organisms for 24 to 48 hours was adequate prophylaxis for endoscopic endonasal ASBS. In this study, none of the 90 patients who underwent ASBS developed postoperative meningitis.<sup>30</sup> Another study recommended that two doses of cefuroxime is adequate for transsphenoidal pituitary surgery.<sup>29</sup> In a retrospective analysis of 145 patients who underwent endoscopic endonasal transsphenoidal surgery who received an intraoperative and single postoperative dose of cefazolin, none developed meningitis.<sup>31</sup> Based on these studies, an evidence-based review recommended less than 24 hours of postoperative antibiotic prophylaxis for clean-contaminated ASBS, except in cases where nasal packing or splints are left in for over 48 hours.<sup>2</sup>

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Interestingly, we found that European surgeons were three times less likely than surgeons in other geographic regions to give postoperative prophylaxis, which suggests that there are geographic influences on antibiotic practice patterns. An Italian study of 2,039 patients who underwent ASBS followed an antibiotic protocol that did not use any postoperative antibiotics with a postoperative meningitis rate of only 0.69%.<sup>18</sup> The reasons for these geographic disparities in postoperative antibiotic use have not been evaluated. Potential explanations may be related to the centralization of SBS in Europe to select large volume academic centers. Adherence to strict antibiotic stewardship guidelines could be more common in these centers. Similarly, the nationalized healthcare systems in many Western European countries prioritize cost containment and in the United Kingdom, for example, bodies such as the National Institute for Health and Care Excellence (NICE) provide evidence-based guidance which strongly recommend against treatments for which there is no strong evidence base.

In our study, the most common reason cited for use of postoperative antibiotics was to prevent postoperative infection (82.1%), and the second most common reason was for prophylaxis in the setting of non-absorbable packing (38.1%). This is similar to findings in a survey of the ARS, in which 39.1% of respondents prescribed a seven-day course of oral antibiotics in the setting of nasal packing.<sup>11</sup> This is a much lower percentage than reported by the prior survey of the NASBS, where 88.5% of respondents who used non-absorbable packing gave postoperative antibiotics.<sup>12</sup> Antibiotics are commonly prescribed in the setting of non-absorbable packing for fear of toxic shock syndrome despite its extremely rare incidence. There is limited data supporting postoperative antibiotic use in the setting of nasal packing following ASBS.<sup>32</sup> Despite the lack of evidence, one-quarter (25.4%) of those surveyed modified their use of postoperative antibiotics depending on patient comorbidities with history of transplantation having the greatest effect on decision-making.

The limitations of this study include those that are inherent to survey studies. Web-based surveys often have response rates below 20%.<sup>7,8</sup> Though the response rate of approximately 25% in the current study is marginally better, this rate is still significantly lower than that achieved through other modes of survey distribution, some of which use incentives, which increase study costs.<sup>8</sup> The relatively low response rate achieved in the current study may lead to non-response bias. The sample population represents a self-selected group of NASBS members who chose to participate in the distributed survey. Consequently, the generalizability of results across the 75% of NASBS members who did not respond to this survey, and to the wider population of surgeons cannot be assured. To illustrate, 60.4% of respondents were in an academic practice and may manage higher complexity cases in environments that tend to have standardized perioperative workflows biasing responses in favor of antibiotic use. This may underlie the observed association between practicing in an academic environment and increased intraoperative antibiotic use compared to non-academic surgeons. Recall bias of case numbers and other details by respondents is another possible limitation. Questions were asked in a multiple-choice format. For example, respondents were given different options as to why they prescribed intraoperative or postoperative antibiotics. Responses other than those designated by the survey authors were not permitted, potentially introducing a selection bias. Permitting respondents to free text responses may have reduced—but would not have ameliorated—this bias. The implications are that there may be factors which influence antibiotic use that were not identified in this study. In addition, most respondents were from North America, likely biasing the reported practices in this study towards those implemented in North America where antibiotic overuse is widely acknowledged. Reported responses in this study represent the opinions of the survey respondents and do not represent the view of the NASBS.

## **CONCLUSION**

Despite the lack of high-quality evidence supporting the use and duration of perioperative antibiotics in ASBS, our survey study demonstrates that a large proportion of our respondents give intraoperative and postoperative antibiotic prophylaxis. Several patient factors, including comorbid conditions, influence surgeon decision-making as it pertains to prescribing intra- and postoperative antibiotics. Practice setting and geographic location may also play a role in prescribing practices. A prospective randomized controlled trial evaluating perioperative antibiotic use in ASBS is necessary to develop high-quality evidence-based practice guidelines.

## REFERENCES

1. Lai LT, Trooboff S, Morgan MK, Harvey RJ. The risk of meningitis following expanded endoscopic endonasal skull base surgery: a systematic review. *J Neurol Surg B Skull Base*. 2014;75(1):18-26.
2. Patel PN, Jayawardena ADL, Walden RL, Penn EB, Francis DO. Evidence-Based Use of Perioperative Antibiotics in Otolaryngology. *Otolaryngol Head Neck Surg*. 2018;158(5):783-800.
3. Savitz SI, Rivlin MM, Savitz MH. The ethics of prophylactic antibiotics for neurosurgical procedures. *J Med Ethics*. 2002;28(6):358-363.
4. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev*. 1997;10(3):505-520.
5. Korinek AM, Golmard JL, Elcheick A, et al. Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. *Br J Neurosurg*. 2005;19(2):155-162.
6. Wang EW, Gardner PA, Zanation AM. International consensus statement on endoscopic skull-base surgery: executive summary. *Int Forum Allergy Rhinol*. 2019.
7. Dykema J, Jones NR, Piche T, Stevenson J. Surveying clinicians by web: current issues in design and administration. *Eval Health Prof*. 2013;36(3):352-381.
8. Cook DA, Wittich CM, Daniels WL, West CP, Harris AM, Beebe TJ. Incentive and Reminder Strategies to Improve Response Rate for Internet-Based Physician Surveys: A Randomized Experiment. *J Med Internet Res*. 2016;18(9):e244.
9. Dodson KM, Appelbaum NP, Lee N, Amendola M, Kaplan B. Otolaryngology Resident Well-Being and Perceptions of the Clinical Learning Environment. *Ear Nose Throat J*. 2019:145561319840125.



10. Reid JW, Rotenberg BW, Sowerby LJ. Contemporary decongestant practices of Canadian otolaryngologists for endoscopic sinus surgery. *J Otolaryngol Head Neck Surg.* 2019;48(1):15.
11. Wannemuehler TJ, Rabbani CC, Burgeson JE, et al. Survey of endoscopic skull base surgery practice patterns among otolaryngologists. *Laryngoscope Invest Otolaryngol.* 2018;3(3):143-155.
12. Roxbury CR, Lobo BC, Kshetry VR, et al. Perioperative management in endoscopic endonasal skull-base surgery: a survey of the North American Skull Base Society. *Int Forum Allergy Rhinol.* 2018;8(5):631-640.
13. Lee JT, Kingdom TT, Smith TL, Setzen M, Brown S, Batra PS. Practice patterns in endoscopic skull base surgery: survey of the American Rhinologic Society. *Int Forum Allergy Rhinol.* 2014;4(2):124-131.
14. Batra PS, Lee J, Barnett SL, Senior BA, Setzen M, Kraus DH. Endoscopic skull base surgery practice patterns: survey of the North American Skull Base Society. *Int Forum Allergy Rhinol.* 2013;3(8):659-663.
15. Kono Y, Prevedello DM, Snyderman CH, et al. One thousand endoscopic skull base surgical procedures demystifying the infection potential: incidence and description of postoperative meningitis and brain abscesses. *Infect Control Hosp Epidemiol.* 2011;32(1):77-83.
16. Kraus DH, Gonen M, Mener D, Brown AE, Bilsky MH, Shah JP. A standardized regimen of antibiotics prevents infectious complications in skull base surgery. *Laryngoscope.* 2005;115(8):1347-1357.
17. Horowitz G, Fliss DM, Margalit N, Wasserzug O, Gil Z. Association between cerebrospinal fluid leak and meningitis after skull base surgery. *Otolaryngol Head Neck Surg.* 2011;145(4):689-693.
18. Milanese L, Zoli M, Sollini G, et al. Antibiotic Prophylaxis in Endoscopic Endonasal Pituitary and Skull Base Surgery. *World Neurosurg.* 2017;106:912-918.
19. Orlando R, Cappabianca P, Tosone G, Esposito F, Piazza M, de Divitiis E. Retrospective analysis of a new antibiotic chemoprophylaxis regimen in 170 patients undergoing endoscopic endonasal transsphenoidal surgery. *Surg Neurol.* 2007;68(2):145-148; discussion 148.
20. Ciric I, Ragin A, Baumgartner C, Pierce D. Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. *Neurosurgery.* 1997;40(2):225-236; discussion 236-227.
21. Gallia GL, Asemota AO, Blitz AM, et al. Endonasal endoscopic resection of olfactory neuroblastoma: an 11-year experience. *J Neurosurg.* 2018:1-7.
22. Naunheim MR, Goyal N, Dedmon MM, et al. An Algorithm for Surgical Approach to the Anterior Skull Base. *J Neurol Surg B Skull Base.* 2016;77(4):364-370.

23. Solero CL, DiMeco F, Sampath P, et al. Combined anterior craniofacial resection for tumors involving the cribriform plate: early postoperative complications and technical considerations. *Neurosurgery*. 2000;47(6):1296-1304; discussion 1304-1295.
24. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm*. 2013;70(3):195-283.
25. Marshall WF, Blair JE. The cephalosporins. *Mayo Clin Proc*. 1999;74(2):187-195.
26. Kernodle DS KA. Post-operative infections and antimicrobial prophylaxis. . In: Mandell GL BJ, Dolin R, ed. *Douglas and Bennett's principle and practice of infectious diseases*. . Churchill Livingstone Inc; 1995:2742-2756.
27. Carrau RL, Snyderman C, Janecka IP, Sekhar L, Sen C, D'Amico F. Antibiotic prophylaxis in cranial base surgery. *Head Neck*. 1991;13(4):311-317.
28. Little AS, White WL. Prophylactic antibiotic trends in transsphenoidal surgery for pituitary lesions. *Pituitary*. 2011;14(2):99-104.
29. Little AS, White WL. Short-duration, single-agent antibiotic prophylaxis for meningitis in trans-sphenoidal surgery. *Pituitary*. 2011;14(4):335-339.
30. Brown SM, Anand VK, Tabaei A, Schwartz TH. Role of perioperative antibiotics in endoscopic skull base surgery. *Laryngoscope*. 2007;117(9):1528-1532.
31. Somma T, Maraolo AE, Esposito F, et al. Efficacy of ultra-short single agent regimen antibiotic chemo-prophylaxis in reducing the risk of meningitis in patients undergoing endoscopic endonasal transsphenoidal surgery. *Clin Neurol Neurosurg*. 2015;139:206-209.
32. Pepper C, Lo S, Toma A. Prospective study of the risk of not using prophylactic antibiotics in nasal packing for epistaxis. *J Laryngol Otol*. 2012;126(3):257-259.

## TABLES

Surgeon Characteristic	Overall (n=182)	Column % <sup>a</sup>	Antibiotics Prescribing Patterns			
			Intraoperative antibiotic		Postoperative antibiotic	
			overall: 173 (95%) n (%Rx)	p-value	overall: n=134 (74%) n(%Rx)	p-value
Overall	182		173 (95%)		134 (74%)	

# of Skull Base Cases	-	-	0.38	0.62
0-10	19	10%	18 (95%)	16 (84%)
11-25	42	23%	40 (95%)	33 (79%)
25-50	55	30%	50 (91%)	38 (69%)
51-100	41	23%	41 (100%)	30 (73%)
100+	25	14%	24 (96%)	17 (68%)
Skull Base as % of Practice	-	-	0.79	0.20
<25%	58	32%	55 (95%)	45 (78%)
25-50%	65	36%	62 (95%)	49 (75%)
51-75%	45	25%	42 (93%)	28 (62%)
76-100%	14	8%	14 (100%)	12 (86%)
Type of Operation	-	-	0.99	0.78
Endoscopic	37	20%	35 (95%)	26 (70%)
Open	19	10%	18 (95%)	15 (79%)
Both	126	69%	120 (95%)	93 (74%)
Work Setting	-	-	<b>0.01</b>	0.17
Academic/Gov.	130	71%	127 (98%)	92 (71%)
Private practice	52	29%	46 (88%)	42 (81%)
Geographic Location	-	-	0.93	<b>0.01</b>
North America	112	62%	27 (100%)	83 (74%)
Europe	27	15%	25 (93%)	14 (52%)
South and Central America	12	7%	11 (92%)	12 (100%)
Africa	3	2%	3 (100%)	3 (100%)
Australia and Asia	23	13%	22 (96%)	19 (83%)
Primary Field	-	-	0.25	0.23
Otolaryngology	74	41%	72 (97%)	58 (78%)
Neurosurgery	108	59%	101 (94%)	76 (70%)
Fellowship Trained	-	-	0.33	0.96
Yes	137	75%	129 (94%)	101 (74%)
No	45	25%	44 (98%)	33 (73%)
Years in Practice	-	-	0.31	0.24
0-5	57	31%	53 (93%)	48 (84%)
5-10	38	21%	37 (97%)	26 (68%)
11-15	31	17%	28 (90%)	23 (74%)

a) % may not add to 100% due to rounding in column 3.

**Table 1: Respondent demographic and practice characteristics.**

<b>How often do you prescribe antibiotics</b>	<b>Intraoperative antibiotic (n)</b>	<b>%</b>	<b>Postoperative antibiotic (n)</b>	<b>%</b>
0% of the time	9	5%	48	26%
1-29% of the time	4	2%	4	2%
30-69% of the time	5	3%	8	4%
70-99% of the time	9	5%	10	5%
100% of the time	155	85%	112	62%
<b>Antibiotic Class</b>	<b>Intraoperative antibiotic (n)</b>	<b>%</b>	<b>Postoperative antibiotic (n)</b>	<b>%</b>
Non-extended spectrum, 1st-2nd generation cephalosporin (e.g. cefazolin, cefuroxime)	96	55%	68	51%
Extended spectrum, 3rd-5th generation cephalosporin (e.g. cefotaxime, cefepime, ceftaroline, ceftobiprole)	75	43%	59	44%
Penicillins (e.g. oxacillin)	17	10%	24	18%
Anti-pseudomonal penicillins (e.g. piperacillin-tazobactam)	8	5%	9	7%
Aminoglycosides (e.g. gentamicin)	9	5%	6	5%
Quinolones (e.g. ciprofloxacin)	3	2%	6	5%
Macrolides (e.g. erythromycin)	1	1%	0	0%

Lincosamides (e.g. clindamycin)	15	9%	6	5%
Nitroimidazole (e.g. metronidazole)	15	9%	13	10%
Folate inhibitors (e.g. trimethoprim-sulfamethoxazole)	1	1%	4	3%
Glycopeptides (e.g. vancomycin)	43	25%	31	23%
Tetracyclines (e.g. doxycycline)	0	0%	2	1%
Carbapenems (e.g. meropenem)	4	2%	3	2%

**Table 2. Frequency and types of antibiotics prescribed.** Respondents were given answer choices of which they could select multiple answers.

Reasons for prescribing	Intraoperative antibiotic (n)	%	Postoperative antibiotic (n)	%	p-value	OR
<b><i>Intraoperative antibiotics</i></b>						
Actively infected sinuses	47	27%			<b>0.027</b>	<b>0.3 (0.1,0.8)</b>
Active CSF leak	49	28%			0.298	
To reduce risk of bacteremia	45	26%			0.346	
To reduce risk of postoperative infection	157	91%			0.346	
Use of non-absorbable packing	41	24%			0.060	
Use of lumbar drain	16	9%			0.540	
That's how I was taught	28	16%			0.216	

<b>Postoperative antibiotics</b>						
To prevent postoperative infection		110	82%	0.113		
Concern for active CSF leak		31	23%	0.511		
To reduce postoperative mucosal inflammation, scarring, synechiae, crusting		25	19%	0.251		
To prevent postoperative sinonasal symptoms		24	18%	0.884		
Use of lumbar drain		17	13%	0.250		
Use of absorbable packing		30	22%	<b>0.003</b>	<b>0.2 (0.1, 0.6)</b>	
Use of non-absorbable packing		51	38%	0.176		
That's how I was taught		23	17%	<b>0.027</b>	<b>0.3 (0.1,0.8)</b>	

**Table 3. Reasons for prescribing intraoperative and postoperative antibiotics.** Respondents were given answer choices of which they could select multiple answers. Odds ratio and p-value are from logistic regression modelling frequency among prescribers of antibiotics. Model is predicting probability that the surgeon prescribes antibiotics 100% of the time. Abbreviation: CSF, cerebrospinal fluid.

Comorbidity that may change prescribing decision	Intra-operative antibiotic	%	p-value	OR	Post-operative antibiotic	%	p-value	OR
No, I do not change my prescribing pattern based on comorbidities.	148	86%	<0.0001	<b>8.7 (3.0, 25.0)</b>	100	75%	<b>0.0012</b>	<b>4.9 (1.9, 12.8)</b>
HIV/AIDs	14	8%	<b>0.0003</b>	<b>0.1 (0.03, 0.4)</b>	16	12%	<b>0.0212</b>	<b>0.3 (0.1, 0.8)</b>
Cystic fibrosis	9	5%	0.2493		15	11%	<b>0.0138</b>	<b>0.2 (0.1, 0.7)</b>
Diabetes	17	10%	<b>0.0001</b>	<b>0.1 (0.04, 0.3)</b>	25	19%	<b>0.0243</b>	<b>0.3 (0.1, 0.9)</b>
Transplant patient	19	11%	<0.0001	<b>0.1 (0.03, 0.3)</b>	24	18%	<b>&lt;0.0001</b>	<b>0.1 (0.04, 0.4)</b>
Cardiac disease	7	4%	0.1316		9	7%	0.1712	0.4 (0.1, 1.6)
Pulmonary disease	7	4%	<b>0.0126</b>	<b>0.1 (0.03, 0.6)</b>	11	8%	<b>0.0125</b>	<b>0.2 (0.1, 0.7)</b>

**Table 4. Factors that potentially influence prescribing decision.** Respondents were given answer choices of which they could select multiple answers. Odds ratio and p-value are from logistic regression modelling frequency among prescribers of antibiotics. Model is predicting probability that the surgeon prescribes antibiotics 100% of the time. Abbreviations: HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome.