Antibiotic Prescriptions of Pediatric Dentists in a University and Adherence to Official Guidelines

ΒY

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THESIS

Submitted as partial fulfillment of the requirements for the degree of Master of Science in Oral Sciences in the Graduate College of the University of Illinois Chicago, 2021

Chicago, Illinois

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This thesis is dedicated to all of the faculty and staff in the Department of Pediatric Dentistry. Thank you to all of the staff who provide immense support on a daily basis so that I may pursue and achieve my endeavors. Thank you to all of the faculty members who each provide me with their own unique insight into this wonderful career. I will treasure all the knowledge and mentorship absorbed during my time in residency to help me become the best provider and educator that I can be. I can only hope that one day I can also pass it forward to the generation ahead. Finally, this is dedicated to all of my family and friends who provide me with the never-ending support to keep me pushing ahead.

ACKNOWLEDGEMENTS

Dr. Kratunova for not only being my research mentor but a constant source of inspiration through her daily expression of compassion towards patients, students, and colleagues. I am beyond grateful to have the opportunity to work so closely with someone I admire so greatly.

Dr. da Fonseca for all the knowledge and support he provides as our department head. Thank you for always believing in me and giving me the many opportunities to learn and grow as a provider.

Dr. Avenetti for all the hard work he puts in as our program director to try to provide me with the best possible experience as a resident. I am so thankful for all the time you dedicate to the residents and to this program.

Dr. Lamberghini for being such a wonderful clinical mentor. Thank you for always providing your time and I am so thankful for the unique opportunities that you have given me.

Dr. Han for his dedication to this process. Thank you for not only being such a great source of knowledge but also being an educator who is so thoughtful and generous.

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LIST OF ABBREVIATIONS

AAPD	American Academy of Pediatric Dentistry
AB	Antibiotic
ADA	American Dental Association
AHA	American Heart Association
AP	Antibiotic Prophylaxis
BID/TID/QID	2x/day, 3x/day, 4x/day
CSS	Cross Sectional Study/Survey
DCF	Data Collection Form
EHR	Electronic Health Record
IV/IM/PO	Intravenous/Intramuscular/By Mouth
MeSH	Medical Subject Headings
MRSA	Methicillin-resistant Staphylococcus aureus
NICE	National Institute for Health and Care Excellence
NUG	Necrotizing Ulcerative Gingivitis
PI	Principal Investigator
SBE	Subacute Bacterial Endocarditis
SDCEP	Scottish Dental Clinical Effectiveness Programme
UIC	University of Illinois Chicago

SUMMARY

The increase in antibiotic resistance worldwide is a recognized public health care problem. The excessive administration of antibiotics by health care professionals has contributed to the rise in prevalence of drug-resistant bacterial infections. Governmental bodies and professional associations have urged for judicious antimicrobial prescribing to eliminate the misuse and overuse of antibiotics as this can limit the growing problem of bacterial resistance.

Although dental practitioners may not treat patients with antibiotics as frequently as physicians, it has been estimated that dentists prescribe between 7 to 11% of all common antibiotics. Dentists may prescribe antibiotics to manage existing infections or prophylactically (to prevent an infection occurring).

The American Academy of Pediatric Dentistry (AAPD) has developed an evidencebased best practice recommendation document with specific clinical indications for antibiotic usage in pediatric dental patients and has strongly advised practitioners to adhere to the outlined general principles.

A number of studies (surveys) in the dental literature have described the selfreported compliance of dentists to antibiotic guidelines as medium to low. There is a lack of research reporting on antibiotic prescribing practices evaluated by assessment of clinical records. Reducing the incidence of antibiotic misuse and overuse requires altering clinicians' practices. This can be a challenging process that requires identifying noncompliance and addressing barriers to practice change.

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SUMMARY (continued)

This was a retrospective cross-sectional study. The dental electronic health record (EHR) system of the Pediatric Dentistry Department, College of Dentistry (COD), University of Illinois Chicago (UIC) was searched to identify all patients who had received an antibiotic prescription in the twenty-seven-month period from 03/10/2018 till 06/02/2020. Of this cohort, pediatric patients who fulfilled the study's inclusion criteria were enrolled as subjects. Each subject received a study number. The subjects' EHR and the day notes corresponding to the dates of antibiotic prescriptions were accessed and assessed by the principal investigator. Subjects' demographics (age at the time of prescription, weight at the time of prescription, sex, race, ethnicity) as well as information regarding the dental diagnosis of the tooth requiring antibiotic administration, the type and duration of the prescribed antibiotic and the treatment intervention were recorded in a data collection sheet. Prescribing practices were evaluated according to the AAPD best practice recommendations with compliance scores assigned. A second examiner reviewed all collected data and has also made determinations of the appropriateness of antibiotic prescribing. Both examiners were trained and calibrated for the purposes of this study. Examiner disagreements were resolved by reassessment of the subjects' EHR and discussion between the examiners. The inter- and intra-examiner reliability was assessed using Cohen's Kappa. The data was analyzed using descriptive statistics, including univariate and multivariate analyses as well as a chi-square test and bivariate logistic regression. A p-value of <0.05 was used to determine statistical significance.

The study findings provide knowledge of current antibiotic prescribing practices amongst pediatric dentists and their compliance with the official professional organization recommendations. It highlights the need for practice change to prevent future misuse and overuse of antibiotics.

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I INTRODUCTION

I.1 Background

I.1.1 Antibiotics and Bacterial Resistance

The terms antimicrobial, anti-infective and antibiotic, refer to a wide range of pharmaceutical agents that include antibacterial, antifungal, antiviral, and antiparasitic drugs. Of this list, antibacterial agents are by far the most commonly used medication. In everyday life and clinical practice, the term antibiotic is generally known as an equivalent to antibacterial agent and it is applied with this meaning herein (Leekha, Terrell, and Edson 2011).

In pre-antibiotic America, the three main causes of death were tuberculosis, pneumonia, and gastrointestinal infections (Fair and Tor 2014). The discovery of penicillin by Fleming, over 90 years ago, revolutionized the medicine of the 20th century and paved the way to the development of modern antibiotics (Tan and Tatsumura 2015). It is also considered one of the most important scientific advances in human history (Tan and Tatsumura 2015). Antibiotics are indicated for the management of active infectious diseases or for preventing further systemic spread of infections caused by bacteria and as such are ineffective and should not be used in treating viral diseases (Leekha, Terrell, and Edson 2011). They are intended to assist the host immune system in gaining control over the bacterial invasion and ultimately in eliminating the infection). However, their application may be associated with negative effects as well such as allergy, toxicity, potential for superinfection with resistant bacteria, expression of dormant resistant genes, chromosomal mutations to resistance and gene transfer to vulnerable organisms).

The phenomenon of antibiotic resistance is owed to self-modification of bacteria either by mutations or by exchanging resistant genetic determinants with other bacteria (Ventola 2015). Developing resistance allows bacteria to successfully survive in environment of antibacterial drugs being used (Ventola 2015). There is strong evidence that frequent personal exposure to antibiotics enhances the risk of an individual harboring resistant microorganisms (Ventola 2015; Meyer et al. 2013). At a larger scale, this principle also applies to communities (Ventola 2015; Meyer et al. 2013). While the reliance on the use of antibiotic medications has been critical to successful medical management and patient survival, there has been an emergence and continuous increase of deadly resistant bacterial strains in the past 20 years (Fair and Tor 2014).

The increase in antibiotic resistance worldwide has become a growing public health problem to the stage of a true global health emergency (Toner et al. 2015). The widespread use of antibiotics by healthcare professions and the livestock industry has been directly linked to the an alarming increase in prevalence of drug-resistant bacteria (Musoke 2000). In the United States (US), it is estimated annually that this surge in antibacterial resistance has cost upward of 20 billion dollars in excess of healthcare costs, including 1.1 billion dollars in unnecessary antibiotic prescriptions. Additionally, antibacterial resistance has also resulted an estimated 8 million days in hospital stays annually (Fair and Tor 2014). Another study found that in the US in the 1990's more antibiotics were sold yearly than over-the-counter medications (Haas, Epstein, and Eggert 1998).

The cause of this surge in antibacterial resistance is multifactorial (Ventola 2015; Meyer et al. 2013). Not only are providers overprescribing but the problem is compounded by a deficiency in research and development by the major pharmaceutical companies (Projan 2003). The fight against the rising bacterial resistance is limited due to diminishing incentives such as a low return on investment on the development of new antibiotic drugs (Power 2006). Moreover, an insufficiency in public knowledge has contributed to this health crisis as many patients are too willing to accept or are even seeking antibiotic prescriptions for non-indicated conditions (Fair and Tor 2014).

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Currently, the major players of bacterial resistance include gram positive species such as Methicillin-resistant Staphylococcus aureus (MRSA) (Boucher et al. 2009). MRSA currently stands as the most commonly observed resistant bacterial species and is responsible for up to 89% of nosocomial infections (Fair and Tor 2014; Jacobs 2004). Streptococcus pneumoniae, which is the leading cause of bacterial pneumonia, has up to 40% of strains that are resistant to penicillin (Boucher et al. 2009; Jacobs 2004). And Clostridium difficile, which is highly prevalent among hospital patients with associated colitis (Fair and Tor 2014; Jacobs 2004).

It is important for pediatric dentists to be educated on appropriate antibiotic prescribing practices as the misuse and overuse of the most commonly prescribed antibiotics in dentistry is directly related to the resistance of aforementioned bacterial species (Tan and Tatsumura 2015). Furthermore, while there has been a strong emphasis on the emerging gram-positive resistant species, there is also an up and coming rise of gram-negative resistant species, most often connected to tuberculosis drugs (Fair and Tor 2014; Jacobs 2004). All in all, providers should be increasingly aware of these trends to always be mindful towards careful prescription of antibiotics.

Government bodies and professional associations worldwide have urged for judicious antimicrobial prescribing to eliminate the misuse and overuse of antibiotics which can curb the growing problem of bacterial resistance. Antimicrobial stewardship has been promoted globally as a systematic effort to educate and motivate prescribers to follow evidence-based prescribing practices. The evidence-based practice guidelines from the Infectious Diseases Society of America are regularly updated and are an excellent information resource for all medical professionals. In dentistry, many organizations, such as American Dental Association (ADA), AAPD, American Association of Endodontics, and others have developed specific guidance to aid their members in the appropriate decision making process when prescribing antibiotics.

I.1.2 Prescribing Practices in Dentistry

While dentists treat less patients with antibiotics then physicians, antibiotic therapy is a valuable adjunct management modality for certain dental infections.(Oberoi et al. 2015) Analgesics and antibiotics are found to be the most commonly prescribed medicaments by dentists and an estimated 10% of all annual US antibiotic prescriptions are dentally-related (Roda et al., n.d.).

When prescribing antibiotics in dentistry it is important to differentiate between prophylactic and therapeutic antibiotic prescribing. Prophylactic prescribing means to prescribe in order to prevent an infection while therapeutic prescribing means to prescribe at the time of an active infection (Stein et al. 2018). While understanding proper prophylactic prescribing practices is extremely important, the main objective here will be on therapeutic prescribing.

In a study surveying Express Scripts Holding Company's (ESHC) records, one of the largest independent prescription benefits manager in the United States, dentists were found to be among the third most prescriber of antibiotics just behind family medicine and internal medicine physicians (Durkin et al. 2017). Among these dentists, 2.9 million prescriptions were written with the majority of them being amoxicillin (57%), followed by clindamycin (15%) and penicillin V (12%) (Durkin et al. 2017). The same is true among pediatric dentists. In a cross-sectional survey sent to members of the AAPD, most of the antibiotic prescriptions were for amoxicillin (78%), followed by penicillin (20%) and <1% of clindamycin and Augmentin ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). In general, this survey suggested inappropriate antibiotic prescriptions with a tendency to overprescribe and inconsistent adherence to the AAPD guidelines ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). It was also found that while a lack of knowledge may be the majority of cases in improper prescription, many nonclinical factors also played a part in prescribing antibiotics when not indicated. An example of a nonclinical factor includes mounting

pressure from parents of patients to prescribe, particularly when the clinician is unable to provide prompt treatment to a symptomatic patient. This is common for dental emergencies that may occur over the weekend or the holidays when the dental office is closed ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). While the ADA recommends an overall conservative use of antibiotics and the AAPD specifically describes clinical situations where antibiotics are indicated, the data continues to show limited adherence to guidelines by providers when prescribing ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017).

I.1.3 Current Recommendations for Antibiotic Therapy for Pediatric Dental Patients

The AAPD recognizes the persistence of overuse and misuse of antibiotics and the potential for an enormous health crisis if improper prescribing practices continue to exist.⁴ Fortunately, the AAPD has consistently updated guidelines on antibiotic therapy for pediatric dentists. These recommendations should provide the proper guidelines needed to help improve prescribing practices (Pallasch 2003).

Administration of antibiotics for oral wounds needs to be evaluated according to host risk as well as type and severity of the wound. This will determine the level of risk for infection to decide whether systemic antibiotics will need to be prescribed ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). If it is decided that antibiotics are needed, antibiotics (consider IV, IM, oral administration) should typically be administered immediately as timing becomes critical in order to help support the natural host immune system ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). It is imperative to monitor clinical symptoms after drug administration as it is recommended that there needs to be a minimum of 5 days of administration after substantial improvement of symptoms ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). In a typical prescription, antibiotics are prescribed as a 5

to 7 day course depending on the medication ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017).

In accordance with the AAPD, systemic antibiotics should be prescribed therapeutically in instances of systemic involvement and septicemia secondary to an odontogenic infection ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). Thus a child presenting with pulpitis, apical periodontitis, or localized intraoral swelling without associated systemic involvement should be treated surgically instead ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). In its recently published new guideline, the ADA also advises practitioners to recommend over-the-counter pain relief medications such as acetaminophen and ibuprofen for such conditions and to actively avoid prescribing antibiotics (Lockhart et al. 2019). Administration of antibiotics for these conditions is ineffective as the dental infection is contained within the pulpal and/or the periapical periodontal tissues. ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). Pulpally involved teeth exhibit compromised pulpal circulation, making it unlikely for systemic antibiotics to reach the infected areas and to achieve therapeutic concentrations (Sivaraman, Hassan, and Pearson 2013). Signs of systemic spread include facial (extraoral) swelling, diffuse intraoral swelling, trismus, fever, lymphadenopathy, dysphagia, tachycardia, and respiratory distress ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). In cases of systemic involvement, antibiotic therapy is indicated with penicillin derivatives being the first choice and cephalosporins as the alternative. In cases of severe infection, metronidazole may be added to the antibiotic regimen for anaerobic bacterial involvement ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). The amoxicillin and metronidazole combination can also be prescribed in cases of necrotizing ulcerative gingivitis (NUG) and systemically involved pericoronitis (Stein et al. 2018).

In cases of dental trauma, aside from specific associated soft tissue injuries, systemic antibiotics are only indicated in replantation of avulsed permanent teeth ("Use of

Antibiotic Therapy for Pediatric Dental Patients' 2017). In these cases, appropriate antibiotic prescriptions would be tetracycline (e.g., doxycycline) for those over the age of 12 and penicillin V or amoxicillin for those under the age of 12 in order to avoid discoloration of developing permanent dentition ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017).

Therapeutic antibiotics are also indicated in cases of salivary gland infections where amoxicillin/clavulanate is often the antibiotic of choice with clindamycin being the alternative in the event of a penicillin allergy ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). Common salivary gland infections may include acute/chronic bacterial submandibular sialadenitis or juvenile recurrent parotitis ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017).

With respect to antibiotic course duration, the recommendations are to choose the shortest course that will prevent both clinical and microbiological relapse. Clinical judgement must be applied, but most acute odontogenic infections resolve within three to seven days. The only practical guide for determining the effectiveness of antimicrobial treatment, and hence the duration of therapy, is clinical improvement of the patient as judged by remission of the infection. When the clinical evidence indicates that the infection is reasonably certain to resolve or is resolved, the antibiotic therapy should be terminated.

II LITERATURE REVIEW

A review of the literature was conducted to evaluate pediatric dentists' adherence to official professional recommendations and guidelines when prescribing antibiotics to their patients. A search in the PubMed database with the MeSH terms "anti-bacterial agents", "child", "dentists", "pediatric dentistry" were used in various combinations. All articles included in the review were cross-sectional studies, published in English, published in the last 10 years, and critically reviewed antibiotic prescribing practices in dentistry according to various professional guidelines. A total of 9 articles were included in the review.

TABLE I

Author	Study Type	Guideline	Area	Participants	Methods and Materials	Results	Comments
Cherry et al. 2012	Cross sectional survey (CSS)	AAPD Infections	US	154 Dentists	Demographic questions & 5 scenarios	10-42% adherence to AAPD & ADA guidelines	Objective evaluations with scenarios Compliance Range: Very low to low Large Sample
Farook et al. 2012	CSS	NICE IE	UK	155 Dentists	Survey of awareness, reading, & compliance of NICE guidelines	94-97% awareness of NICE guidelines, 62-69% have read guidelines, 48-77% self-reported compliance	Subjective/self- reported Compliance Range: Medium Large sample
Leong et al. 2012	CSS	ADA/AHA IE	US	78 Orthodontists	29 questions, demographics, knowledge & management	63% self-reported adherence to guidelines; 58%, 58% consult for medical clearance; 25% had knowledge of correct risk assessment	Subjective/self- reported compliance Compliance Range: Medium Small sample
Lockhart et al.	CSS	ADA/AHA IE	US	878 Dentists	Survey of demographics	75% pleased with ADA guidelines,	Subjective/self- reported

SUMMARY OF REVIEWED LITERATURE

2013					& satisfaction of ADA guidelines	70% had patients who took AP when not recommended	compliance Compliance Range: Low Large sample
Sivarama n et al. 2013	CSS	AAPD Infections & IE	US	984 Pediatric Dentists	19 demographic and scenario- based survey	32-42% AB overprescribed for irreversible pulpitis; 39-68% localized dentoalveolar abscess; 43% for mitral valve prolapse, 15% for intrusion, 13% for extrusion, 12% for rheumatoid arthritis	Objective evaluation with scenarios Compliance Range: Low for odontogenic infections & IE, High for trauma Large sample
Dayer et al. 2013	CSS	NICE IE	UK	664 Dentists, 502 Medical Specialists	Survey awareness & satisfaction of NICE guidelines	99% awareness of NICE guidelines all specialties, 87% Dentists follow NICE	Subjective/self- reported Compliance Range: High Large sample
Jain et al. 2015	CSS	ADA/AHA IE	CA	149 Dental Hygienists & 194 Dentists	5-part survey, demographics & scenarios	42-54% inappropriately recommended AP for low-risk conditions, 81-91% fail to recommend AP for high risk conditions	Objective evaluation with scenarios Compliance Range: Very low to low Large sample
Tomczyk et al. 2018	CSS	ADA/AHA IE	USA	437 Dentists	22-question online survey of antibiotic usage guidelines and prescribing practices	Overall, dentists reported greater antibiotic use than currently recommended by guidelines	Objective evaluation with scenarios Compliance Range: Low Large sample
Ahsan et al. 2020	Cross sectional interview	AAPD Infections & IE	РК	380 Dentists	Pre-designed validated questionnaire used for interview with demographic profile and clinical cases	26.1-42% adherence to AAPD guidelines	Objective evaluation with scenarios Compliance Range: Low Large sample

In general, most of the included studies were cross-sectional surveys with predominantly self-reported compliance. Some of the studies included general surveys to its participants such as questions regarding their awareness of antibiotic prescribing guidelines as seen in the studies by Farook et al., (2012) (Farook et al. 2012) and Dayer

et al., (2013) (Dayer et al. 2013). Other studies included more specific clinical scenario surveys to test their participant's knowledge as seen in the studies conducted by Cherry et al., (2012) (Cherry et al. 2012) and Sivaraman et al., (2013) (Sivaraman, Hassan, and Pearson 2013). Ahsan et al., (2020) (Ahsan et al. 2020) provided the only study that was conducted as a cross sectional interview. Only 3 of the 9 studies used the AAPD guidelines on antibiotic therapy and only 2 of the studies focused strictly on the prescribing practices of pediatric dentists. In contrast, Leong et al., (2012) (Leong, Kunzel, and Cangialosi 2012), Jain et al., (2015) (Jain et al. 2015), and Tomczyk., (2018) (Tomczyk et al. 2018) focused on compliance to the guidelines given by the ADA and the American Heart Association (AHA) for infective endocarditis. All other included studies used the National Institute of Clinical Excellence (NICE) guidelines for adherence to prescribing of infective endocarditis. Overall, as seen in the literature, the dentist's adherence to their respective guidelines were found to be medium to low.

Apart from the study by Ahsan et al., (2020) (Ahsan et al. 2020), all other studies in the literature review suffer from nonresponse bias due to low response rates of the distributed surveys. With nonresponse bias, the sample targeted by the researchers may not be representative of the desired population. Survey research would also exhibit response bias as questions answered may not actually be representative of each provider's clinical decision making.

II.1 Gaps in the Literature

Across the literature, studies reporting on the adherence of pediatric dentists' prescribing practices according to the AAPD guidelines on antibiotic therapy are low. Additionally, no studies were found within the inclusion criteria, that critically review clinical records to critique prescribing practices. The limited available studies are survey based and self-reported.

Reducing the incidence of antibiotic misuse and overuse requires altering practitioners' practices. This can be a challenging process that requires identifying and addressing barriers to practice change. Implementation of clinical audit as well as continued research and education for health-care providers are effective and important tools for clinical practice improvement.

III AIM AND OBJECTIVES

III.1 <u>Aim</u>

The aim of this study was to retrospectively review the antibiotic prescribing practices of dentists at a university-based pediatric dental clinic and to evaluate these practices against the current professional (AAPD) best practice recommendations for antibiotic prescribing in dentistry for children.

III.2 Objectives

- To examine dentists' adherence to the AAPD best practice recommendations with respect to prescribing correctly for oral/dental conditions that are indicated for antimicrobial therapy.
- To evaluate the dentists' compliance with the AAPD drug therapy guidance with respect to:
 - Prescribing adequate types of antibiotics advised for treatment of oral and odontogenic disorders.
 - Administrating the correct strength, frequency, and duration of antibiotic courses.
- To expose practices of misuse or overuse of antibiotics that potentially can lead to antibiotic resistance.
- To search for associations between inappropriate antibiotic prescribing and patient's factors such as age, medical status and/or type of tooth (permanent or primary) involved.
- To make recommendations on improvement of antibiotic prescribing practices as well as on the record keeping with regard to antibiotic prescribing.

IV HYPOTHESIS OF THE STUDY

IV.1 Overarching Hypothesis

The null hypothesis of the study was that there is no difference between the prescribing practices of dentists at the university-based pediatric dental clinic and the AAPD best practice recommendations for antibiotic prescribing in dentistry for children.

The alternative hypothesis was that there is a difference between the prescribing practices of dentists at the university-based pediatric dental clinic and the AAPD best practice recommendations for antibiotic prescribing in dentistry for children. Therefore, the adherence to professional recommendations is less than ideal.

IV.2 Additional Hypotheses

In this study three additional hypotheses were examined:

- There is no statistically significant difference between the inappropriate antibiotic prescribing practices for medically healthy versus medically compromised pediatric dental patients.
- There is no statistically significant difference between the inappropriate antibiotic prescribing practices for pediatric dental patients in the age group
 0 to 7 years of age versus the age group 7 to 17 years of age.
- There is no statistically significant difference between the inappropriate antibiotic prescribing practices for pediatric dental patients presenting with a problem associated with a primary tooth versus permanent tooth.

V MATERIALS AND METHODS

V.1 <u>Ethical Approval</u>

This study was approved by the Institutional Review Board on June 5th, 2020 at the University of Illinois Chicago with protocol number 2020-0717 (Appendix). No external funding was provided or used for this study.

V.2 Study Site

This study was conducted at the College of Dentistry (COD), University of Illinois Chicago (UIC) in the Pediatric Dentistry Department.

V.3 <u>Study Design and Procedures</u>

This study utilized a retrospective cross-sectional cohort design. The AxiUm EHR system administrator generated a report of all patients younger than 17 years of age that were given prescriptions for antibiotics in the period from 03/10/2018 to 06/02/2020. The principal investigator (PI) reviewed all records from this list. Patients that fulfilled the study's selection criteria were enrolled as subjects and received study numbers. Each study number corresponded to a respective EHR number. The key to the code (document containing the list of all EHR numbers and the respective study participant's numbers) was kept in a separate encrypted file in a password protected computer for the duration of the study. None of the data was collected elsewhere and no paper copies of this file were made. The data itself was numerically coded and entered into an encrypted Excel spreadsheet file that was also kept in a password protected computer at Room 269-D, Pediatric Dentistry Department, College of Dentistry, UIC. Only the appointed study investigators had access to the collected information.

V.3.1 Inclusion and Exclusion Criteria of the Study

The eligibility criteria for included pediatric dental patients (0-17 years) that attended the Pediatric Dentistry Department Clinic, COD, UIC in the period from 03/10/2018 to 06/02/2020 and were given a prescription for an antibiotic for a dental problem. Patient records were selected from both the post-graduate and undergraduate clinics of the Pediatric Dentistry Department. If the patient record met these criteria but the antibiotic prescription was completed outside of the Pediatric Dentistry department, then the record was excluded. Additionally, records that had duplicate prescriptions on the same day, records with no associated note with the prescription, or records prescribing on the basis of Subacute Bacterial Endocarditis (SBE) prophylaxis were also excluded (Table 2). No patient records were excluded on the basis of ethnicity, gender, religion, or economic background.

TABLE II

SUMMARY OF THE STUDY'S ELIGIBILITY CRITERIA

Inclusion Criteria	Exclusion Criteria
• Pediatric dental patients from 0 to 17 years	• Adult dental patients (17 years and older).
of age.	• Pediatric patients attending dental clinic at a
Patients of the post-graduate and	different department than the Pediatric
undergraduate clinics, Pediatric Dentistry	Dentistry, College of Dentistry, UIC.
Department, College of Dentistry, UIC.	• Pediatric patients seen outside of the period
• Patients seen in the period from 03/10/2018	from 03/10/2018 to 06/02/2020.
to 06/02/2020.	• Pediatric patients that did not receive an
Patients who received antibiotic	antibiotic prescription at the dental visit.
prescription at their dental visit.	

V.3.2 Study Examiners

Two study examiners (PI and a faculty mentor) had access to all data and were specifically trained and calibrated for the purposes of this research. The PI was a postgraduate student in pediatric dentistry and the second examiner (faculty mentor) was a specialist in Pediatric Dentistry.

V.3.3 Data Collection Procedures

For the records that met the selection criteria, the PI reviewed the EHR information, and the day note corresponding to the prescribed antibiotic and gathered information pertinent to this study in an initial data collection form (Figure 1).

The data collection included subjects' demographics (date of birth, date of antibiotic prescription, weight, gender, race, ethnicity) at the time of the prescription. The

age on the day of prescribing was calculated from the date of birth and the date of the dental visit. To find the weight of the patient at that time, the PI searched the pediatric exam form from the visit (identified by the AxiUm administrator) or the day note. If no weight was recorded in the EHR, the weight range, from the 10th to the 90th percentile according to subject's age was estimated from the CDC growth charts. The subject's health status was also documented, including all listed in the EHR medical diagnoses.

Subject Study number
Rx Date
DOB (Age)
Sex
Race
Ethnicity
Weight (kg)
Weight estimates to age (kg)
Antibiotic Type
Antibiotic Dose
Antibiotic Frequency
Antibiotic Course Duration
Medical Status
Radiographic Examination (yes/no)
Patient Complaint
Clinical Diagnosis
Systemic Involvement Recorded
Type of patient visit (Urgent/Routine)
Immediate treatment
Follow up



Information about the type of tooth (primary or permanent), or the soft tissue disorder for which the antibiotic was prescribed was gathered. Furthermore, it was noted whether or not a radiographic examination was performed if the issue was related to teeth. This was important as the establishment of appropriate diagnosis often requires both clinical and radiographic examination.

The data collection also included the type of prescribed antibiotic, as well as its strength, frequency of daily administration, and course duration. From the day notes entered by the clinical providers, the PI identified the chief patient complaint and the clinical diagnosis of the oral condition for which the antibiotic was prescribed. Most importantly, the PI reviewed thoroughly the day notes to look for description of signs and symptoms of systemic spread of the infection for which the antibiotic was given and recorded the findings. The immediate and the follow up clinical management were documented as separate categories to assess the adherence to the set of relevant clinical standards and to determine the overall quality of the patient care. In addition, the type of patient visit was also noted. The information collected from the EHR was used for assessment of adherence to prescribing for oral conditions indicated for antibiotic administration by the AAPD clinical best practice recommendations.

After the initial data collection was completed by the PI, both examiners reviewed the gathered information independently and made determinations on the appropriateness of antibiotic prescribing with respect to variables related to the actual prescription and to the clinical scenario. The results were recorded in data outcome forms (Figure 2).

Appropriateness of immediate care

Figure 2. Data Outcome Form

The appropriateness of antibiotic type was determined by comparing the findings with the AAPD best practice recommendations "Use of Antibiotic Therapy for Pediatric Dental Patients".

The appropriateness of antibiotic dose, frequency and course duration were decided by comparing the data with the information available in the AAPD "Useful Medications for Oral Conditions" document. The dosing of the antibiotics is provided in a range with a minimum to a maximum (in mg/kg/day) limit. For subjects, whose weight was known, the minimum and maximum daily doses were calculated and if the prescribed dose was within that range, it was determined that the dose prescribing was appropriate. However, if the prescribed dose was lower than the minimum or higher that the maximum, then the dosing was deemed inappropriate. For subjects, whose exact weight was not recorded, the CDC growth charts (for boys and girls respectively) were used to determine the 10th and the 90th percentile weight range according to age. Similarly, if the prescribed dose according to the minimum limit was lower than that calculated for the 10th percentile weight, then the dose was deemed inappropriate. In all other cases, where the dose was within the range, the dosing was determined to be appropriate.

The selection of effective dose within the recommended range is also generally governed by the severity of infection. If the inflammatory process and the systemic spread are limited, choosing medicament strength within the lower to medium dose range would be effective to fight the bacterial invasion. However, in cases where the infection and the systemic involvement are advanced, selecting a dose in the higher range or at the maximum limit might be necessary. These principles were applied by the examiners to make the determinations of the appropriateness of antibiotic prescription dose according to the diagnosis and systemic involvement. While in the existing literature no official grading scales for adherence to guidelines were defined or validated, most authors deemed adherence below 25% to be very low, between 25% and 50% to be low, from 50% to 75% to be medium and over 75% to be high. In our study we adopted the same grading scale.

V.4 Intra- and Inter-examiner Reliability

The two examiners of the study were trained and calibrated. Their study training included review and familiarization with all relevant publications in the AAPD Reference Manual such as the best practice recommendations on "Use of Antibiotic Therapy for Pediatric Dental Patients" (latest revision 2019), "Useful Medications for Oral Conditions", the National Center for Chronic Disease Prevention and Health Promotion (CDC) growth charts, as well as other applicable publications on antibiotic prescribing (including all of those discussed in the background and the literature review section of this thesis).

The calibration process included a number of steps. Using Excel random number generator, ten patient records were selected. Each examiner completed the data collection and antibiotic appropriateness determinations for those records independently and on two separate occasions with more than ten days period apart. The scores were analyzed for inter- and intra-examiner reliability using Cohen's Kappa statistics.

V.5 <u>Statistical Analysis</u>

All study data gathered throughout the forms was numerically converted and transferred into Microsoft[®] Excel 2019 (Microsoft Inc., Redmond, WA, USA). The Microsoft Excel data was then transferred and analyzed using SPSS statistical software (IBM Corporation, Armonk, NY, USA, 2019).

The data was analyzed using descriptive statistics, including univariate and bivariate analyses as well as a chi-square test and logistic regression. A p-value of <0.05

was used to determine statistical significance. Odds ratio and 95% confidence interval were also calculated for each risk factor in the analysis.

VI RESULTS

VI.1 Descriptive Data Analysis

The AxiUm EHR system administrator generated a list of 341 patient numbers in response to the electronic query to identify all records of pediatric patients who have had an antibiotic prescription completed at the COD, UIC in the twenty-seven-month period from 03/10/2018 to 06/02/2020. The PI accessed and reviewed all 341 patient records against the inclusion criteria of the study. Twenty-nine records (8.3%) were excluded as the antibiotics were prescribed for subacute infective endocarditis prophylaxis. Another 5 records (1.5%) were removed as they lacked day notes of patient encounters and further 28 records (8.2%) were excluded as the antibiotic prescriptions were completed at other departments at the COD than the Pediatric Dentistry department, such as the Oral and Maxillofacial Surgery Department, Endodontic department, and the Department of Periodontics. The final sample of eligible for the study records included 279 Axium numbers and those patients were enrolled as subjects for the study.

VI.1.1 Demographic Data

Demographic data analysis of the 279 subjects was completed. The sex distribution of the patient population showed a slightly higher male prevalence with 55% (n=153) males and 45% (n=126) females (Figure 3).

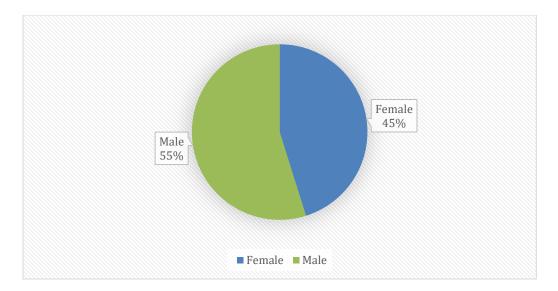


Figure 3. Sex Distribution of Patient Population

The age range of the participants was 1.4 to 16.7 years old. The median age was 6.9 years, and the mean (average) age was 7.5 years (Table 3). The distribution of the number of prescriptions according to the age of the participants is presented in Figure 4.

TABLE III

Age in Years				
Minimum	Maximum	Median	Average	Interquartile Range
1.4	16.7	6.9	7.5	4.7

STUDY SAMPLE AGE IN YEARS RESULTS

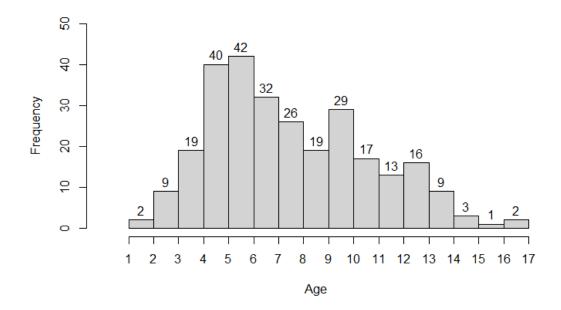


Figure 4. Distribution of Number of Prescriptions according to Patient Age

Race was reported for 79.2% (n=221) of the subjects and for 20.8% (n=58) of the sample the race was not recorded. The majority of participants (49.5%, n=138) self-reported White race. The rest were 25.8% (n=72) Black, 3.6% (n=10) Asian and 0.4% (n=1) Native participants (Figure 5).

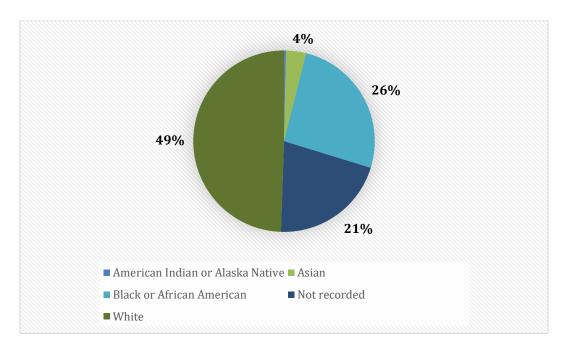


Figure 5. Racial Distribution of Patient Population

Ethnicity was reported for 79.2% (n=221) of the sample. The distribution showed a higher prevalence of Not Hispanic or Latino patients at 41.9% (n=117) compared to 37.3% (n=104) Hispanic or Latino subjects. For 20.8% (n=58) of the subjects, ethnicity was not disclosed (Figure 6).

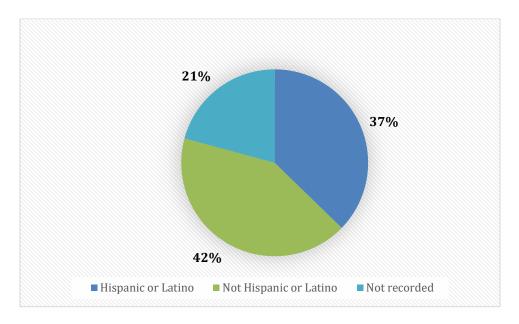


Figure 6. Ethnic Distribution of Patient Population

With respect to medical status, 66.7% (n=186) of the participants were healthy, while the remaining 33.3% (n=93) were medically compromised (Figure 7). Furthermore, 75.3% (n=70) of the medically compromised participants had more than one medical condition on record and 24.7% (n=23) had a singular diagnosis. For subjects with multiple conditions on record, the leading diagnosis was utilized for the purposes of the analysis and the medical diseases were grouped into their respective systemic categories. Hence, of the whole sample (n=279), 6.5% (n=18) of the subjects were diagnosed with asthma, 6.5% (n=18) with autism, 5% (n=14) with an allergic disorder, 4.3% (n=12) presented with a syndrome, 2.9% (n=8) had developmental and learning delays, 2.9% (n=8) had a cardiovascular disorder, 1.4% (n=4) had a hematologic disorder, 1% (n=5) had other disorders.

The distribution of the medical issues within the medically compromised patient sample (n=93) is presented in Figure 8.

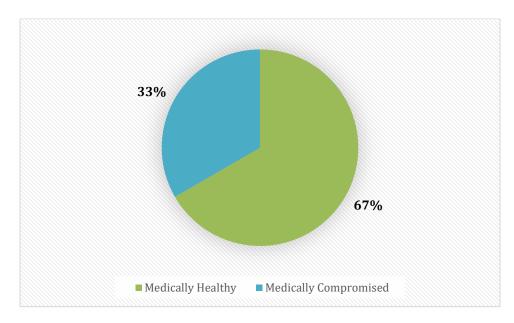
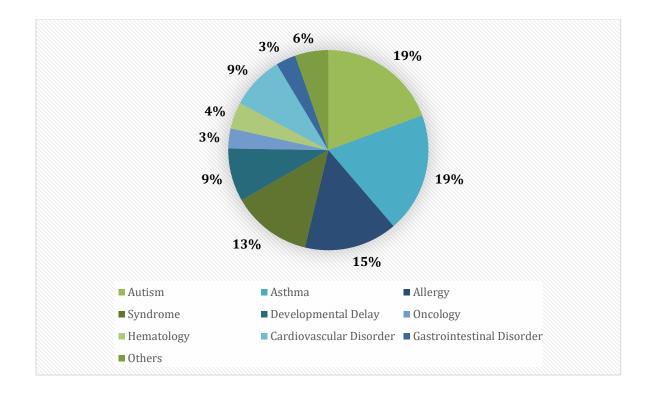
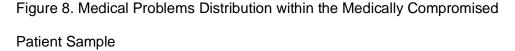


Figure 7. Medical Status Distribution of Patient Population





The majority of the participants, 80.3% (n=224) had their weight recorded in the EHR at the time when the antibiotic was prescribed. The actual number was retrieved either by the AxiUm administrator directly from the pediatric patient medical status form or by the PI from the EHR day note. The remaining 19.3% (n=55) of participants had no available recorded information of their weight on the date of prescribing (Figure 9).

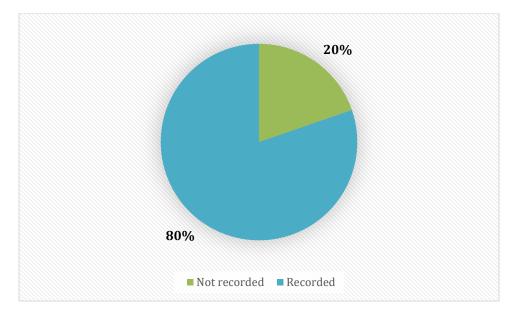


Figure 9. Weight Record Distribution of The Sample

With respect to the recorded weight of the subjects, the range was from 11.4kg to 115kg with median of 25.1kg and mean (average) of 29.5kg (Table 4).

TABLE IV

RECORDED WEIGHT IN KILOGRAMS RESULTS

Weight in Kilograms				
Minimum	Maximum	Median	Average	Interquartile Range
11.4	115	25.1	29.5	15.8

VI.1.2 Descriptive Data of the Prescribed Antibiotics

The majority of the prescriptions were completed for a single type antibiotic 91% (n=254), while 9% (n=25) included a combination of two medicaments (Figure 10).

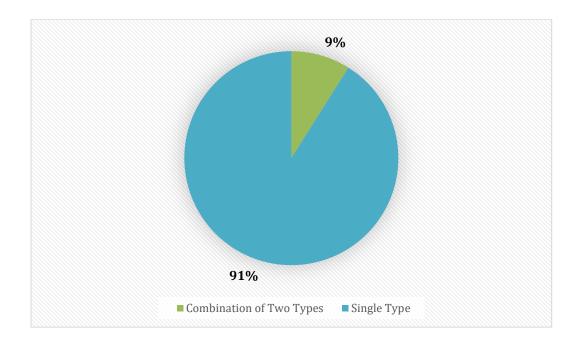


Figure 10. Distribution of Number of Antibiotics Prescribed

The most frequently prescribed type of antibiotic was Amoxicillin 77.1% (n=215), followed by the combination of Amoxicillin and Metronidazole (9.3%, n=26). In 8.2% (n=23) of the cases Clindamycin was chosen (Figure 11). Of these 23 subjects, 16 (5.7% of the whole study sample) had documented Penicillin allergy and for the remaining 8

participants, the reason for choosing Clindamycin as a first-choice antibiotic was not recorded by the clinical provider in the EHR. Less commonly prescribed in this cohort were Augmentin (1.8%, n=5) and Penicillin V (0.7%, n=2). Metronidazole was prescribed as a single choice in 2.9% (n=8) of the cases. In all of these cases, the patients had another wide spectrum antibiotic already prescribed from an outside provider, so Metronidazole was a complimentary medication. On all occasions (12.2%, n=38) when Metronidazole was prescribed both as a single drug or in combination with Amoxicillin, an extraoral swelling was implicated in the clinical cases.

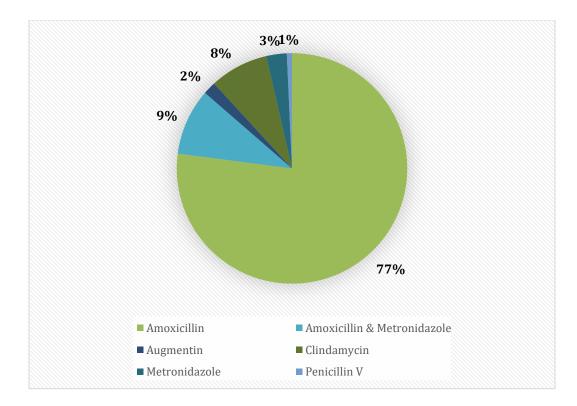


Figure 11. Distribution of Antibiotic Types Prescribed

The vast majority (95.3%, n=266) of the prescriptions were advised for three times daily (TID) administration, while 2.9% (n=8) were written for every 12 hours medication intake (BID) and the remaining 1.8% (n=5) for four times daily (QID) administration (Figure 12).

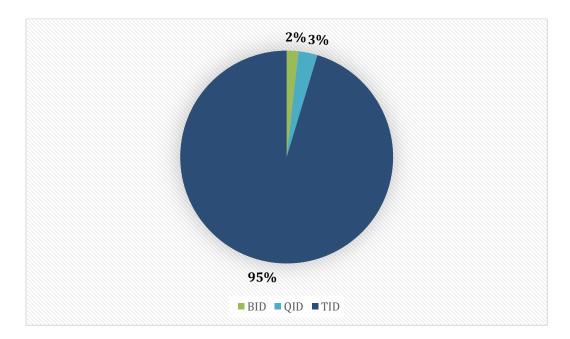


Figure 12. Distribution of Antibiotic Administration Times

With respect to course duration, the clinicians most frequently prescribed for 7 days (74.6%, n=208), followed by 10 days (21.9%, n=61) and least often for 5 days (3.6%, n=10), (Figure 13).

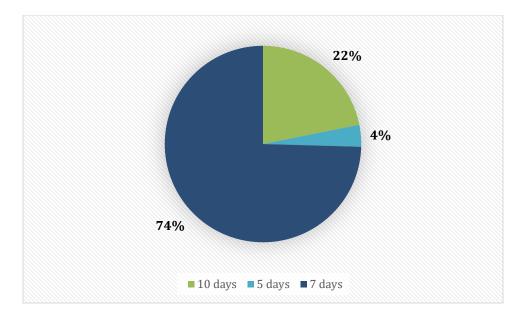


Figure 13. Distribution of Antibiotic Course Length

VI.1.3 <u>Descriptive Data of the Clinical Case Scenarios, which Received Antibiotic</u> <u>Prescription</u>

The most common chief patient complaint for which an antibiotic was prescribed in this study cohort was extraoral swelling (42.3%, n=118). Other issues included pain (40,1%, n=112), dental trauma (8.2%, n=23), intraoral swelling (7.5%, n=21) and bleeding gums (0.7%, n=2). Singular items (0.4%, n=1) included post-operative bleeding, soft tissue trauma and dental checkup (Figure 14).

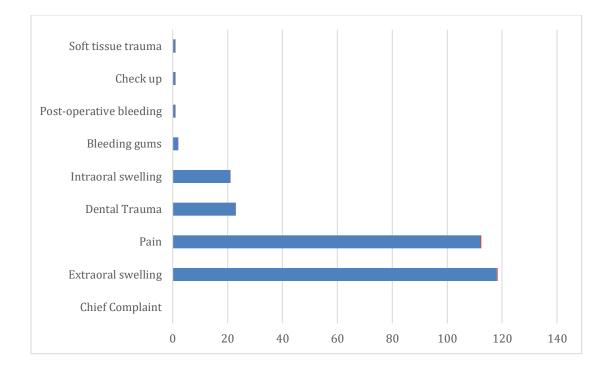


Figure 14. Distribution of Chief Patient Complaint Types

The EHR contained a documented clinical diagnosis of the issue requiring antibiotic prescription in almost all cases (98.9%, n=276). Three (1.1%) of the patient encounters had no record of diagnosis.

The distribution of diagnostic descriptions recorded by the providers in the EHR and deemed indicated for systemic antibiotic administration are presented in Table 5.

TABLE V

DISTRIBUTION OF DIAGNOSTIC DESCRIPTIONS

Type Diagnosis	Number	Percent
Abscess	132	47.3%
Acute Periapical Periodontitis	61	21.9%
Irreversible pulpitis	37	13.3%
Luxation	6	2.2%
Necrotic Pulp	6	2.2%
Pericoronitis	5	1.8%
Subluxation	5	1.8%
Avulsion	4	1.4%
Dry Socket	3	1.1%
Intrusion	3	1.1%
No record	3	1.1%
Acute Necrotizing Ulcerative Gingivitis	2	0.7%
Draining Chronic Abscess	2	0.7%
Reversible Pulpitis	2	0.7%
Aphthous stomatitis	1	0.4%
Extrusion	1	0.4%
Foreign body reaction	1	0.4%
Grossly decayed primary tooth	1	0.4%
Laceration	1	0.4%
Liver clot	1	0.4%
Odontalgia	1	0.4%
Post-operative swelling	1	0.4%

With respect to the implicated oral anatomical structure, the majority of the antibiotic prescriptions were given to manage odontogenic infections associated with primary teeth (57.3%, n=160), followed by permanent teeth (35.1%, n=98) and infections associated with soft tissues (5%, n=14) were ranked third most common. On a few occasions (1.4%, n=4), the subjects had both primary and permanent teeth involved. Three of the records did not specify the source of the oral infection (Figure. 15).

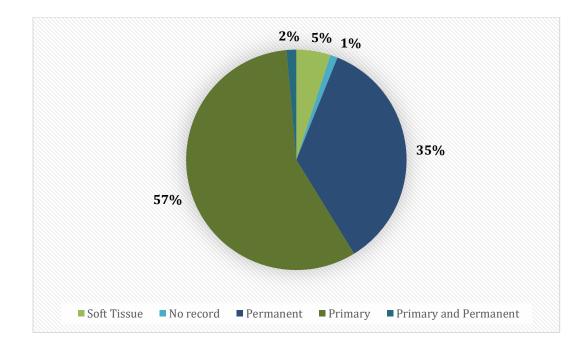


Figure 15. Distribution of Implicated Oral Anatomical Structures

Where soft tissue pathology (5%, n=14) was the cause of the problem, understandably a dental radiograph may not have been indicated and was not exposed. A dental x-ray was taken in 90% of the cases, in which teeth were causing the problem. However, there were instances (5.4%, n=15) in which radiographs were not exposed (Figure 16).

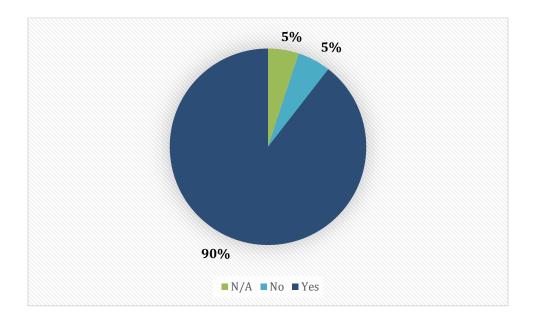


Figure 16. Radiographic Exam Case Distribution

The clinical providers have recorded in the EHR day notes evidence of systemic involvement of the oral infection/issue deemed to require antibiotic prescription in 59.1% (n=165) of the cases, while in the remaining 40.9% (n=114) occasions such information was not documented (Figure 17).

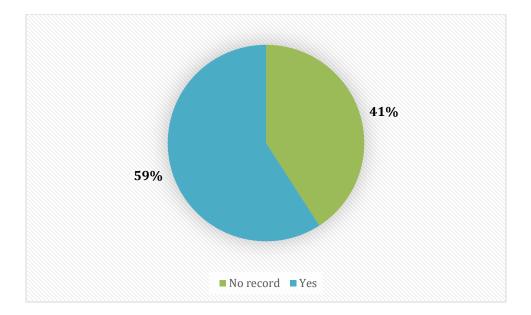


Figure 17. Distribution of Recorded Evidence of Systemic Involvement of the Oral Infection/Problem

VI.1.4 Descriptive Data of the Type of Patient Care

Only 5.7% (n=16) of the subjects were seen as routine care patients, while the majority 94.3% (n=263) attended the urgent care clinic.

With respect to the dental therapy completed at the time of the patient visit, 60.6% (n=169) only received antibiotic prescription, 21.9% (n=61) had a tooth extraction, 4.7% (n=13) had a root canal treatment commenced on a permanent tooth, 3.2% (n=9) received antimicrobial mouthwash with 0.12% Chlorhexidine, 3.2% (n=9) had a tooth splint applied, 2.5% (n=7) had Incision and Drainage procedure completed, 1.4% (n=4) were referred to the Department of Endodontics while 0.7% (n=2) were referred to the Oral and Maxillofacial Surgery Department. An MTA pulpotomy, primary tooth pulpectomy and suture placement were single subject interventions each accounting for 0.4% of all cases (Table 6).

TABLE IV

Immediate Treatment	Ν	%
Prescription only	169	60.6%
Extraction	61	21.9%
RCT	13	4.7%
Chlorhexidine irrigation	9	3.2%
Splint	9	3.2%
Incision & Drainage	7	2.5%
Referral to Endo	4	1.4%
Referral to OMFS	2	0.7%
Tele-dentistry	2	0.7%
MTA pulpotomy	1	0.4%
Pulpectomy	1	0.4%
Suture	1	0.4%

DISTRIBUTION OF IMMEDIATE DENTAL MANAGEMENT TYPE

Following the visit of antibiotic prescription, all subjects were given an appointment for subsequent care. At that visit, the majority (32.6%, n=91) of the participants had a dental extraction, while 27.2% (n=76) had a follow up examination. The distribution of the remaining type of dental care are presented in Table 7.

TABLE 1

DISTRIBUTION OF FOLLOW-UP MANAGEMENT TYPE

Follow up care	Number	%
Extraction	91	32.6%
Clinical Exam	76	27.2%
None	63	22.6%
Operative Treatment	18	6.5%
RCT Stage II	16	5.7%
RCT Stage I	7	2.5%
Did not attend	4	1.4%
General Anesthesia	3	1.1%
Incision and Drainage	1	0.4%

VI.2 Antibiotic Prescribing Appropriateness Determination Results

The choices of antibiotic type, administration daily frequency/timing and course duration were determined to be appropriate on all occasions (100%, n=279).

With respect to accurate dosing according to patient's weight, most of the prescriptions (93.5%, n=261) were determined to be appropriate, however in 6.5% of the cases (n=18) the prescribed dose of medication was outside of the recommended limits (Figure 18). Within the sample of 18 prescriptions deemed inaccurately dosed according to patient's weight, 72.2% (n=13) were dosed lower than the minimum dose range limit and 27.8%

(n=5) had antibiotic dose calculated higher than the recommended maximum dose range limit.

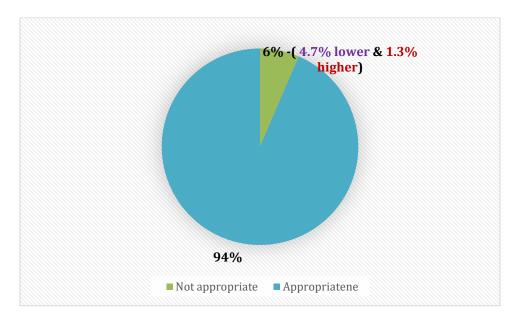


Figure 18. Distribution of Accurate Antibiotic Dosing Determinations according to Patient's Weight

The determinations of the appropriate range of antibiotic dosing according to severity of the documented oral infection showed that the majority of the prescriptions were appropriate (81.7%, n=228), however 18.3% (n=51) were evaluated as inappropriate of which 12.2% (n=34) were dosed higher and 6.1% (n=17) lower than recommended (Figure 19).

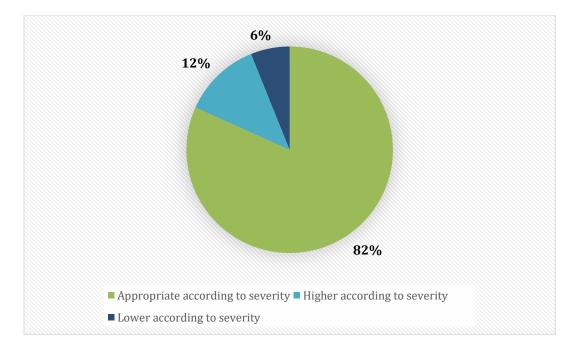


Figure 19. Distribution of Appropriate Range Antibiotic Dosing Determinations according to Infection Severity

The results from determining the overall appropriateness of prescribing antibiotics with respect to the documented in the EHR oral clinical diagnosis as well as evidence of presence of systemic involvement of the infection demonstrated that 61.6% (n=172) of the prescriptions were appropriate and 38.4% (n=107) were not properly justified (Figure 20).

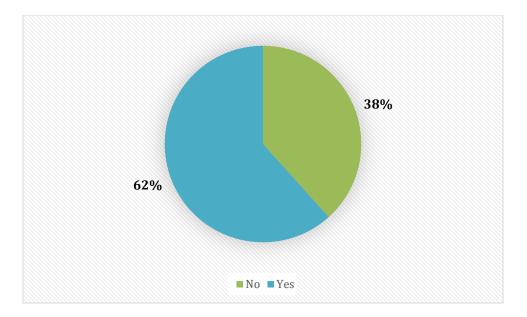


Figure 20. Distribution of Prescribing Antibiotic Appropriateness Determinations according to Diagnosis and Evidence of Systemic Involvement of the Infection

According to the adopted rating scale, defining low (0 to 50%), medium (50% to 57%) and high (75% to 100%) adherence to official recommendations, the result of 61.6% in our study portrays the adherence of prescribing as medium.

The null hypothesis of the study was that there is no difference between the prescribing practices of dentists at the university-based pediatric dental clinic and the AAPD best practice recommendations for antibiotic prescribing in dentistry for children (high adherence of 100%). Since, the results demonstrated differences (medium adherence of 61.6%), we reject the null hypothesis and accept the alternative hypothesis.

VI.3 Descriptive Results for the Period of COVID-19 Impacted Clinic Closure

The dental clinics at the COD, UIC were operating on emergency basis only for the period from 03/17/2020 to 06/02/2020, which was included in the study. All routine dental care was discontinued, due to infection control restrictions posed by the COVID-19 pandemic.

During this time, a total of 20 urgent care pediatric patients, given antibiotic prescriptions satisfied the selection criteria and were included in this subsample. Of those, only two (10%) were assessed via teledentistry, while the rest (90%, n=19) were seen inperson.

This subsample size was 7.2% of the whole study sample. Of the 20 prescriptions, 25% (n=5) were determined to be inappropriate. This figure however, was just 4.7% of all cases deemed to have inappropriately prescribed antibiotics.

Overall, for the 24-month period from 03/10/2018 to 03/10/2020 a total 259 prescriptions were completed, averaging to 10.8 prescriptions per month. For the 3-month period of clinic closures from 03/10/2020 to 06/02/2020, monthly average was 6.7 prescriptions per month, lower than the previous average.

VI.4 Associations of Inappropriate Antibiotic Prescribing with Patient Factors

VI.4.1 Patient Medical Status

With respect to the patient medical status, the statistical analysis determined that there was a statistically significant difference between the inappropriate antibiotic prescribing practices for medically compromised versus medically healthy pediatric dental patients (p=0.0033).

The odds of inappropriate antibiotic prescribing practice for medically compromised pediatric dental patients was 2.15 times of the odds of inappropriate antibiotic prescribing practice for medically healthy dental patients (OR 95%; CI=1.29, 3.57).

Furthermore, various diagnoses were evaluated for associations with inappropriate prescribing and the analysis returned the following:

- There was not statistically significant difference between the odds of inappropriate antibiotic prescribing practices for autistic patients comparing to all other pediatric dental patients (OR=2.11, p=0.128, OR 95% CI = (0.81, 5.54)).
- There was not statistically significant difference between the odds of inappropriate antibiotic prescribing practices for patients with asthma comparing to all other pediatric dental patients (p =0.9613, OR = 0.98 (0.37, 2.60)).
- There was not statistically significant difference between the odds of inappropriate antibiotic prescribing practices for patients with allergies comparing to all other pediatric dental patients (p =0.362, OR = 0.61 (0.21, 1.78)).

However, when such association was assessed for patients diagnosed with a syndrome the results showed that there was a statistically significant difference between the odds of inappropriate antibiotic prescribing practices for syndromic patients comparing to all other pediatric dental patients (p=0.0278, OR = 0.22 (0.05, 0.85), protective factor).

The first additional hypothesis stated that there was not statistically significant difference between the inappropriate antibiotic prescribing practices for medically healthy

versus medically compromised pediatric dental patients. The study results demonstrated the opposite; hence we reject this additional hypothesis.

VI.4.2 Patients Age Group

With respect to patient age, the statistical analysis determined that there was a statistically significant difference between the inappropriate antibiotic prescribing practices for pediatric dental patients in the younger age group (0 to 7 years of age) versus older children (age group 7 to 17 years), (p-value = 0.039).

The odds of inappropriate antibiotic prescribing practice for young kids in the age group 0 to 7 was 1.58 of the odds of inappropriate antibiotic prescribing practice for older children (95% CI is (0.97, 2.57)).

Furthermore, the odds of inappropriate antibiotic prescribing for young kids in the age group 0 to 3 years was 2.34 of the odds of inappropriate antibiotic prescribing practice for older children (4 to 17 years of age), (95% CI is (0.91, 6.00)).

The second additional hypothesis stated that there was not statistically significant difference between the inappropriate antibiotic prescribing practices for pediatric dental patients in the age group 0 to 7 years of age versus the age group 8 to 17 years of age. The study results demonstrated a difference; hence we reject this additional hypothesis.

VI.4.3 Type of Tooth

The data was analyzed to determine if the type of tooth, primary or permanent was a factor associated with inappropriate prescribing.

The results showed that there was a statistically significant difference between the inappropriate antibiotic prescribing practices for pediatric dental patients presenting with a problem associated with a permanent tooth versus primary tooth (p-value = 0.0353).

The odds of inappropriate antibiotic prescribing practice for pediatric dental patients presenting with a problem associated with a permanent tooth was 1.72 of the odds of inappropriate antibiotic prescribing practice with primary tooth (OR 95% CI = (1.04, 2.86)).

The third additional hypothesis stated that there was no statistically significant difference between the inappropriate antibiotic prescribing practices for pediatric dental patients presenting with a problem associated with a primary tooth versus permanent tooth. The study results demonstrated a difference; hence we also reject this additional hypothesis.

VI.5 Intra- and Inter-examiner Reliability

An intra-class analysis was run to assess intra-rater reliability of the two examiners, which yielded a 100% match in responses between tests.

An inter-class analysis was run to assess inter-rater reliability between the two examiners (the PI and the faculty mentor). This yielded a 95% match in response. Any discrepancy was resolved between the two raters.

VII DISCUSSION

VII.1 Demographics of the Patient Population

The Pediatric Dentistry Department of the COD, UIC has multiple dental providers and includes a postgraduate and an undergraduate dental clinic. In the twenty-seven-month study period, a total of 279 antibiotic prescriptions were found eligible for research. Antibiotic prescribing is part of routine dental care and odontogenic infection management is considered regular practice within the scope of clinical pediatric dentistry. Therefore, it was reasonable to expect that acquiring a study sample from over a two-year period of routine clinical operations would achieve a number representable for the usual patient flow and care provided at the Pediatric Dentistry Department. A prospective power analysis was not feasible to complete, as there was no previously published research with similar design. Our study is the first in the current literature to examine actual (not self-reported) antibiotic prescribing practices, evident by patient records and clinical documentation. The sample size of 279 prescriptions highlighted deficiencies in care and demonstrated statistically significant results. Therefore, the study sample size may be deemed appropriate for meaningful statistical results.

The Pediatric Dentistry Department of the COD, UIC typically has a busy clinic schedule. The postgraduate clinic usually accommodates 6 to 14 providers daily and each sees about seven pediatric patients throughout a morning and an afternoon clinical session. A similar number of dental students serve about four patients per day in the undergraduate dental clinic. While calculating the monthly patient flow was not subject for our study, it is important to note that only a small percentage of the patient population (around 10 patients per month) received antibiotic prescriptions. Overall, the Pediatric Dentistry department does not appear to be a frequent antibiotic prescriber. However, this

fact does not diminish the importance of properly justifying every single prescription that is completed and alerting for any irregularities in that regard.

The Pediatric Dentistry Department, COD, UIC is primarily a secondary setting and serves a diverse patient population. The majority of patients referred to the clinic are from primary providers and typically have extensive and unique oral healthcare needs. Many pediatric patients present with severe early childhood caries and may complain of acute complications of their dental disease. Our university-based clinical setting serves a broad range of ages among the pediatric population from newborns up to 17 years old, however children from younger age groups, who are in primary and mixed dentitions, form larger proportions of the patient flow. The patient population is largely made up of Hispanic or Latino and Black Americans with a smaller subset of patients of European and Asian descent. A fair number of patients who are either medically complex or have special health care needs are also seen at the department. The demographic results obtained by the study fully mirror the typical patient population makeup of the clinic.

VII.2 Appropriateness of Antibiotic Type

Among all assessed patient records, it was found that the antibiotic types were appropriately selected from the recommended list by the AAPD common antibacterial drugs. Amoxicillin was the most frequently prescribed antibiotic (77.1%), followed by the combination of amoxicillin and metronidazole (9.3%), and clindamycin (8.2%) holding the third place. These choices are in compliance with the recommended choices of antibiotics advised by the AAPD.

The AAPD states that penicillin derivates remain the empirical choice when prescribing for odontogenic infections with metronidazole as an appropriate adjunct and clindamycin and azithromycin as suitable alternatives for those with penicillin allergies ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017; "Useful Medications for Oral Conditions" 2017). Metronidazole is useful in targeting anerobic bacteria and may be given in combination with amoxicillin for severe odontogenic infections or as a stand-alone drug in cases of periodontal disease such as acute necrotizing ulcerative gingivitis (NUG) ("Useful Medications for Oral Conditions" 2017). This antibiotic has not been a popular choice in pediatric dentistry in the US until recently. The AAPD has included it in its recommendations only about five years ago. The fact that it has been used in this study confirms that the dentists at the department have knowledge and experience with up-todate practices. While both clindamycin and azithromycin are effective alternatives in patients with penicillin allergies, they each come with their own associated risks further precluding them as first-choice antibiotics for those without penicillin allergies.

Clindamycin is often associated with an increased risk of colitis and azithromycin is associated with cardiac arrhythmias in patients with pre-existing cardiac conduction defects ("Useful Medications for Oral Conditions" 2017; Scottish Dental Clinical Effectiveness Programme et al. 2016). Eight of the clindamycin prescriptions in our study were given to patients without a penicillin allergy and there was no other record in the dental note for its justification in choosing it over amoxicillin. Typically, if a patient had taken an antibiotic course in the last month and a new one is required, it is a good practice to change the type in order to reduce the risk of resistance development (Scottish Dental Clinical Effectiveness Programme et al. 2016). Otherwise, selecting an antibiotic from the first line choices is more appropriate. Furthermore, our results demonstrated that clindamycin was the only used penicillin alternative as no prescriptions with azithromycin were found in the sample. An advantage of azithromycin is the single daily dose regimen with an additional loading dose on the first day as opposed to 3-4 doses per day for clindamycin ("Useful Medications for Oral Conditions" 2017). Therefore, azithromycin may be considered for patients where non-compliance is an issue. Dental providers should be informed on these advantages which will enable their better medication selection.

Other less commonly prescribed antibiotics captured in the data included Augmentin and penicillin V. While penicillin V is considered a narrow spectrum first line agent against odontogenic infections with potential to develop less resistance (Stein et al. 2018), it was much less prescribed in comparison to amoxicillin. Compliance with penicillin V regiment could be an issue particularly in children, as it is given in 4 doses per day and must be taken on an empty stomach versus 3 doses for amoxicillin with no restrictions to diet ("Useful Medications for Oral Conditions" 2017). Augmentin may be useful against bacteria with beta lactamase but should only be given if the patient does not respond to amoxicillin initially and as with clindamycin (Scottish Dental Clinical Effectiveness Programme et al. 2016). Its use can also result in associated colitis (Scottish Dental Clinical Effectiveness Programme et al. 2016).

Both Augmentin and clindamycin are considered second line antibiotics (Scottish Dental Clinical Effectiveness Programme et al. 2016). As a general principle, second line agents should only be considered if the patient does not respond to first line agents such as amoxicillin, penicillin V and metronidazole (Scottish Dental Clinical Effectiveness Programme et al. 2016). If the patient develops a hypersensitivity reaction to penicillin, subsequently clindamycin or azithromycin should be given ("Useful Medications for Oral Conditions" 2017).

Of the 8 different recommended antibiotics by the AAPD, there were also no prescriptions of doxycycline or cephalexin. Doxycycline has its uses with NUG, sinusitis, or trauma but is largely avoided particularly in patients less than 8 years of age due to its intrinsic discoloration effects on tooth development ("Useful Medications for Oral

Conditions" 2017). Cephalexin may also be useful in odontogenic infections ("Useful Medications for Oral Conditions" 2017). Since it has no advantage to other first line antibiotics, it may be considered if the patents had a recent course of amoxicillin to avoid repetition of the same drug (Scottish Dental Clinical Effectiveness Programme et al. 2016).

VII.3 Appropriateness of Antibiotic Dose and Course

After choosing the proper antibiotic type for a given clinical situation, the provider must determine the correct amount of antibiotic that is given to the patient. Overall, 100% of the choices for frequency/timing of prescriptions and course duration were deemed appropriate, while 94% of all prescriptions were found appropriate according to the patient's weight. Moreover, 82% of all of the captured prescriptions were determined to be within the appropriate range of antibiotic dosing according to the infection severity in correspondence with the EHR and day note. To be within the appropriate range, the prescriber must correctly determine the dose, frequency, and duration of the antibiotic. All of these factors are imperative to maximize clinical efficacy while minimizing bacterial resistance. Suboptimal antibiotic dose will not achieve drug levels in the infected tissue required for minimal inhibitory concentration of the target microorganism (Calhoun, Wermuth, and Hall 2021). Such practices of lower strength prescribing contribute to the occurrence of antimicrobial resistance and need to be avoided (Calhoun, Wermuth, and Hall 2021). Prescribing very high doses may lead to adverse effects of toxicity, hence care must be exercised when making the appropriate dose calculations (Calhoun, Wermuth, and Hall 2021). Within our sample, 18 prescriptions were deemed inaccurately dosed according to patient's weight and of those prescriptions, 72.2% (n=13) were dosed lower than the minimum dose range limit while 27.8% (n=5) had antibiotic dose calculated higher than the recommended maximum dose range limit. It is important to educate providers to avoid such errors.

In the study, 95% of the prescriptions were administered every 8 hours (TID), followed by 2.9% administered every 12 hours (BID), and 1.8% administered every 6 hours (QID). This was in line with the most frequently prescribed antibiotics as amoxicillin, metronidazole, and clindamycin are typically administered three times daily ("Useful Medications for Oral Conditions" 2017). With respect to course duration, the most commonly administered course was 7 days at 74%, followed by 10 days at 22%, and 5 days at just 4%. For indicated oral infections, therapeutic antibiotics are typically prescribed for 5-7 days (Stein et al. 2018), mostly depending on the severity of the infection and the clinical response of the patient (Scottish Dental Clinical Effectiveness Programme et al. 2016). Ideally, the clinical response should be monitored and the antibiotic discontinued until a 3 day resolution of symptoms (Stein et al. 2018). Further prolonging the course of antibiotic treatment is subclinical as choosing to keep the patient on antibiotics even after the resolution of symptoms may lead to antibacterial resistance (Scottish Dental Clinical Effectiveness Programme et al. 2016). While 10 day antibiotic prescriptions used to be common practice in dentistry, this is no longer recommended. The AAPD best practice recommendation does not advice anymore on a 10-day course of antibiotics ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). While in our study, we accepted the 10-day period as conventional, clinical providers should be educated on averting from prescribing antibiotics for so long (Scottish Dental Clinical Effectiveness Programme et al. 2016).

VII.4 Justification of Antibiotic Prescription

While prescribing the correct type, dose, and course of antibiotic is important, the initial justification for antibiotic prescription is the imperative factor in preventing misuse and limiting the risk of bacterial resistance. The AAPD has clear recommendations for therapeutic antibiotic prescribing indications in various clinical situations. It is important to

note that most odontogenic infections are self-limiting ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). Antimicrobial therapy is best administered only as an adjunct to operative management and considered as first line of care only in cases of sepsis with advanced systemic spread (Stein et al. 2018).

In pediatric dentistry, there are several situations, in which prescription of antibiotics are justified. The most pervasive indication for prescription is in relation to odontogenic infections. In the majority of cases with odontogenic infections, operative/surgical intervention is sufficient to achieve drainage and help treat the infection ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). It is only in situations that the infection becomes systemically involved should systemic antibiotics be administered ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). In this study, the most prevalent chief complaint documented by the providers was extraoral swelling (42.3%), followed by pain (40.1%), and dental trauma (8.2%). Additionally, the most common clinical diagnosis at these visits were dental abscess (47.3%), acute periapical periodontitis (21.9%), and irreversible pulpitis (13.3%). It is difficult to qualify adherence based on the chief complaint and diagnosis alone, so a separate category was created to determine if proper justification with respect to evidence of systemic spread for the prescription was made. The diagnosis dental abscess for example is broad and often the clinical notes did not have a record of any specific details on the affected dental tissues or the type of infection, acute or chronic. Each record was critically evaluated for evidence of systemic involvement of the oral infection. We found this to be the case for only 59% of all records. However, in some instances without documented findings of systemic involvement, the examiners evaluated the prescribing as appropriate. Examples are permanent tooth avulsion, substantial soft tissue laceration or in cases of patients whose

(Stein et al. 2018; "Use of Antibiotic Therapy for Pediatric Dental Patients" 2017).

Diagnoses, recorded by our providers, such as gross caries, draining chronic abscess, odontalgia, reversible/irreversible pulpitis, aphthous stomatitis, and dental trauma like subluxation/luxation are usually contraindicated for antibiotic use ("Useful Medications for Oral Conditions" 2017). For these diagnoses, the more appropriate method of treatment should have been through operative means rather than pharmacological (Stein et al. 2018).

The current AAPD best practice recommendation document was reinforced within the profession as a guideline only until recently. About 4 years ago, the AAPD scientific committee concluded that the quality of evidence supporting the recommendations is lower than the required for a guideline ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017). At the moment, there were only three studies to evaluate prescribing practices of pediatric dentists with the use of the AAPD recommendations as a guide. In addition, these studies were mainly survey based and self-reported. Our study qualified the overall adherence to the recommended practices to be medium (62%). This result was overall better than the findings of Ahsan et al., (2020), which showed that among the 380 interviewed dentists the adherence to the AAPD was only 26% to 42% (very low to low) (Ahsan et al. 2020). In another study that based compliance on the AAPD recommendations, Sivaram et al., (2013), demonstrated that the 984 pediatric dentists completing the questionnaire were knowledgeable of the appropriate management in between 13% and 68% of the various case scenarios (Sivaraman, Hassan, and Pearson 2013). Our result was also higher than the concluded by Cherry et al., (2012). The authors found that the 154 dentists in this cross-sectional survey demonstrated adherence to the AAPD guidelines of 10-42% (very low to low) (Cherry et al. 2012).

This study also looked into the type of therapy provided to patients at the visit as well as at follow up. At initial presentation, the majority of participants did not have any interventional care (60.6%) with some of them (2.8%) being only referred to other departments.

A positive finding is that about a third of the subjects (29.5%) received dental care that seemingly provided infection drainage with extraction (21.9%), incision and drainage (2.5%) and pulpectomy procedure (0.4%) completed to the offending tooth. Furthermore, at the follow up care a total of 42.3% of the subjects had an intervention (such as extraction, root canal treatment, comprehensive care under general anesthesia and, incision and drainage) that suggested obtaining infection drainage from the problematic tooth. It is difficult to draw any conclusions from these results, but if the figures are added it would appear that only about 72% of the cases received care consistent with infection drainage. Therefore, it is important to emphasize that antibiotic prescribing is only an adjunct management and all efforts should be made to achieve definitive care of the problem.

VII.5 Hypotheses Evaluation

Overall, taking into account the proper justification of antibiotics, appropriate antibiotic type, dosage, and course, it was determined that 61.2% of prescriptions were justified. This is comparable to the adherence found in the literature review as the range of adherence in this study was categorized as medium, thus rejecting the null hypotheses to demonstrate a difference in the prescribing practices in our university-based setting and the AAPD best practice recommendations.

Among the most prevalent medical alerts in this sample including asthma, autism, and allergy disorder, none were found to be statistically significant for inappropriate prescribing practices when compared to healthy patients. However, the opposite was true for syndromic patients and medically compromised patients, indicating that there may be a tendency to overprescribe in specific types of medically compromised patients.

In relation to prescriptions by patient age group, inappropriate prescriptions in the younger age group (0 to 7) was found to be statistically significant compared to the older age group (7 to 14). This may indicate a tendency to overprescribe in younger age groups as well. In both the younger age groups and in specific types of medically compromised patients, barriers to care such as a lack of familiarity on the provider's end on how to treat these types of patients may lead to a tendency to prescribe antibiotics even when not indicated. Another consequence to unfamiliarity may mean that providers may either under or overdose these patients out of increased caution to the either bacterial resistance or the infection itself. Another consideration is uncooperative behavior, which may prevent appropriate treatment over an antibiotic prescription.

It was also found to be statistically significant to inappropriately prescribe in permanent teeth involvement versus primary teeth involvement. There may be several factors into why this might be the case. In many cases of odontogenic infection, extraction is often a definitive solution to the problem. Among pediatric dentists and accompanying parents, there is often minimal hesitation to extract an infected primary tooth as the tooth will often be replaced by its successor. However, in a clinical situation involving a permanent tooth, the decision to extract a permanent tooth is not so clear. Hesitation may come from both the provider and accompanying parent, as there is no successor to replace the offending tooth. In other cases, such as in an infected restorable tooth, the pediatric dentist may not be able to provide the endodontic treatment required to clear the infection and save the tooth. All of these factors may lead the provider to inappropriately prescribe antibiotics in permanent tooth involvement.

Antibiotic prescribing as a way of delaying treatment is a poor clinical choice and all other possible management options should be considered beforehand. Antibiotics should not be used instead of pain-relief and anti-inflammatory medication. Every patient is entitled to the best standard of clinical care.

VII.6 Study Strengths and Limitations

This study had several strengths including a sizable sample that was captured over a twenty-seven-month period to best replicate daily patient flow at the university. The study also included two trained and calibrated investigators prior to auditing the records. Both an intra-class and inter-class analysis were run to determine reliability, which were found to be a 100% match and 95% match, respectively. Unlike all previous studies, which examined self-reported prescribing, our research investigated actual prescribing practices that have a direct impact on patients. Our results could be perceived closer to reality as in the surveys, prescribers may show bias towards providing ideal answers. Another strength of our study is the selected setting. The university-based clinics provide an academic environment, where both the educators and the trainees have access to pertinent and current literature. There is a continuous educational incentive to demonstrate and provide service to the highest standard. Identifying practices of antibiotic misuse in such a setting, highlights the need of raising the awareness for appropriate prescribing amongst clinical providers at all levels.

This study also had limitations, mainly related to the inherent disadvantages of the retrospective design. Our study depended on obtaining reliable data from patient records. Poor record keeping and inconsistent documentation may have resulted in negative study findings and bias toward lower scoring. During data collection, documentation with information commissions was found among the records. This included either no definitive weights being recorded, no clear indication or rationale for prescription, and in a few cases

no associated notes (records had to be excluded). If no weight was recorded, a weight estimation by age had to be made, creating an additional layer of bias that may lead to under or overestimating the correct dose of that particular record. This in turn may have led to an incorrect determination of appropriateness of a particular prescription. If no clear indication or rationale for prescription was made, the record was assumed to be of an incorrect justification for antibiotic prescription. Lastly, despite having two trained and calibrated investigators for data collection, there is always the aspect of inherent human error during data collection as could be the case with numerous records and data points that needed to be collected.

Our study also underscores the importance of appropriate record keeping. The EHR documentation of medical history, clinical findings, and diagnosis should be detailed and specific. The patient's file is a legal document that can be used for direct judgement of clinicians' management decisions.

VII.7 Prospects of Future Studies

Future studies should be conducted to further evaluate the prescribing practices of pediatric dentists in various clinical settings. Furthermore, after completing this type of research, the providers whose practices have been evaluated should be made aware of the results and provided with continuous educational opportunities to enable them to improve their professional performance. After a period of time, a subsequent study can be conducted in the same setting to demonstrate if positive changes have been made.

A future study may also involve a prospective one consisting of an experimental group and a control group of clinical providers. The experimental group would receive standardized educational training for proper antibiotic prescriptions and the control group would not. The proper prescription adherence from providers of both groups could then be compared to assess if there are other determinants of professional decision making apart from knowledge and problem awareness.

VII.8 Recommendations for Prescribing Therapeutic Antibiotics in Clinical Practice

Based on this study and the existing literature evaluating adherence of pediatric dentists to antibiotic prescribing guidance, it is evident that there is need for improvement. Practice change and decision-making modifications be challenging and should be facilitated with proper education and introduction of stewardship controls. An opportunity and a tool for improvement is the regular audit of clinical practices in various clinical settings. The audit results should be communicated with the actual prescribers and direct instruction for changes provided. The PI of this study summarized the following basic recommendations based on the information supplied by the AAPD, the SDCEP, and other pertinent and up to date literature.

- The patient should be properly triaged and diagnosed to determine presence of bacterial infection: ascertain chief complaint, assess symptoms, complete thorough clinical and radiographic exam (Scottish Dental Clinical Effectiveness Programme et al. 2016).
- If the infection has been determined to have no systemic spread and involvement (cellulitis, lymph node involvement, diffuse intraoral swelling, extraoral swelling, fever, malaise, trismus) use local drainage to manage infection (extraction, incision and drainage, root canal therapy) ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017; Scottish Dental Clinical Effectiveness Programme et al. 2016). Over-the counter pain relief and anti-inflammatory medication (such as acetaminophen and ibuprofen) can be prescribed to patients.

- If the infection has evidence of systemic spread and involvement, administer systemic antibiotics in conjunction with local drainage on same day or after antibiotic administration in an effort to control the spread of infection first ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017; Scottish Dental Clinical Effectiveness Programme et al. 2016).
 - If patient presents with significant systemic involvement such as severe trismus, floor of mouth swelling, and compromised airway, patient should be sent to the emergency room (Scottish Dental Clinical Effectiveness Programme et al. 2016).
- First line antibiotics include amoxicillin, penicillin V, and metronidazole (Scottish Dental Clinical Effectiveness Programme et al. 2016).
- Amoxicillin may be given alone or in combination with metronidazole for severe systemic infections ("Useful Medications for Oral Conditions" 2017; Scottish Dental Clinical Effectiveness Programme et al. 2016).
- If patients are allergic or develop hypersensitivity reactions to penicillin, consider an alternative such as (clindamycin or ,azithromycin) ("Useful Medications for Oral Conditions" 2017).
- Second line antibiotics include clindamycin, Augmentin, and azithromycin. Second line antibiotics should only be used if first line antibiotics are not an option. Caution should be used as clindamycin and Augmentin come with an increased chance of colitis and azithromycin is associated with cardiac arrhythmias in patients with preexisting cardiac conduction defects (Scottish Dental Clinical Effectiveness Programme et al. 2016).
- Dose of the antibiotic should be calculated according to weight ("Useful Medications for Oral Conditions" 2017; Scottish Dental Clinical Effectiveness

Programme et al. 2016). For more severe infections, dose should be calculated according to the upper recommended limit for the particular type of antibiotic (Scottish Dental Clinical Effectiveness Programme et al. 2016).

- Duration of the antibiotic will depend on the severity of infection and the clinical response from the patient. Antibiotics are typically given for at least 5-7 days either BID, TID, or QID depending on the antibiotic type and half-life of the drug ("Useful Medications for Oral Conditions" 2017; Scottish Dental Clinical Effectiveness Programme et al. 2016).
- Ideally after antibiotic prescription is given, clinical signs should be monitored in response to the antibiotic. The patient should be instructed to finish the course of antibiotics or until the patient is symptom free for 3 days. Prolonging the course of antibiotics any longer may result in an increased chance of bacterial resistance (Stein et al. 2018; Scottish Dental Clinical Effectiveness Programme et al. 2016).
- Follow up with the patient and carry out local treatment if still needed ("Use of Antibiotic Therapy for Pediatric Dental Patients" 2017).
- Documentation is key. Documentation should include the patient's chief complaint, updated weight, antibiotic type, antibiotic dosage (dose, frequency, duration) prescribed, diagnosis and indication for the antibiotic, and appropriate care given and planned follow up care.

VIII CONCLUSIONS

The following conclusions can be made based on the results of this study:

- The adherence to AAPD best practice recommendations was found to be medium with 38.2% of the antibiotic prescriptions deemed inappropriate.
- Significantly more inappropriate prescriptions were given to medically compromised patients, syndromic patients, children younger than 7 years of age and patients presenting with a dental problem associated with a permanent tooth.
- A stewardship program is needed to improve antibiotic prescribing practices and should include accountability, tracking, reporting, education, and action.

APPENDIX A



Exemption Granted

June 5, 2020

Justin Baik Pediatric Dentistry

RE: Protocol # 2020-0717 "Antibiotic Prescribing Practices of Pediatric Dentists in a University Setting and Adherence to Official Guidelines: A Retrospective Study"

Dear Justin Baik:

Your Claim of Exemption was reviewed on **June 5**, 2020 and it was determined that your research meets the criteria for exemption as defined in the U.S. Department of Health and Human Services Regulations for the Protection of Human Subjects [45 CFR 46.104(d)]. You may now begin your research.

Exemption Granted Date: June 5, 2020 Sponsor: None

The specific exemption category under 45 CFR 46.104(d) is: 4

Waiver of HIPAA Authorization:

A waiver of HIPAA Authorization has been granted [45 CFR 164.512(i)(1)(i)] for the use of protected health information (PHI) for research purposes. Please note that this research has been determined to meet the criteria for exemption under category 4. Under the revised Common Rule regulations (2018 Requirements, effective January 21, 2019), research involving secondary analysis of UIC medical records data qualifies for exempt category 4 when the research is limited to the collection and analysis of UIC protected health information within the UIC covered entity per HIPAA. The exemption does not apply to the research use of PHI from non-UIC entities, or to research that involves disclosure of UIC PHI outside of the UIC covered entity. Any future plans to disclose PHI outside of the UIC covered entity will require a protocol amendment and re-review by the IRB.

You are reminded that investigators whose research involving human subjects is determined to be exempt from the federal regulations for the protection of human subjects still have responsibilities for the ethical conduct of the research under state law and UIC policy.

Please remember to:

- → Use your research protocol number (2020-0717) on any documents or correspondence with the IRB concerning your research protocol.
- → Review and comply with the <u>policies</u> of the UIC Human Subjects Protection Program (HSPP) and the guidance <u>Investigator Responsibilities</u>.

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Phone (312) 888-1711

APPENDIX A (continued)



We wish you the best as you conduct your research. If you have any questions or need further help, please contact me at (312) 355-2908 or the OPRS office at (312) 996-1711. Please send any correspondence about this protocol to OPRS via <u>OPRS Live</u>.

Sincerely, Charles W. Hoehne, B.S., C.I.P. Assistant Director, IRB #7 Office for the Protection of Research Subjects

cc: Marcio Da. Fonseca Evelina Kratunova

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Education and Training

University of Illinois Chicago, College of Dentistry, Chicago, IL

- Certificate in the specialty of Pediatric Dentistry, June 2020
- Master of Science in Oral Biology, June 2020
- Doctor of Dental Medicine, May 2019

Rush University

• Master of Science in Biotechnology, May 2014

University of Illinois at Urbana-Champaign

• Bachelor of Science, December 2011

Licensure

Licensed in Dentistry, Illinois

Professional Experience

Apple Dental Care

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• Provide comprehensive oral health care to infants, children, and adolescents in a private practice setting

Research Experience

• Antibiotic Prescribing Practices of Pediatric Dentists in a University Setting and Adherence to Official Recommendations (2021)

Awards and Honors

- Dr. Indru C. Punwani Graduate Student Research Award (2021)
- International College of Dentists Student Leadership Award (2019)
- Bisco, Inc. Award in Pediatric Dentistry (2019)

Professional Affiliations

- American Academy of Pediatric Dentistry
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