

THE PENNSYLVANIA STATE UNIVERSITY
SCHREYER HONORS COLLEGE

DEPARTMENT OF HEALTH POLICY AND ADMINISTRATION

A STUDY OF THE EFFECTIVENESS OF ANTIBIOTICS ON POSTOPERATIVE
COMPLICATIONS AFTER THE REMOVAL OF THIRD MOLARS.

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FALL 2013

A thesis
submitted in partial fulfillment
of the requirements
for a baccalaureate degree
in Science
with honors in Health Policy and Administration

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ABSTRACT

While studies have been conducted to examine how to decrease the incidence of osteitis and secondary infections following the removal of third molars, these complications still remain the two most prominent complications after third molar extractions. The findings from this study, however, shed some light on issues that have not been widely supported by previous research.

This study was designed to explore the effects of antibiotics on the incidence rates of osteitis and secondary infections, with the expectation that antibiotics would lower the incidence of both osteitis and infections. For this double-blinded, randomized study, data was collected on 254 patients, but the sample population was based on the number of teeth extracted ($n=508$). Four different interventions were used in this study: 1) placebo on tooth 17; 2) placebo on tooth 32; 3) antibiotic on tooth 17; and 4) antibiotic on tooth 32. Each patient received one of those four interventions in one extraction site, and the other extraction site was the control site. To analyze the effects of interventions on postoperative complications, I created two regression models in which various intrinsic and extrinsic factors were controlled for. The intrinsic variables included gender, age, level of tooth impaction, and tooth number. The extrinsic variables consisted of doctor, location, number of medications, birth control, allergy medications, and nutrition.

While the results show that antibiotics significantly decrease the rates of osteitis compared to the placebo intervention and the control site, I find no evidence to support the benefits of antibiotics in preventing infection. Moreover, it is worthy of note that the results suggest that males have significantly higher rates of osteitis when controlling for the use of birth control among women. These findings differ from previous studies. They may suggest that antibiotics are not as useful as they were previously thought to be for combating infections, perhaps due to increased antibiotic resistance, and that there is a gender difference in favor of females, which counters prior studies and prevailing wisdom in the industry.

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ACKNOWLEDGEMENTS

I would like to thank all of the people who were involved in making the completion of this project possible. Most notably, I would like to thank my thesis supervisor, Dr. Jonathan Clark, who guided me through the entire course of this thesis. His support, which ranged from fine-tuning a research question to helping me create analytical models to editing my final paper, was invaluable to the success of this project. I would also like to thank Dr. Rhonda BeLue for serving as the second reader for this project. Lastly, I would like to thank the oral surgery practice that provided me with all the data that was analyzed in this study.

Chapter 1

Introduction

Overview

The surgical removal of impacted third molars, also known as wisdom teeth, can result in various postoperative complications, all of which cause a lot of pain, swelling, and dysfunction (Sisk, Hammer, Shelton, Joy, 1986). Many factors contribute to these postoperative complications, and due to this complexity, it can be difficult to determine what is responsible for an inflammatory response for any given person (Baqain, Karaky, Sawair, Khaisat, & Lamis, 2008; Sisk et al., 1986). Previous research suggests that meticulous surgical techniques and procedures, such as using antibiotics, may help minimize the risk of complications (Cardoso, Rodrigues, Junior, Garlet, & de Carvalho, 2010).

In order to understand postoperative complications, it is essential to recognize that many factors may play a role (Bui, Seldin, Dodson, 2003; Baqain et al., 2008). For example, intrinsic factors such as age, gender, medical history, tooth location, and level of impaction may play a role (Cardoso et al., 2010; Baqain et al., 2008). Moreover, extrinsic factors should also be considered, including medications, the operating doctor, the office location where the procedures are taking place, and different interventions, such as antibiotics (Cardoso et al., 2010; Chuang, Perrot, & Dodson, 2008; Larsen, 1992). While there have been studies that aim to determine the effects of different interventions on postoperative complications, there has yet to be a consensus on what interventions work best because certain unavoidable complications will always occur due to the intricacy of their nature (Baqain et al., 2008; Sisk et al., 1986).

Tooth Extractions and Postoperative Complications

The most common complication following the removal of third molars, commonly referred to as wisdom teeth, is dry socket, which is also known as alveolar osteitis or localized osteitis (Krogh, 1948). Osteitis is a postoperative complication that is characterized by the inception of severe pain around 3 to 5 days after the extraction of the tooth (Larsen, 1992). Clinically, osteitis reveals a necrotic blood clot in the extraction wound, which will unveil alveolar bone upon disintegration of the clot (Heasman & Jacobs, 1984). The disintegration of the clot can be a result of bacterial invasion (Larsen, 1992). The alveolar bone appears to have a “dry” appearance, which is why Crawford termed this condition “dry socket” in 1876 (Cardoso et al., 2010). An intense pain that radiates from the ear and neck and a foul odor from the mouth clinically characterize the onset of osteitis (Crawford, 1896). Pain is the most important symptom of osteitis, and it can vary in frequency and intensity (Cardoso et al., 2010). However, the pain can lead to other symptoms, such as headache, insomnia, and dizziness (Cardoso et al., 2010).

The incidence of osteitis following the removal of third molars has a wide range. It has been reported as ranging anywhere from 0.5 to greater than 50%, although most authors have reported an incidence of 5 to 20% (Chuang et al., 2008). The large differences in the reported incidence of osteitis may be due to differences in diagnostic criteria, in intraoperative and postoperative treatment of the extraction sites, in patient populations with respect to age, medical status, or tooth positions, or in surgical techniques and skills (Sisk et al., 1986). Mandibular or lower third molars have a higher incidence of osteitis compared to maxillary or upper third molars because of the reduced thickness of the buccal alveolar bone in the upper regions (Turner, 1982). Several studies have reported the incidence rates of osteitis after removal of impacted mandibular third molars to be 20 to 30% (Larsen, 1992).

Secondary infection is another common postoperative complication that occurs following the removal of third molars. Secondary infections have an onset several days after the tooth

extraction (Bui et al., 2003). Symptoms that may accompany a secondary infection are fever, abnormal swelling, pain, or a salty or prolonged bad taste with or without discharge from the surgical site (Shwetha Dental Hospital, 2012). Reported secondary infection rates usually range from 0.9 to 5% (Chuang et al., 2008; Bui et al., 2003). To avoid secondary infections, it is crucial to maintain good oral hygiene, avoid drinking, and avoid smoking (Shwetha Dental Hospital, 2012).

Intrinsic Factors Related to Postoperative Complications

There are many factors that have the potential to influence the incidence of postoperative complications. Some of these factors are intrinsic, such as age, gender, medical history, tooth location, and level of impaction. Evidence supports the notion that older patients typically have a higher risk of postoperative complications (Bui et al., 2003). Therefore, age can be considered a predisposing factor. This may be due to the fact that younger bone is much more plastic and vascularized, or it may be due to fact that bone density increases with age, thus requiring more manipulation during surgery (Bui et al., 2003; Kraver, 2011). Increased age is also associated with a complete root formation and diminished wound healing capabilities, which often leads to higher operative and inflammatory complications (Bui et al., 2003).

Gender is another factor that is often studied when determining the incidence of postoperative complications, particularly with regard to osteitis. While many studies show that there is no significant difference between men and women with regard to osteitis (Bui et al., 2003; Heasman & Jacobs, 1984), some studies do show that men typically have lower rates of osteitis, with the ratio of men to women being 2:3 (MacGregor, 1969). For the studies that do show a significantly higher rate of complications among women, this may be due to the increased usage of oral contraceptives among females in the study (Bui et al., 2003). This idea will be

discussed in a later section where I address the role birth control plays in postoperative complications.

Medical history impacts the likelihood that someone will have postoperative complications. Diabetes and liver disease can slow the healing power of a patient (Kolokythas, Olech, & Miloro, 2010), and it is known that people who have wound healing problems are especially likely to have a complication following the extraction of third molars (Bui et al., 2003). In addition, people who have an organ transplant, HIV, or blood disorders, such as hemophilia, were considered at greater risk for the complications (Bui et al., 2003). Patients who have a positive dental history, which is one that includes bleeding gums, sensitive teeth, and difficulty with jaw movements, were also more inclined to experiencing postoperative complications (Bui et al., 2003).

The incidence of postoperative complications varies based on location of the extraction site. Osteitis and infections are more common in the mandible than in the maxilla (Larsen, 1992). The reason for this is that the mandible has a relatively low blood supply compared to the maxilla, and this predisposes the mandible to osteitis (Amir, 2011). The mandible bone is also thicker, which results in more trauma to the extraction site and, in turn, increases the chance of complications (Turner, 1982). Osteitis also increases as one goes further back into the mouth, with the highest osteitis incidence being in the third molar mandibular region (Amir, 2011). Lastly, food debris tends to gather in the lower sockets more readily than the upper sockets, and this can increase osteitis and secondary infection rates (Amir, 2011).

The chance of postoperative complications may also increase with the difficulty of the extraction, which is usually associated with the level of impaction. A full bony impacted tooth occurs when the tooth is stuck entirely within the bone and is covered completely by gum tissue, while a partial bony impaction occurs when the tooth gets stuck halfway through the bone (Bui et al., 2003; Kraver, 2011). Full bony impaction tends to have higher incidence rates in comparison

to partial bony impactions and soft tissue impactions, which could be explained by the increase in extraction trauma (Bui et al., 2003). When teeth are more impacted, it often takes more force to extract the teeth, and this force could increase the incidence of osteitis (Amir, 2011). When the surgery has a longer duration in which the surgical site is exposed longer, it also increases the chance that bacteria enter the site, resulting in complications (Capuzzi & Montebugnoli, 1994). If bone cutting is done during the tooth extraction due to the deep level of impaction, infections and osteitis are more likely (Shwetha Dental Hosiptal)).

Extrinsic Factors Related to Postoperative Complications

Postoperative complications are more likely to occur if a person smokes and uses birth control pills (Bui et al., 2003). In addition, the doctors' experience and office location may also affect the rates of postoperative complications (Sisk et al., 1986).

Smoking often increases the chance that one will have a postoperative complication (Kolokythas et al., 2010). This may occur because nicotine has a significant vasoconstrictor effect on the small vessels that occur in smokers, which decreases the blood supply and oxygen to the site and inhibits wound healing (Amir, 2011). In addition, nicotine inhibits the proliferation of fibroblasts and macrophages, which results in disintegration of the blood clot and, in turn, osteitis (Kolokythas et al., 2010). Smoking also introduces harmful substances that can act as contaminants to the surgical wound, thereby leading to infections and osteitis (Kolokythas et al., 2010).

As stated above, some studies show that women have a higher rate of osteitis when compared to men, and this may be due to the fact that many women take oral contraceptives (Larsen, 1992). Most oral contraceptives contain high levels of estrogen, and estrogen can prevent one's body from healing by preventing clotting, thus increasing postoperative complication rates (Kolokythas et al., 2010). In addition, oral contraceptives appear to lower a woman's pain

tolerance level, which will make her more susceptible to the pain associated with osteitis (De Vizio, n.d.).

Doctors also play a part in postoperative complications. Differences in surgical techniques have been shown to result in varying incident rates (Baquin et al., 2008; Sisk et al., 1986). For example, more inexperienced surgeons tend to use more force when extracting third molars, and the extra force can lead to a more traumatic extraction, increasing the likelihood of postoperative complications (Sisk et al., 1986). In addition, the location of the practice may affect the chances of getting postoperative complications due to economic disparities. Practices that are in less affluent areas will bring in a different population of patients than those in more affluent areas, and the populations may display different behaviors and habits, which could affect the rates of postoperative complications (Koopu & Boyd, 2009). For instance, since it is known that oral hygiene affects the rates of postoperative complications (Bui et al., 2003), an increase of postoperative complications in less affluent areas with patients of lower socioeconomic status could be due to the fact that the general pool of patients cannot afford upkeep with good oral hygiene and healthy diets compared to populations that come from more affluent areas (Koopu & Boyd, 2009). In general, lower costs can limit access to services and resources needed to support healthy lifestyles (Koopu & Booyd, 2009).

Interventions for Postoperative Complications

Over the years, many studies have been conducted in order to try and reduce the incidence of postoperative complications (Larsen, 1992). Previous studies show that various methods are successful in reducing the incidence of postoperative complications, and these interventions include using intraoperative irrigation, placing stabilizing clot factors into the socket, using systemic antibiotics, and using topical antibiotics, such as Tetracycline, Neomycin, and Bacitracin, in the socket (Larsen, 1992; Cardoso et al., 2010). When placing topical

antibiotics into the socket, they are usually placed on gelfoam, which is methylcellulose that is utilized to control bleeding during surgery (Cardoso et al., 2010). The reason why antibiotics are typically successful in reducing the rates of postoperative complications is because they attack the bacteria that play a role in the development of osteitis and infections (Cardoso et al., 2010).

Although many studies have been conducted on osteitis and secondary infections, these are still the most common postoperative complications that plague many oral surgery practices today. In past studies, the antibiotic Minocycline has been shown to reduce delayed clinical recovery of patients predicted to be at higher risk of delayed recovery after third molar removal by reducing the pain and complications associated with the extractions (Stavropoulos, Shugars, Phillips, Conrad, Fleuchaus, White, 2006). As such, this study aims to examine the affect of using the topical antibiotic Minocycline as an intervention for the postoperative complications of osteitis and secondary infections. Due to the role antibiotics have with fighting bacteria and Minocycline has with reducing clinical recovery, I expect two results from this study:

- Hypothesis 1: The use of antibiotics will decrease the incidence of osteitis.
- Hypothesis 2: The use of antibiotics will decrease the incidence of infections.

Aftercare and Treatments for Postoperative Complications

Despite using interventions like those mentioned above, postoperative complications will still persist to some degree. According to the National Health Services [NHS] (2013), following aftercare instructions will help lessen the chance of getting a postoperative complication. After the surgical removal of third molars, patients must avoid rinsing the site that day, keep gauze in for at least twenty minutes, and avoid hard food and using straws; these methods will help the blood clot stay in place (Amir, 2011). In addition, patients should continue brushing their teeth, and after the first day, they should rinse the site with salt water to reduce swelling and relieve pain (Husney & Christen, 2011).

If a patient has a postoperative complication even after following the aftercare instructions, then the doctor will treat the patient. When a patient is diagnosed with osteitis, the doctor must flush out the socket with a saline solution in order to remove food particles and other debris that may contribute to pain or infection (Mayo Clinic, 2013). They also pack the socket with medicated dressings and prescribe pain medications (Mayo Clinic, 2013). When a patient has a secondary infection, doctors will prescribe systemic antibiotics to fight the infections (Mayo Clinic, 2013).

Working with an Oral and Maxillofacial Surgeons (OMS) Practice

This study was conducted in collaboration with an oral surgery practice that has five offices throughout a metropolitan area in a mid-Atlantic state. The study had 254 patients, and it ran during the summer and fall of 2012. This was a double-blinded, randomized study. For each patient, there was one control site and one intervention site, with the intervention site containing either Minocycline on gelfoam or a placebo on gelfoam.

In order to understand the impact that antibiotics have on the postoperative complications, patients were followed up one week after surgery to determine if there were any complications. The diagnostic criteria for osteitis in this study was the postoperative return of the patient with pain and bone showing and the placement of a medicated dressing in the extraction site. The diagnostic criteria for infection was the postoperative return of a patient with swelling, redness, pain, pus, and/or temperature for which systemic antibiotics were prescribed. If a patient returned to the follow-up appointment and was not treated for any complications, then this study assumed no complications. This thesis will analyze the data collected from this oral surgery practice in order to study the effects of antibiotics on postoperative complications of the general population.

Chapter 2

Methods

Sources of Data

Almost all patients treated at the study practice live in two counties, with a population of over 625,000 and 800,000, respectively (U.S. Census Bureau, 2013). The five offices are spread throughout different areas of the one county, and as such, the population demographics at each office may vary. Based on per capita income, the order of the office location from the most to least affluent area is as follows: Location 1, Location 5, Location 2, Location 3, and Location 4 (Sperling's Best Places, 2013). The mean per capita income spanned from about \$42,000 in the most affluent area to \$33,000 in the least affluent area (Sperling's Best Places, 2013). Third molar extractions only occurred at Location 1, Location 5, Location 3, and Location 4 for this study.

The study practice has five surgeons, all of whom were part of the study that ranged from May to November of 2012. Throughout the study, Doctor 3 was the primary informant. Approximately 300 patients were recruited for this study. To be included in the study, the patients had to be non-smokers between 13 and 25 years old, and all patients had to have two lower third molars, both of which were impacted to some degree, either partially or fully. This was to ensure that one lower third molar site was the control site and the other was the intervention site. In addition, patients had to sign a consent form. The doctors administered this form on the consultation day, and if the surgery took place a month after that consultation, the patients had to resign the consent.

Each patient in the study represented one of four intervention options, with each intervention initially having 75 patients ($n=75$). The four intervention options were based on the

site of intervention, which was indicated by the tooth number, and the actual intervention rendered, which could either be an antibiotic or placebo. The control site was the other lower third molar site that was not being treated. Table 1, below, outlines the different treatment options given to the patients.

Table 1. Interventions

Treatment option (randomly assigned):	Treatment tooth number:	Actual treatment rendered:	Control tooth number:
#17 GP	#17	Gelfoam Placebo	#32
#17 GA	#17	Gelfoam Antibiotic	#32
#32 GP	#32	Gelfoam Placebo	#17
#32 GA	#32	Gelfoam Antibiotic	#17

Despite recruiting 300 patients, a sample of only 254 people with a total of 508 ($n=508$) extracted teeth qualified for final inclusion in the study. This was due to patient drop out prior to the procedure or not showing up for the follow-up appointments. Table 2 shows the adjusted intervention numbers. The fact that the number of patients receiving each treatment is not the exact same for both teeth can be attributed to the randomness of the study and to the dropouts. However, 127 patients received the antibiotic and 127 received the placebo.

Table 2. Adjusted Numbers for the Four Interventions and the Control Sites

Intervention	Tooth 17	Tooth 32	Total
	Number of Patients (<i>n</i>)	Number of Patients (<i>n</i>)	Number of Patients (<i>n</i>)
Antibiotic	60	67	127
Placebo	65	62	127
Control	129	125	254

Methodology

This was a double-blinded study that was approved by the Office for Research Protections (ORP) at Penn State (Appendix A). For this study, the doctors and patients did not know the intervention, so nurses throughout the four offices were in charge of preparing the intervention for each patient at the time of surgery and filling out a form for each patient (Appendix B). This form indicated age, medications, gender, doctor, level of impaction for both of the lower third molars, and postoperative statuses for both teeth. The nurses also wrote down the office that the surgery was performed at on this form. In addition to the form, the nurses had 300 manila envelopes that indicated the intervention for each patient, which was randomly assigned at the start of the study. By looking into the manila envelope attached to the patient form, nurses were able to prepare the correct intervention for each patient without the surgeons knowing the treatment. During the surgery, the nurses told the doctors which tooth was the site of intervention, and from there, the doctors placed the gelfoam with either the placebo or antibiotic into that site. Nothing was placed into the control site. At the completion of the study, which

occurred after all patients came back for their follow-up appointment, the nurses provided all of the data forms to me so that I could run statistical analyses.

Statistical Analysis

To better understand the data, descriptive statistics were used to show the frequency distributions of the different variables used in this study. These variables included the type of postoperative complication, age, gender, level of impaction, tooth number, doctor, location, intervention, number of medications, and types of medications, such as birth control, nutrition supplements, and allergy medications.

In order to examine the major hypotheses and determine the statistical significance of the effects of antibiotics on postoperative complications, I designed two separate regression models, each to examine one of the two key outcome variables: osteitis or infection. The intervention and control variables for the models are listed in Table 3.

In each of the models, the intervention variable was the primary variable of interest in relationship to the outcome variables of osteitis and infection. Intervention was a categorical variable that identified the type of intervention that the patient was receiving: antibiotic, placebo or control. The other ten variables in Table 3 were included as control variables.

I included the doctor and location variables in order to control for differences that might exist among the doctors and the office locations, e.g., the number of teeth extracted by each doctor and at each location. Both of these variables are categorical variables, and they identify each practice and each doctor in the study. The other extrinsic factors I controlled for were the number of medications and the types of medications. I included these variables in order to control for the potential effects that medications may have on the outcome variables. The number of medications is a discrete variable that identifies the number of medications a particular patient

takes, while birth control, nutrition supplements, and allergy medications are dichotomous variables in which a person either took those medications or did not.

I also controlled for intrinsic variables such as age, gender, level of impaction, and tooth number. Age is a continuous variable in this study that ranged from 13-25, while gender is a dichotomous variable. These variables were controlled for to account for the potential impact that gender and age may have on the incidence of complications. In addition, I controlled for the tooth number and level of impaction, which were both dichotomous variables.

Table 3. Intervention and Control Variables in the Regression Model

Variables	
1. Intervention Antibiotic Placebo Control	7. Doctor Doctor 1 Doctor 2 Doctor 3 Doctor 4 Doctor 5
2. Location Location 1 Location 3 Location 4 Location 5	8. Number of Medications 1 2 3 4 5
3. Age	9. Birth Control
4. Gender Male Female	10. Nutrition Supplements
5. Level of Impaction Partially Fully	11. Allergy Medications
6. Tooth Number Tooth 17 Tooth 32	

Chapter 3

Results

Descriptive Statistics

The final sample population included 254 patients with 135 females (53.15%) and 119 males (46.85%). While the initial study population included 75 patients ($n=75$) in each of the four treatment options, the final study population had a different number of patients receiving each treatment due to the dropout rate. Table 2 in the Methods section shows the final number of patients receiving each of the four treatment options, and it also shows the final split of the control according to the extraction site.

Table 4 provides an overview of the incidence of osteitis and infections after the study was completed. There were a total of 20 sites plagued with osteitis with an incidence rate of 3.94%, and 33 sites had infections with an incidence rate of 6.50%. In addition, there was one patient who developed both osteitis and infection. Of the 508 teeth extracted, 454 extraction sites showed no complications. Therefore, there was a success rate of 89.37%.

Table 4. Number and Frequency of Osteitis, Secondary Infections, and No Complications

Postoperative Status	Number (n)	Frequency (%)
Osteitis	20	3.94
Infection	33	6.50
Infection and Osteitis	1	0.20
No Complications	454	89.37

Table 5, below, shows descriptive statistics for the intrinsic factors of gender, age, level of impaction, and tooth number. More specifically, it shows the mean, standard deviation, minimum, and maximum for each of these variables.

Table 5. Descriptive Statistics for the Intrinsic Factors: Gender, Age, Level of Impaction, and Tooth Number

Variable	Sample Size of Each Variable (Based on Extracted Teeth)		Descriptive Statistics			
	<i>n</i>	%	Mean	Std. Dev.	Min	Max
Gender						
Male	238	46.85	.4685	.4995	0	1
Female	270	53.15	.5315	.4995	0	1
Total	508	100.00				
Age			16.99	2.081	13	25
13	8	1.57				
14	34	6.69				
15	78	15.35				
16	126	24.80				
17	92	18.11				
18	52	10.24				
19	44	8.66				
20	46	9.10				
21	16	3.15				
22	8	1.57				
23	-	-				
24	2	0.39				
25	2	0.39				
Total	508	100.00				
Level of Impaction						
Fully	421	82.87	.8287	.3771	0	1
Partially	87	17.13	.1713	.3771	0	1
Total	508	100.00				
Tooth Number						
Tooth 17	254	50.00	.5	.5005	0	1
Tooth 32	254	50.00	.5	.5005	0	1
Total	508	100.00				

Each variable has multiple levels, i.e. the variable gender has two levels: male and female. As can be seen from Table 4, there were more females than males in the study, with females making up 53.15% of the study population. The most common age for third molar removal was 16 years old ($n=126$). The next two ages with the most teeth extracted were 17 year olds ($n=92$) and 15 year olds ($n=78$), respectively. The mean age of people in the study is approximately 17 years old, with a standard deviation of about 2. This shows that there was a narrow distribution of ages within the study. In the study, 421 teeth were fully impacted, while on 87 teeth were partially impacted. Therefore, 82.87% of all teeth extracted were fully impacted. Lastly, because all patients included in the study had to have two lower third molars, there were even numbers of tooth 17 and tooth 32 extracted.

Table 6 shows descriptive statistics for the extrinsic factors of doctor, location, intervention, number of medications, birth control, nutrition supplements, and allergy medications. More specifically, it shows the mean, standard deviation, minimum, and maximum for each of these variables.

In table 6, each variable has multiple levels. Based on the doctor variable, Doctor 3 extracted the most teeth ($n=154$), which was about 30% of all teeth extracted, and Doctor 1 extracted the least number of teeth ($n=54$). Location 1 is where most teeth were extracted ($n=212$), and Location 4 is where the least number of teeth were extracted ($n=60$). There were the exact same number of antibiotic and placebo interventions at $n=127$. The mean number of medications taken by a patient was .7323 with a standard deviation of about 1. This shows that there was a narrow distribution with regard to number of medications taken. It was rare for people to take more than two medications, with only 0.79% of the population taking five medications. In addition, 13.39% of the population took birth control, 14.96% of the population took nutritional supplements, and 12.99% of the population took allergy medications.

Table 6. Descriptive Statistics for the Extrinsic Factors: Doctor, Location, Intervention, Number of Medications, Birth Control, Nutrition Supplements, and Allergy Medications

Variable	Sample Size of Each Variable (Based on Extracted Teeth)		Descriptive Statistics			
	<i>n</i>	%	Mean	Std. Dev.	Min	Max
Doctor						
1	54	10.63	.1063	.3085	0	1
2	124	24.41	.2441	.4300	0	1
3	154	30.31	.3031	.4601	0	1
4	118	23.23	.2323	.4227	0	1
5	58	11.42	.1142	.3183	0	1
Total	508	100.00				
Location						
1 (D)	212	41.73	.4173	.4936	0	1
3 (Q)	118	23.23	.2323	.4227	0	1
4 (W)	60	11.81	.1181	.3231	0	1
5 (C)	118	23.23	.2323	.4227	0	1
Total	508	100.00				
Intervention						
Antibiotic	127	25.00	.25	.4334	0	1
Placebo	127	25.00	.25	.4334	0	1
Control	254	50.00	.5	.5004	0	1
Total	508	100.00				
Number of Medications			.7323	1.005	0	5
0	276	54.33				
1	140	27.56				
2	58	11.42				
3	24	4.72				
4	6	1.18				
5	4	.079				
Total	508	100.00				
Birth Control	68	13.39	.1339	.3408	0	1
Nutrition Supplements	76	14.96	.1496	.3570	0	1
Allergy Medications	66	12.99	.1299	.3365	0	1

Analytical Statistics

A controlled logistic regression was run to examine the relationship between various factors, both intrinsic and extrinsic, and postoperative complications. The tests of my hypotheses were based on the p-values from each regression model. While a p-value of less than 0.05 represented a very strong significant correlation, a p-value of less than 0.1 was also considered significant for the sake of this study, though I note that as p-values get larger, confidence in the estimates weakens. I used the odds ratio in order to determine the direction and magnitude of the correlation between the benchmark, or comparison, variable and the control variables listed in Table 3.

Table 7, below, shows the logistic regression for osteitis. Based on the results in Table 7, the antibiotic intervention was shown to be successful in decreasing the incidence of postoperative complications. With regard to the control site, the antibiotic intervention was statistically significant at conventional levels ($p=0.077$), with the control site being 3.30 times more likely to get osteitis. With regard to the placebo intervention, the antibiotic showed even stronger statistical significance ($p=0.016$), with the placebo sites being 7.30 times more likely to get osteitis.

There was a statistically significant difference ($p=0.019$) between males and females, with males being 1.87 times more likely than females to get osteitis when birth control was controlled for. There was also a statistically significant difference ($p=0.036$) between Doctor 1 and Doctor 2, with Doctor 2 being 5.3 times more likely to cause osteitis. Location 4 was statistically significant compared to Location 1 ($p=0.015$), with the chance of osteitis being two thirds less likely to occur in Location 4. Lastly, there is a very large statistical significance with respect to birth control ($p=0.008$). A female taking birth control is 18.39 times more likely to get osteitis than a female who does not take birth control. There was no statistically significant

difference based on age, level of impaction, tooth number, or medications, such and allergy medications.

Table 7. Controlled Logistic Regression for Osteitis

Variable	Odds Ratio	Significance by P-value
Gender <i>(Compared to Females)</i>		
Male	1.87	0.019
Age	1.07	0.680
Level of Impaction <i>(Compared to Fully Impacted)</i>		
Partially	1.13	0.810
Tooth Number <i>(Compared to tooth 17)</i>		
32	0.81	0.117
Doctor <i>(Compared to Doctor 1)</i>		
Doctor 2	5.30	0.036
Doctor 3	1.84	0.599
Doctor 4	1.39	0.588
Doctor 5	3.67	0.106
Office Location <i>(Compared to Location 1)</i>		
Location 3	1.07	0.793
Location 4	0.69	0.015
Location 5	0.89	0.777
Intervention <i>(Compared to Antibiotic)</i>		
Control	3.30	0.077
Placebo	7.30	0.016
Number of Medications	0.72	0.645
BCP	18.39	0.008
Nutrition Supplements	2.97	0.301
Allergy	0.91	0.962

Table 8 shows the controlled logistic regression with infections being the postoperative complication. All of the variables are the same as in Table 7. When examining the effects of the antibiotic intervention, the results show that there was no statistically significant difference between the antibiotics and the placebo or the control ($p=0.724$ and 0.359 , respectively). This is contrary to my expectations, since prior studies by Larsen (1992), Cardoso et al. (2010), and Stavropoulos et al. (2006) have suggested that antibiotics would significantly decrease the incidence of infections.

Beyond the intervention, the level of impaction and office location resulted in statistically significant results. First, there was a statistically significant difference between partially impacted teeth and fully impacted teeth ($p=0.027$). The extraction sites of partially impacted teeth were one-third less likely to get an infection than the extraction sites of fully impacted teeth. Based on location, Location 3 and Location 4 were both significantly different from Location 1, with p -values of 0.023 and 0.016 , respectively. In Location 3, infections were 1.34 times more likely to occur than in Location 1, and in Location 4, infections were 2.66 times more likely to occur than in Location 1.

Gender, age, tooth number, doctor, and medications, such as birth control, nutrition supplements, and allergy medications, did not play a statistically significant role in infection rates.

Table 8. Controlled Logistic Regression for Infection

Variable	Odds Ratio	Significance by P-value
Gender <i>(Compared to Females)</i>		
Male	0.58	0.328
Age	1.01	0.939
Level of Impaction <i>(Compared to Fully Impacted)</i>		
Partially	0.30	0.027
Tooth Number <i>(Compared to tooth 17)</i>		
32	1.36	0.332
Doctor <i>(Compared to Doctor 1)</i>		
Doctor 2	1.43	0.668
Doctor 3	1.14	0.624
Doctor 4	0.94	0.248
Doctor 5	1.05	0.173
Office Location <i>(Compared to Location 1)</i>		
Location 3	1.34	0.023
Location 4	2.66	0.016
Location 5	1.02	0.888
Intervention <i>(Compared to Antibiotic)</i>		
Control	0.79	0.359
Placebo	1.15	0.724
Number of Medications	1.38	0.131
BCP	0.25	0.352
Nutrition Supplements	0.68	0.414
Allergy	0.64	0.645

Chapter 4

Discussion

The main purpose of this study was to evaluate the effect that the antibiotic intervention had on the incidence of postoperative complications, such as osteitis and secondary infections. This study further aimed to examine the various effects that intrinsic and extrinsic factors had on postoperative complications. The intrinsic factors that were examined in this study included gender, age, and level of impaction, while the extrinsic factors included doctor, location, and various medications.

From the two hypotheses of this study, only one was supported. I predicted that antibiotics would decrease the incidence rates of both osteitis and infections, but the results from this study only supported the reduced incidence rates of osteitis. Compared to many other studies that have been run, this study had a low overall incidence rate of osteitis at 3.94% (Chuang et al., 2008; Sisk et al., 1986). However, the 6.5% infection rate from this study was high compared to other studies in which the common infection rate was between 0.9% and 5% (Chuang et al., 2008; Bui et al., 2003).

While I believed that the antibiotic would decrease the incidence of osteitis, I also believed that the gelfoam, which was used in the placebo and antibiotic interventions, would help decrease the rates of osteitis. My findings did not support the gelfoam expectation. Compared to the control sites, which were the extraction sites that had no gelfoam or antibiotics, the sites with the antibiotics were 3.30 times less likely to develop osteitis ($p=0.077$), which is statistically significant at conventional levels with an alpha value of 0.1. However, interestingly, the statistical difference between the placebo sites, which were the sites with the gelfoam, and the antibiotic

sites was even more significant than the difference between the control and antibiotic site. The placebo sites had significantly higher incidence rates of osteitis ($p=0.016$), with those sites being 7.30 times more likely to develop osteitis. Both results, however, show that the antibiotics were successful in decreasing the rates of osteitis.

Although I expected the gelfoam to aid in decreasing the incidence of osteitis due to the role it plays as a clotting agent (Cardoso et al., 2010), my interviews suggest that the discrepancy of the placebo intervention having a stronger significant difference than the control when compared to the antibiotic sites could be because the control site allows the site to heal naturally. The gelfoam that is placed in the placebo site could be a potential source of bacteria, and bacteria have been known to irritate the bone and blood clot, thereby resulting in osteitis (Cardoso et al., 2010). However, by using an antibiotic on the gelfoam, the antibiotic may be able to fight off much of the bacteria that were present, which prevented irritation of the bone and dissolution of the blood clot, thereby resulting in lower incidence rates.

While one would expect antibiotics to also decrease the incidence rates of infections, this study did not support that idea. The antibiotics used in this study showed no significant effect on infections when compared to the placebo and control, which is a fascinating finding in opposition to previous studies (Larsen, 1992; Cardoso et al., 2010; Stavropoulos et al., 2006). An interesting explanation for this result may be that the rampant use of antibiotics to fight childhood infections has led to a gradual increase in antibiotic resistance among teens and young adults (Andersson & Levin, 1999).

Another possible way to explain why antibiotics did not significantly decrease infection rates is to consider hygiene factors. Many bacteria are found in the mouth, and the infections could have arisen if the patient was not keeping his/her surgical site clean (Bui et al., 2003; Hoopu & Boyd, 2009). Moreover, my study interviews suggest that the antibiotics may not work in fighting infection if the antibiotic gets overwhelmed by all the bacteria and, therefore, can only

do so much to fight the bacteria. The antibiotic in this study was placed directly in the socket, so it may not have been able to directly impact bacteria that were seeded into different tissues other than the socket. For example, bacteria could have been displaced to the soft tissue surrounding the extraction site at the time of surgery, and if this occurred, the antibiotic in the socket would not have been able to fight the infections that arose from the soft tissue bacteria.

Another aspect that this study examined was the role that birth control plays on postoperative complications. Past research has studied the effects of birth control on osteitis rates (Bui et al., 2003; Chuang et al., 2008). Studies have shown that oral contraceptives increase the occurrence of osteitis because most oral contraceptives contain high levels of estrogen, which can prevent one's body from healing by preventing clotting, thus increasing osteitis rates (Kolokythas et al., 2010). Consequently, I expected that birth control would increase the rates of osteitis, but I did not expect birth control to affect infection rates. These expectations were supported by this study. Birth control was found to have a statistically significant impact ($p=0.008$) on osteitis. Women who took birth control were 18.39 times more likely to get osteitis. There was no significant result for the affect of birth control on infections ($p=0.352$).

One of the most fascinating findings from this study was with regard to gender and the birth control effect. Most studies show that gender does not play a role in osteitis (Bui et al., 2003; Heasman & Jacobs, 1984), or if it does, women have higher rates due to the birth control effect (MacGregor, 1969). For this study, I expected that women would have significantly higher rates of osteitis due to birth control, but the results show that there was no statistical difference between men and women when birth control was not controlled for. However, when controlling for birth control, women were actually significantly less likely ($p=0.019$) than men to have osteitis, with men being 1.87 times more likely to get osteitis. Table 9, below, shows the differences in the significance value of gender with and without controlling for birth control.

Table 9. Effects of Controlling for Birth Control on the Statistical Significance Between Genders

Variable	With Controlling for Birth Control		Without Controlling for Birth Control	
	Odds Ratio	P-Value	Odds Ratio	P-Value
Male <i>(Compared to Females)</i>	1.87	0.019	.568	0.309

The finding that men have significantly higher rates of osteitis when controlling for birth control is a very intriguing finding that has not been widely supported or explored by previous studies. Interviews from this study suggest that men may have been less likely to listen to instructions on how to care for their surgical site, and neglecting to care for the surgical wound could impact the blood clot and result in higher rates of osteitis (NHS, 2013). In addition, men may have been more likely to eat hard foods before their wound healed, which would greatly increase the chances of dislodging the blood clot, thereby exposing the bone and getting a dry socket (Amir, 2011; Larsen, 1992). An interesting follow-up to this study would be to examine the differences in aftercare between men and women.

While it was expected that postoperative complications would increase with increasing age due to the increased bone density and decreased plasticity (Bui et al., 2003; Kraver, 2011), this prediction was not supported by the study. However, the limited number of patients that were older than 20 years old could easily explain this. In the study, only 14 out of 254 patients were older than 20 years old. This does not provide a good representation of the older age groups. In order to really study the effect that age has on postoperative complications, a larger poll of older patients should be used.

Another expectation from this study was that the level of impaction would have an impact on the incidence of both osteitis and infections, with partially impacted teeth being less likely to result in complications, because one would expect more trauma and more exposure of the surgical site to coincide with the removal of fully impacted teeth (Capuzzi & Montebugnoli, 1994; Bui et al., 2003). Greater exposure of the surgical site allows more opportunities for bacteria to get into the wound, which would increase both infection and osteitis rates (Capuzzi & Montebugnoli, 1994). Moreover, forceful extractions have been shown to increase osteitis rates (Amir, 2011).

This expectation was supported with regard to infections but not with regard to osteitis, which is difficult to explain. The statistically significant results ($p=0.027$) that support lower incidence of infections with partially impacted teeth compared to fully impacted teeth can be explained by the fact that partially impacted sites have less exposure during surgery and usually less trauma (Capuzzi & Montebugnoli, 1994; Bui et al., 2003). As interviews suggest, the fact that there was no difference in osteitis based on the level of impaction may be a result of fully bony impacted teeth having larger extraction sites that allow for larger clots, which helps with osteitis prevention.

During this study, I also looked at some extrinsic factors that could impact the rates of postoperative complications. I predicted that there would be no difference in postoperative complications among doctors because they were all at a similar experience level (Sisk et al., 1986). My expectation that there would be no difference between doctors was not supported by the results with regard to osteitis, but it was supported with regard to infections. In the study, Doctor 2 had a higher rate of osteitis that was statistically significant ($p=0.036$). This may be explained by surgical techniques, since it is well known that techniques vary across surgeons (Sisk et al., 1986). For example, some surgeons may use more force when extracting teeth, which could result in more trauma and, thus, higher rates of osteitis (Amir, 2011).

In addition to expecting no difference among doctors, I also expected there to be no significant difference among office locations because the four office locations are in relatively close proximity to each other, and the doctors rotate among the offices. My prediction that there would be no difference in postoperative complications among office locations was not supported by this study because one location showed significantly lower rates of osteitis compared to Location 1 and two offices showed significantly higher rates of infection compared to Location 1.

With regard to osteitis, Location 4 had a significantly lower rate of osteitis ($p=0.015$) when compared to the main office. In an effort to explain this effect, I considered the supporting nursing staff. While most of the offices rotate nursing staff members, Location 4 remains relatively constant with regard to nursing staff. The two main nurses are among the most experienced nurses at that practice, so they may be gentler when it comes to assisting the surgeries, and they may have more polished techniques (Sisk et al., 1986).

With regard to infections, it was very interesting that two offices had significantly higher rates of infections compared to the main office. One of the two offices with higher infection rates was Location 4, which had a lower rate of osteitis. As seen in Table 4, infections and osteitis very rarely occur together, so these outcomes are likely a function of different things. Consequently, it makes sense that Location 4 could be lower in osteitis rates and higher in infection rates. Location 3 and Location 4 ($p= 0.023$ and 0.016) are the offices that are in the least affluent areas. As a result, socioeconomic factors may again play a role in the frequency of infections (Koopu & Boyd, 2009). Interviews suggest that the people from these areas may not be as concerned with hygiene and healthy diets or they may not have access to services and resources needed to live healthy lifestyles, which would play a role in fostering infections (Koopu & Boyd, 2009).

Another interesting finding was that Location 4, the office with the highest infection rates, had the sterility room in the basement, which was in the same area as the lunchroom and supplies. This layout may foster more bacteria, which could lead to greater infection rates. In

addition, shuffling the instruments from the basement to the surgical rooms could also increase the level of bacteria that the instruments are introduced to. While the instruments typically remain in sterility bags until they get into the operating rooms, sometimes there are so many patients that the instruments get sterilized without bagging for quicker turn-around. As such, bacteria could contaminate these instruments more easily as they are taken from the basement to the operating room.

It cannot be ignored that there are several limitations in this study due to the nature of the collection and analysis of the data. While there were 254 patients in this study, the ages of the patients were extremely skewed, so it was difficult to determine the relationship between postoperative complications and age. Moreover, the doctors and offices each had varying number of extractions, which made it more difficult to accurately determine associations between those variables and the postoperative complications. Another limitation that arose from this study was the timing of the follow-up. Some patients may have developed infections or osteitis after they had their postoperative follow-up. Because the data forms were collected at the end of the first follow-up, any additional follow-up appointments would not have been recorded for this study.

One of the biggest limitations from this study is that my model did not control for all variables that could have impacted the rates of postoperative complications. For instance, controlling for the nursing staff would be very challenging because most of the nurses move from office to office, but the nursing staff could play a role in the rates of postoperative complications. Moreover, I did not take into account whether patients followed all aftercare instructions when they came back for the follow-up, so I could not control for this factor in my regression model. In addition, while socioeconomic effects may play an indirect role in postoperative complications, the study did not take into account the socioeconomic status of the patient. The socioeconomic status of the patients was generalized based on the office location where they had surgery, which would not be completely representative of all the patients at that office. Lastly, this study did not

take into account the difficulty level of the extractions, and having this information could have provided more accurate information about the relationship between trauma and postoperative complication rates (Turner, 1982).

There are a few future studies that would be a very fascinating follow-up to the findings of this study. It would be interesting to do a cost-benefit analysis of using antibiotics to see if using the antibiotics would decrease the number of postoperative complication appointments, thereby freeing up time to see additional patients. In addition, a follow-up study could examine the work and organizational flow of the practices to determine why there are differences in postoperative complications between offices. Lastly, it would be interesting to examine a few of the factors that I did not take into account for this study, such as the socioeconomic effect on postoperative complications and the effect of aftercare on postoperative complications.

Despite the limitations of this study, the results do provide information about a topic that continues to plague the extraction of third molars. While many people have studied what affects osteitis and secondary infections, the results from this study shed light onto topics that have not been widely supported or explored. Most notably, the findings that antibiotics did not significantly decrease the rates of infections and that men are significantly more likely to get osteitis when controlling for birth control are fascinating. While antibiotics help decrease the incidence of some postoperative complications, they do not entirely eliminate these complications. One may conclude that the rampant use of antibiotics to treat childhood infections has increased antibiotic resistance among teens and young adults. Consequently, the antibiotics are not as useful in fighting the infections brought about by the removal of third molars. As for the gender effect, one should continue exploring the idea of aftercare in order to determine what is leading to the gender differences seen from this study. Ultimately, it is important to continue studying all the factors that affect postoperative complications so that the incidence of osteitis and infections continue to decrease into the future.

Appendix A

Office of Research Protections (ORP) Approval

	Reply	Reply to All	Forward	Delete	Full Headers	Printer Friendly	Previous	Next	Index
From	"Krout, Stephanie" <sqk2@psu.edu> @								
To	"jrc5496@psu.edu" <jrc5496@psu.edu> @								
Subject	IRB Protocol ID 39669, "The efficacy of topical Tetracycline in reducing infection and topical steroids in reducing localized osteitis following removal of boney impacted third molars"								
Date	Tue, Apr 3, 2012 01:08 PM								
CC	"jrc24@psu.edu" <jrc24@psu.edu> @								
Safe View	On <input type="checkbox"/> Turn Off What is "Safe View"?								
Jessica Cunning,									

The Office for Research Protections (ORP) has received and reviewed the above-referenced eSubmission application. It has been determined that this project does not meet the definition of "human participant research." This project does not require further review by the ORP or the Institutional Review Board (IRB); therefore, your application will be closed out. Your study's Non-Human/Non-Research Determination letter has been uploaded into PRAMS.

To access your letter:

- Log into PRAMS (<http://www.prams.psu.edu>)
- In the blue, left-hand menu, expand the "Human" link (click on the +)
- Click on "Protocol Folder Closed"
- Select your "Protocol ID" (IRB number)
- Select the "Documents" tab
- The letter is located in the "Approval Letter" folder

If you have any questions, please let me know. The above-referenced IRB # MUST be included in any correspondence sent to this office regarding this study.

Thank you,

Stephanie L. Krout

Research Compliance Coordinator

The Pennsylvania State University | Office for Research Protections | The 330 Building, Suite 205 | University Park, PA 16802

Direct Line: (814) 865-2935 | Main Line: (814) 865-1775 | Fax: (814) 863-8699 | www.research.psu.edu/orp

Appendix B

OMS Third Molar Postoperative Complication Study Form

OMS PC 3rd Molar Complication Study

Patient ID/Chart # _____ Date: _____

Patient Age: _____

Medications: _____

Sex: M F

Doctor #: 1 2 3 4 5

Tooth Number:

 #17: Partial Full

 #32: Partial Full

Post Op Status

#17 No Complications ~~Osteitis~~ Infection

Dates of Treatment: _____

Treatment Rendered: _____

#32 No Complications ~~Osteitis~~ Infection

Dates of Treatment: _____

Treatment Rendered: _____

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ACADEMIC VITA

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- President Freshman Award, Sophomore Sparks Award, and Evan Pugh Scholar Award
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ASSOCIATION MEMBERSHIPS/ACTIVITIES:

Scholars for Sharing the Journey International, Penn State

President and Founder, 8/11-Present

- Founded a club to provide support for the non-profit, Sharing the Journey International, by acquiring funds for medical supplies to aid communities in Guatemala
- Organized projects for students to get involved with orphanages and other child foundations in Guatemala.

Sharing the Journey International, Guatemala

Medical Assistant and Volunteer, 12/06-Present

- Responsibilities included helping patients, assisting physicians, and organizing medical supplies
- Provided humanitarian aid to communities in the form of food, water, and clothes.
- Recognized as an 'Honorary Citizen of San Pedro, Guatemala' by the First Lady of Guatemala.

THON, Penn State

Pediatric Cancer Research Fundraiser, 8/11-Present

- Largest student-run philanthropy in the world
- Involved in year-round efforts to raise funds

English Department, Penn State

English Teaching Assistant, 8/11-5/13

- Worked with a team of student leaders to create “Lector: A Virtual Book Club” for first year English students.

PROFESSIONAL EXPERIENCE:

Bristol Myers Squibb (BMS), New Brunswick, NJ

Co-op, Quality Operations-External Manufacturing Department, 1/13-6/13

- Worked as liaison between BMS and 14 contract companies to collect data and ensure BMS was in compliance with new European Medicines Agency regulations and ready for FDA inspection.
- Analyzed 16 products at varying dosages for quantity of heavy metal catalysts and reagents to meet FDA standards and to make BMS products safe for human use, thereby preserving company reputation.
- Led project to create and implement inventory systems to track and update quality documents in support of company success in future audits and inspections.
- Generated reports for change controls in order to present data and trends at monthly Quality Council meetings to validate that no significant issues needed further action.
- Took initiative to create files to detail processes for seamless transition to next co-op and earned unsolicited positive feedback from management team for thinking ahead and saving time and resources during transition.

Oral and Maxillofacial Surgeons, P.C., Doylestown, PA

Research Analyst for Lower Third Molar Removal Study, 5/12-8/12

- Designed quality improvement study to test effect of antibiotics on post-operative complications of lower third molar sites in effort to reduce costs for patients.
- Coordinated and communicated effectively with surgeons, nurses, and administrative staff across four different offices throughout the study, ensuring no data was lost.
- Analyzed data to determine statistical significance of study and recommended results for future journal publications to broaden recognition of practice.

Surgical Assistant, Summers 2010-2012

- Assessed and ensured patient satisfaction and compliance through post-operative care and acted as liaison between operation room and rest of office to provide optimal care.
- Maintained sterility of operation room and instruments to minimize transmission of diseases.

SKILLS:

Leadership, Analysis, Research, Communication, Project management, Mentoring, Multi-tasking, Team-Building, Flexibility, Persistence, Critical thinking, Problem resolution, Time management. Software: SAS, Stata, Minitab, Trackwise, SPSS.

OTHER TRAVEL EXPERIENCE:

International Scholar Laureate Program, National Society of College Scholars

Medical Delegation Scholar, China, 6/12

- Travelled to China in order to learn about the Chinese healthcare system and Traditional Chinese Medicine (TCM).

Biology 499A, Penn State

Coastal Field Ecology Student, Costa Rica, 12/11-1/12

- Travelled to Costa Rica for a Coastal Field Ecology course to learn about tropical biodiversity.

Other Countries Visited

- Guatemala, France, England, Switzerland, Germany, Italy, Hungary, Austria, Belgium, Czech Republic.

OTHER RESEARCH EXPERIENCE:

General and Organic Chemistry Labs, Penn State

Student

- Familiar with micropipetting, titrations, spectroscopy, chromatography (TLC, liquid, gas), distillation, purifications, and crystallization.

General Biology Labs, Penn State

Student

- Familiar with PCR, gel electrophoresis, microscopy, cell counting, and cell staining.