

THE EFFECT OF INTRAWOUND VANCOMYCIN POWDER ON SURGICAL SITE  
INFECTIONS IN POSTERIOR INSTRUMENTED SPINAL ARTHRODESES

BY

AARON HELLER

Submitted to the graduate degree program in Clinical Research and the Graduate Faculty of the  
University of Kansas in partial fulfillment of the requirements for the degree of Master of  
Science.

---

Chairperson Sue-Min Lai, PhD, MS, MBA

---

Terence McIff, PhD, MBA

---

Douglas Burton, MD

Date Defended: 6/20/2012

The Thesis Committee for AARON HELLER

certifies that this is the approved version of the following thesis:

THE EFFECT OF INTRAWOUND VANCOMYCIN POWDER ON SURGICAL SITE  
INFECTIONS IN POSTERIOR INSTRUMENTED SPINAL ARTHRODESES

---

Chairperson Sue-Min Lai, PhD, MS, MBA

Date approved: 7/22/2012

## **Abstract**

**Summary:** We reviewed 371 consecutive patients from Oct. 2008 to Sept. 2011 who underwent posterior instrumented spinal arthrodesis and received intrawound vancomycin powder prior to closure and compared their acute, deep infection rate to 371 consecutive patients from Oct. 2008 to Apr. 2005 who underwent posterior spinal instrumented arthrodesis and did not receive intrawound vancomycin. We found the use of vancomycin powder decreased the acute, deep *Staphylococcus* infection rate from 2.05% to 0 (p=0.008). Vancomycin powder is an effective way to decrease acute, deep *S. aureus* infections following spine surgery.

**Introduction:** Surgical site infection is a serious complication for patients undergoing instrumented spinal surgery. *Staphylococcus aureus* is the most common causative agent associated with post-op wound infections. Recent studies have reported a decreased infection rate with intrawound vancomycin use in spine surgeries. We sought to determine if intrawound vancomycin would decrease the rates of acute, deep *S. aureus* infections in our posterior instrumented spinal arthrodesis patients.

**Methods:** This is a historical cohort study. All procedures were performed by a single surgeon. 371 consecutive patients undergoing posterior instrumented spinal arthrodesis received intrawound vancomycin in addition to standard antimicrobial prophylaxis beginning in Oct. 2008 through Sept. 2011 (Vanco cohort). We compared them to 371 consecutive patients from Oct. 2008 to Apr. 2005 who did not receive intrawound vancomycin (Historical cohort). We excluded any superficial infection (above the lumbosacral fascia) or any infection occurring after 90 days. Infection rates were analyzed with Fisher exact test.

**Results:** We found 8 (2.4%) acute, deep infections in the Historical cohort: 1 *Enterococcus* and 7 (2.05%) *Staphylococcus* (6 of which were *S. aureus*). We found 4 (1.2%) acute, deep infections

in the Vanco group, none of which were *S. aureus*. There were 2 *E.coli*, 1 *Klebsiella oxytoca*, and 1 anaerobic *Streptococcus*. The difference in total acute, deep infection rate between the Historical cohort and Vanco cohort was not significant ( $p= 0.262$ ), but the decrease in *Staphylococcus* infection rate in the Vanco group was significant ( $p=0.008$ ).

**Conclusion:** Intrawound vancomycin powder has decreased the rate of acute, deep *Staphylococcus* infections in our posterior instrumented spinal fusion patient population from 2.05% to 0. Our Vanco cohort was significantly older but otherwise similar in terms of risk factors to the Historical cohort, though had fewer infections. This work is adding to the growing body of evidence in support of this effective adjuvant to standard antimicrobial prophylaxis.

## **Acknowledgements**

I would like to thank Dr. Terence McIff for being my mentor this year. It has been a rare pleasure to work with him and his lab. I would also like to thank Dr. Douglas Burton for giving me the opportunity to work with his patient data, and for allowing me to observe him in the operating room. The Department of Orthopedic Surgery at KUMC has my gratitude as well; especially Michelle Settle, Stephanie Robinson, Jan Brunks, and Cathy Mayfield.

Thank you to all the members of the Kansas University of Medical Center Frontiers: The Heartland Institute for Clinical and Translational Research for their help and support. Especially I am grateful to Dr. Ed Ellerbeck, Dr. Theresa Shireman, and Dr. Sue-Min Lai of the Department of Preventive Medicine and Public Health for their guidance and support this year. I would also like to thank Anita Macan and Marilyn Painter for finding the answers to all of my questions.

I am always thankful for my wife's support. Thank you, Hannah.

## Table of Contents

<b>Abstract</b> .....	iii
<b>Acknowledgments</b> .....	v
<b>Table of Contents</b> .....	vi
<b>List of Tables and Figures</b> .....	vii
<b>Background</b>	
Incidence and cost of surgical site infections .....	1
Risk factors for surgical site infections in spinal surgery.....	3
Current antimicrobial prophylaxis for surgical site infections .....	4
New methods for antimicrobial prophylaxis .....	4
Study purpose .....	6
<b>Materials and Methods</b>	
Study design.....	6
Identification of surgical site infections.....	8
Statistical analysis.....	8
<b>Results</b> .....	9
<b>Discussion</b> .....	17
<b>Conclusion</b> .....	22
<b>References</b> .....	23
<b>Appendices</b>	
Appendix A: Variable definitions and chart locations.....	28
Appendix B: Infections data. ....	34

## List of Tables and Figures

### Tables

Table 1 – Comparison of demographic and hospitalization characteristics for patients receiving and not receiving intrawound vancomycin .....	10
Table 2 – Comparison of operative characteristics for patients receiving and not receiving intrawound vancomycin .....	12
Table 3 – Infections in vancomycin and historical control cohorts.....	13
Table 4 – Comparison of demographic and hospitalization characteristics for patients having and not having surgical site infections .....	14
Table 5 – Comparison of operative characteristics for patients having and not having surgical site infections.....	15
Table 6 – Multi-variable logistic regression analysis of any surgical site infection .....	16

### Figures

Figure 1 – Type of procedures performed by study group per year.....	7
--	---

## **Background**

### *Incidence and cost of surgical site infections*

Surgical site infections (SSIs) are a common concern among the surgical specialties. They dramatically increase the cost associated with the surgical procedure and negatively affect patient outcomes. There are approximately 500,000 SSIs annually in the United States<sup>1</sup>. Klevens et al, using 2002 data from the National Nosocomial Infections Surveillance System, National Hospital Discharge Survey, and American Hospital Association reported that 20% of the 1.7 million hospital acquired infections were SSIs<sup>2</sup>. They found that approximately 2% of all operations result in a SSI<sup>2</sup>. Surgical site infections have been reported to increase the patient's hospital stay by nearly ten days<sup>3</sup>, and SSIs are associated with increased mortality risk and financial costs<sup>4</sup>. Indeed approximately 77% of deaths in those patients with a SSI are attributed to the infection<sup>5</sup>, and nationally the total annual cost of SSIs is estimated to be between \$1 billion and \$10 billion<sup>6,7</sup>.

Similar findings have been reported pertaining to orthopedic procedures specifically. Sampling the Agency of Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project dataset from 2005, de Lissovoy et al used a conservative approach and targeted a single SSI ICD9-CM code<sup>3</sup>. They found that compared to non-SSI controls, a single orthopedic SSI increased the length of the hospital stay by an average of 9.5 days and added an average additional \$15,129 to the cost<sup>3</sup>. The incidence of surgical site infections in spinal surgeries has been reported nationally to be approximately 1.2% for laminectomies and 2.4% for arthrodeses<sup>8</sup>. Surgical site infection rates vary at individual centers depending on surgery type<sup>9</sup>.

The most common cause of an orthopedic SSI is *Staphylococcus aureus* followed by coagulase-negative staphylococci<sup>6,10</sup>. These gram-positive cocci from the patient's own skin flora are the leading source of bacterial inoculums<sup>6,11</sup>. Noskin et al, using the AHRQ Nationwide



Inpatient Sample conducted a retrospective analysis of hospital stays for 2003<sup>12</sup>. Specifically targeting ICD9-CM codes for *S. aureus*, they reported that inpatient stays involving orthopedic surgery had *S. aureus* infection rate of 1.8%. The additional mortality risk and cost associated with such an infection was 2.5% and \$34,202 respectively. From 1998 to 2003 there was a 53% increase in the prevalence of *S. aureus* infections in orthopedic surgery<sup>12</sup>. Total annual economic burden of *S. aureus* SSIs for inpatient orthopedic surgery was estimated to be \$1.5 billion in 2003<sup>12</sup>.

Unfortunately, methicillin-resistant *Staphylococcus aureus* (MRSA) SSIs have recently been shown to have worse health outcomes and higher health service costs compared to methicillin-sensitive *Staphylococcus aureus* (MSSA). In a multi-center matched-outcomes study, Anderson et al<sup>13</sup> compared cardiothoracic, neurosurgical, and orthopedic surgery patients with a MRSA SSI to those with a MSSA SSI or no SSI from 1998 to 2003. They assessed hospital readmissions, mortality, total hospital days, and hospital charges (inflated to 2003 dollars) associated with MRSA SSIs compared to uninfected matched controls and to unmatched MSSA controls. They reported patients with a MRSA SSI were 30 times more likely to have a hospital readmission, and seven times more likely to die within the 90 days post-operative period compared to those patients without an SSI<sup>13</sup>. These MRSA SSI patients had more than \$60,000 of additional hospital charges, and had 16 more days hospitalized compared to uninfected patients. Compared to MSSA SSI, a MRSA SSI was associated with an additional six days of hospitalization and more than \$23,000 of additional hospital charges. They report that preventing a single SSI caused by MRSA can save hospitals \$61,000<sup>13</sup>. A similar increase in mortality risk associated with MRSA bacteremia compared to MSSA was observed in a 2003 meta-analysis by Cosgrove et al<sup>14</sup>.

### *Risk factors for surgical site infections in spinal surgery*

As a result of the significant costs associated with SSIs and specifically those caused by MRSA, infection prevention is a very attractive area of research. Prevention efforts have been two fold; 1) identify and reduce the risk factors associated with SSI and 2) develop prophylactic antimicrobial treatments for SSI. Risk factors for SSI can be classified as preoperative factors, operative factors, and postoperative factors.

Preoperative risk factors for SSI after spinal surgery include history of inflammatory arthritis<sup>15</sup>, diabetes<sup>15,16</sup>, past SSIs<sup>15</sup>, cigarette smoking<sup>17</sup>, immunosuppressant drug use<sup>16</sup>, obesity<sup>16</sup>, serum glucose greater than 125 mg/dL<sup>18</sup>, preoperative shaving with a razor<sup>5</sup>, and nasal colonization with *S. aureus*<sup>19</sup>. Operative risk factors for SSI after spinal surgery include extended length of surgery<sup>15,16,20</sup>, estimated blood loss (EBL) greater than one liter<sup>15,16</sup>, a posterior surgical approach<sup>15,21</sup>, instrumentation<sup>22</sup>, sub-optimal timing of prophylactic antibiotics<sup>18</sup>, two or more residents participating in the surgery<sup>18</sup>, poor homeostasis<sup>5</sup>, and surgical case order<sup>23</sup>. Blood transfusions have been associated with SSIs, but not necessarily linked as a risk factor<sup>20</sup>. Postoperative risk factors include long duration of immobility<sup>16</sup>, use of total-contact braces<sup>16</sup>, and serum glucose greater than 200 mg/dL<sup>18</sup>.

The CDC released a guideline for recommended SSI preventative measures in 1999<sup>5</sup>. According to the guidelines, risk factors that can be modified to prevent SSI include glucose control<sup>5,10,24</sup>, diabetes management<sup>5,10,16</sup>, smoking cessation<sup>5,10,16</sup>, pre-op treatment for unrelated infections (e.g. UTIs)<sup>10,16</sup>, proper hair removal (clippers or depilatory, not razors)<sup>5,10,16</sup>, minimizing operating room traffic flow<sup>5,16</sup>, and proper operative aseptic technique<sup>5,16</sup>.

### *Current antimicrobial prophylaxis for surgical site infections*

Antimicrobial prophylaxis (AMP) is currently recommended for high risk orthopedic surgery, including spinal instrumentation, where infection could result in catastrophic outcomes<sup>5,16</sup>. Standard AMP for spinal orthopedic surgery at Kansas University Medical Center includes 20 mg/kg body weight of Ancef given intravenously within one hour prior to incision and with repeat dosing every four hours during surgery. Post-operatively, patients are given 1 g of Ancef intravenously every eight hours for 24 hours. If the patient is a known MRSA carrier or is allergic to Ancef, 1 g of vancomycin given intravenously can be substituted, as has been done in previous studies<sup>10,16,24-27</sup>. Additionally, all patients are given chlorhexidine towels and instructed to wash with them the night before and the morning of surgery. The operative location is prepped with alcohol, betadine wash and betadine paint prior to incision.

Risk factor reduction protocols and proper AMP therapy are generally part of the surgical standard of care at most facilities. However, maintaining these preventive measures has not resulted in a reduction in SSI incidence in the past decade, and refinement of these techniques is unlikely to cause a significant decrease<sup>20</sup>. Finding new antimicrobial prophylactic treatments for SSIs is now imperative for protecting our patients' quality of life post-operatively and for controlling health care costs.

### *New methods for antimicrobial prophylaxis*

The main AMP techniques being researched and reported on include preoperative bacteria decolonization with chlorhexidine baths<sup>10,16</sup>, routine screening and eradication of intranasal MRSA/MSSA flora<sup>10,16</sup>, and topical application of vancomycin powder to the surgical

wound before closure<sup>25,27,28</sup>. Additional AMP benefit has been demonstrated with soaking the wound with dilute-betadine for three minutes prior to wound closure<sup>29</sup>.

Bathing with chlorhexidine products is not currently recommended for SSI prevention<sup>10,16</sup>. Although chlorhexidine baths, with simultaneous intranasal bacterial eradication with mupirocin, have recently been shown to be effective in preventing SSIs in elective total joint arthroplasty<sup>30</sup>, they have not been shown to be efficacious alone<sup>31</sup>. If chlorhexidine baths are proven effective, computer models have predicted that this will be a cost effective method to prevent SSIs<sup>32</sup>.

Universal screening and eradication of intranasal *S. aureus* with mupirocin is not currently recommended for SSI prevention<sup>10,16</sup>. It was not shown to decrease the rate of SSIs<sup>33,34</sup>. However, it was shown to decrease the rate of SSIs in people colonized with *S. aureus*<sup>33</sup>. Intranasal bacterial eradication with mupirocin has also been shown to be effective in specific surgical populations, like orthopedics<sup>35</sup>. Both chlorhexidine baths and intranasal mupirocin are limited to elective surgery and require patient compliance. Resistance to mupirocin therapy has been demonstrated, which casts doubt on this treatments long-term efficacy potential<sup>6,36</sup>.

Routine use of intravenous vancomycin for SSI prophylaxis is not recommended<sup>10,24</sup>. It has not been shown to be any more effective than using intravenous cephalosporins (e.g. Ancef) in preventing SSIs<sup>37</sup>, nor has it been shown to be any more effective in preventing MRSA SSIs<sup>38</sup>. Recently, administering vancomycin powder locally, directly to the wound, has been shown to decrease SSI rates following spinal surgery procedures<sup>20,22,24</sup>, and this has been shown effective in emergent settings, such as trauma, where pre-operative decolonization would not be possible<sup>22</sup>. This intrawound vancomycin powder AMP appears to have the greatest potential to prevent SSIs in spinal surgery. However, only one of these studies was in a diverse spinal

surgery population<sup>20</sup>, and more studies are needed to confirm the efficacy of intrawound vancomycin powder to prevent surgical site infections in spinal surgeries.

### *Study purpose*

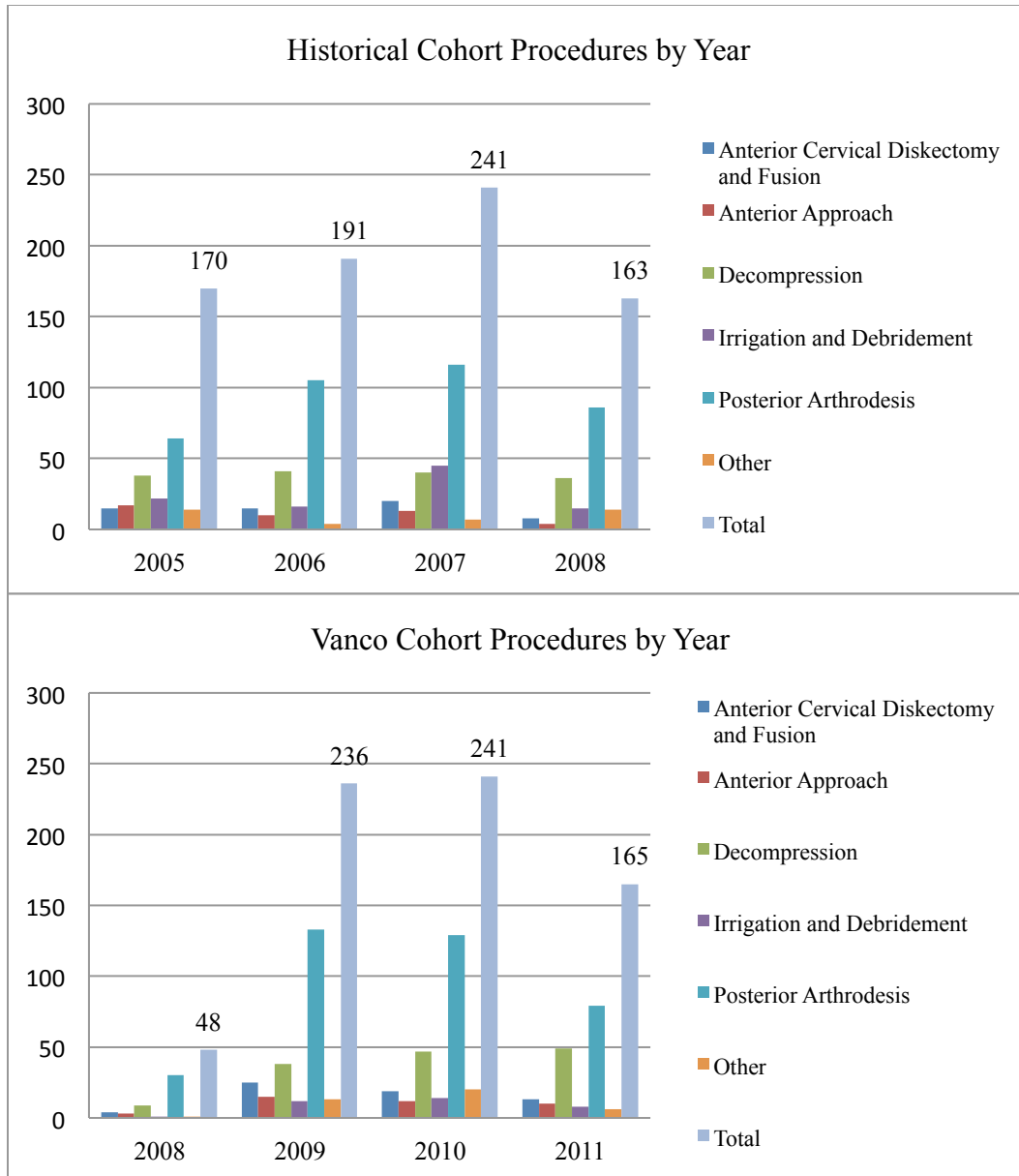
Given the high costs associated with surgical site infections in terms of mortality risk and health services costs and because SSI rates are not decreasing even with increased surveillance and standard AMP measures, new prophylactic measures need to be developed. Of those prophylactic measures currently reported, intrawound vancomycin powder appears to be the most successful at preventing surgical site infections in posterior instrumented spinal surgeries. The purpose of this study was to determine if the use of intrawound vancomycin powder has decreased the rate of acute surgical site infections in posterior instrumented spinal arthrodesis surgeries at the University of Kansas Medical Center.

## **Methods**

### *Study design*

This was a historical cohort study design and was approved by the Human Subjects Committee of the University of Kansas Medical Center. A single surgeon at the University of Kansas Medical Center performed all procedures. Beginning October of 2008 all patients undergoing posterior instrumented spinal arthrodesis received between 0.5 g to 2 g of vancomycin powder applied directly to the wound just prior to closure, in addition to standard AMP. The vancomycin powder dose was based on wound size at the discretion of the surgeon. There were 690 consecutive spinal surgeries performed between October 2008 and September 2011 (Fig. 1). Of these 690 surgeries, 371 of them were posterior instrumented spinal arthrodeses, and these became our Vanco cohort. To identify our Historical control cohort, which did not receive intrawound vancomycin powder, we identified 371 consecutive posterior

instrumented arthrodesis surgeries immediately prior to October 2008. In order to find these 371 surgeries, we examined 765 consecutive spinal surgeries from April 2005 to October of 2008. To be included in our analysis patients had to have a minimum of 90 days of follow-up or a SSI occurring within 90 days of operation. Figure 1 displays the breakdown of surgical procedures performed by year.



**Figure 1: Type of procedures performed by study group per year**

Demographic and operative data were gathered for all patients; including, age, gender, race, BMI, primary insurance, American Society of Anesthesiologists (ASA) grade, prior history of SSI, current cigarette use, any alcohol use, illicit drug use, previous spinal surgeries at the same spinal level, length of hospitalization, discharge location, admitting diagnoses, blood transfusions, number of residents participating in surgery, estimated blood loss, length of surgery, number of levels instrumented and fused, use of an associated anterior approach, a decompression or pelvic fixation, hair removal method, hemovac drain use, co-morbidities, intrawound vancomycin use and surgical site infections. For a complete listing of variable definitions and chart locations see appendix A.

#### *Identification of surgical site infections*

Acute SSI was our primary outcome. We defined an SSI as occurring within 90 days following the operation, requiring an additional operation (i.e. an irrigation and debridement) and having positive wound cultures. Infections were further subdivided into superficial (occurring above the lumbosacral fascia) or deep (beneath the lumbosacral fascia) based on the microbiology wound culture reports and operative reports. For all patients having an SSI, the number of days post-op that the SSI was diagnosed, number of operations needed to treat the SSI, wound vacuum assisted closure use for the SSI, and number of additional days hospitalized were recorded.

#### *Statistical analysis*

Continuous data between the Vanco cohort and Historical control cohort were compared using the T-test and categorical data were compared using chi-square test or Fisher's exact test. The rate of SSIs was compared between the Vanco cohort and the Historical control cohort using chi-square test. Similarly, we compared the rates of deep infections, deep *Staphylococcus*

infections and deep *S. aureus* infections between the two groups. If expected cell counts were five or fewer we used Fisher's exact test.

Univariate analysis was then used to compare those patients who had a SSI and those who did not. We identified those variables that were significantly associated with having any SSI, superficial or deep, ( $p < 0.10$ ) and those that were clinically relevant and fit a multiple variable logistic regression model. We then did a post-hoc power analysis to assess the power of this study to detect a significant decrease in total infections between our study groups. Subjects with missing data points were excluded from analysis of that data. We used two-tailed tests for all analyses with a significance level set at  $p < 0.05$ . All data analysis was performed with SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

## **Results**

We had 92% of the 371 cases with 90 days or greater follow-up in both study groups (N=342 for Vanco cohort and N=341 for Historical cohort). One of the patients in the Historical cohort expired during the operative hospital stay due to a pulmonary embolism, some of the other patients were also deceased at the time of data abstraction but actual death dates were not documented. Most patients without the required 90 days of follow-up were listed in the records as having not kept their follow-up appointment, but without further explanation. Some of the rest of the patients were without follow-up unknown reasons. In the Vanco cohort a small number of the patients were not scheduled back for their follow-up until after the data abstraction period. So while they very well may have complete follow-up, we were not able to capture it.

The demographic and operative data are listed in Table 1 and Table 2 respectively. The Vanco cohort was significantly older with a mean age of 55.3 (standard deviation of 19.1 years) compared to the historical cohort with a mean age of 49.1 (standard deviation of 20.9 years)



( $p < 0.0001$ ). The Vanco cohort had a higher number of patients with hypertension at 56.7% of patients compared to 41.9% in the Historical cohort ( $p < 0.0001$ ). Largely the demographic and hospital stay data were similar across the two study groups.

Patient Characteristics	Vanco Cohort (N= 342)	Historical Cohort (N=341)	T-test or Chi-square
Age, mean (SD)	55.3 (19.1)	49.1 (20.9)	$p < 0.0001$
Gender (%)			$p = 0.302$
Male	45.3	49.3	
Female	54.7	50.7	
Race (%)			$p = 0.101$
Caucasian	85.7	87.7	
African-American	8.2	7.0	
Hispanic	1.8	3.5	
Other	4.39	1.76	
Adult Body Mass Index, mean (SD) <sup>1</sup>	31.6 (7.3)	30.7 (7.0)	$p = 0.130$
Adult BMI group (%) <sup>1</sup>			$p = 0.048$
Normal ( $\leq 25$ kg/m <sup>2</sup> )	15.9	24.4	
Overweight ( $> 25$ and $< 30$ kg/m <sup>2</sup> )	31.1	24.4	
Obese ( $\geq 30$ and $\leq 35$ kg/m <sup>2</sup> )	25.6	25.4	
Morbidly obese ( $> 35$ kg/m <sup>2</sup> )	27.5	25.8	
Co-morbidities (%)			
Diabetes <sup>2</sup>	18.1	15.0	$p = 0.279$
Cardiovascular Disease <sup>2</sup>	17.5	13.3	$p = 0.123$
Respiratory Disease <sup>2</sup>	17.5	14.5	$p = 0.272$
Hypertension <sup>2</sup>	56.7	41.9	$p = 0.0001$
Mean ASA Grade (SD) <sup>3</sup>	2.6 (0.6)	2.5 (0.6)	$p = 0.067$
History of Surgical Site Infection (%) <sup>4</sup>	1.8	3.9	$p = 0.098$
Current Cigarette Use at Time of Surgery (%) <sup>4</sup>	5.6	6.5	$p = 0.602$
Any Alcohol Use (%) <sup>4</sup>	37.1	24.9	$p < 0.001$
Mean Number of Days Hospitalized Until Discharge or SSI (SD)	5.9 (4.5)	6.32 (4.3)	$p = 0.350$
Insurance Type (%) <sup>2</sup>			$p = 0.002$
Commercial	44.4	44.7	
Medicare	35.7	26.5	
Medicaid	5.9	13.5	
Workmen's Comp	14.0	15.3	
Discharge Location (%)			$p = 0.077$
Home	83.3	88.3	
Inpatient Rehabilitation	10.8	9.1	
Skilled Nursing Facility	5.9	2.6	

<sup>1</sup>Historical cohort N=283, Vanco cohort N=309, <sup>2</sup>Historical cohort N=339, <sup>3</sup>Historical cohort N=333, <sup>4</sup>Historical cohort N=338

In the Vanco cohort 53.2% of the patients had a diagnosis of spinal stenosis compared to 43.7% in the historical cohort, which was significantly larger ( $p=0.013$ ), but the groups were similar in terms of other diagnoses. More of the patients in the Vanco cohort had had a previous surgery at the spinal level treated in this study (50.0%) compared to the Historical cohort (39.8%), and this was statistically significant ( $p=0.007$ ). Almost all of the patients in the Vanco cohort had hair removal with electric clippers (98.8%) with the remainder having no hair removal (1.2%) and none of the patients had hair removed with a razor, however the historical cohort had 1.5% with razor hair removal, only 92.5% with electric clippers and the remaining 6.0% had no hair removal. Differences among hair removal types were statistically significant ( $p<0.001$ ).

Table 2: Comparison of Operative Characteristics for Patients Receiving and Not Receiving Intrawound Vancomycin			
Patient Characteristics	Vanco Cohort (N= 342)	Historical Cohort (N=341)	T-test or Chi-square
Diagnosis (%)			
Spinal Stenosis	53.2	43.7	p=0.013
Spondylolisthesis	39.5	44.9	p=0.154
Degenerative Disc Disease/Herniated Disc	15.5	16.7	p=0.665
Scoliosis	14.9	11.1	p=0.144
Pseudoarthrosis	12.0	10.6	p=0.554
Fracture	2.6	4.4	p=0.210
Cancer	0.9	1.8	p=0.340
Other	29.8	23.2	p=0.049
Blood Transfusion (%) <sup>1</sup>	30.1	33.0	p=0.414
Mean Number of Orthopedic Residents Involved in the Surgery (SD)	0.81 (0.43)	0.96 (0.38)	p<0.0001
Mean Estimated Blood Loss in mL (SD) <sup>2</sup>	635 (818)	616 (700)	p=0.747
Mean Length of Surgery in minutes (SD) <sup>3</sup>	298 (125)	312 (129)	p=0.158
Mean Number of Levels Instrumented (SD)	3.8 (3.8)	3.6 (4.1)	p=0.607
Mean Number of Levels Fused (SD)	3.3 (3.6)	3.3 (3.9)	p=0.973
Associated Anterior Approach (%)	20.2	23.8	p=0.259
Decompression (%)	81.9	76.3	p=0.071
Pelvic Fixation (%)	15.2	10.6	p=0.070
Operative Levels (%)			p=0.237
Cervical	7.0	5.6	
Thoracic	1.5	3.8	
Thoraco-lumbar	24.0	22.9	
Lumbar	67.5	67.7	
Previous Surgery (%) <sup>4</sup>	50.0	39.8	p=0.007
Hemovac Drain Used (%)	93.3	91.8	p=0.460
Hair Removal (%) <sup>5</sup>			p<0.001
Clippers	98.8	92.5	
Razor	0.0	1.5	
None	1.2	6.0	
<sup>1</sup> Historical cohort N=336, Vanco cohort N=341, <sup>2</sup> Historical cohort N=332, Vanco cohort N=332,			
<sup>3</sup> Historical cohort N=334, Vanco cohort N=340, <sup>4</sup> Historical cohort N=337,			
<sup>5</sup> Historical cohort N=333, Vanco cohort N=341			

The rates of infection are listed in Table 3. We found an approximately 50% reduction in the rate of total infections in the Vanco cohort (2.1%) compared to the Historical cohort (4.4%), however this was not quite statistically significant (p=0.082). Similarly, there was a 50% reduction in deep infections in the Vanco cohort (1.2%) compared to the Historical cohort

(2.4%), and this was not statistically significant ( $p=0.262$ ). None of the deep infections in the Vanco cohort cultured *Staphylococcus* from the wounds, whereas 7 of the deep infections in the Historical cohort did culture positive for MSSA, MRSA or coagulase-negative *Staphylococcus*, for a deep *Staphylococcus* infection rate of 2.1%. This decrease in deep *Staphylococcus* infections was statistically significant ( $p=0.008$ ). For a complete listing of bacteria cultured from the infections see appendix B. There were no adverse events associated with intrawound vancomycin powder use.

Infections	Vanco Cohort (N= 342)	Historical Cohort (N=341)	Chi-square/Fisher Exact
Any infection, number (%)	7 (2.1)	15 (4.4)	$p=0.082$
Deep infection, number (%)	4 (1.2)	8 (2.4)	$p=0.262$
Deep <i>Staphylococcus</i> <sup>1</sup> , number (%)	0	7 (2.05)	$p=0.008$
Deep <i>S. aureus</i> only, number (%)	0	6 (1.76)	$p=0.014$

<sup>1</sup>Includes *S. aureus* and *S. epidermidis*

When comparing those patients that had an infection (N=22) to those patients that did not have an infection (N=661), we found that those patients who developed a SSI had higher average ASA grades (2.9 compared to 2.5,  $p=0.007$ ), a higher rate of blood transfusions (57.1% compared 30.8%,  $p=0.010$ ), higher average length of surgery (366 minutes compared to 303 minutes,  $p=0.024$ ), higher rates of fracture diagnoses (18.2% compared to 3.0%,  $p=0.006$ ), and a higher rate of having a past SSI (18.2% compared to 2.3%,  $p=0.002$ ). Differences in demographic and operative characteristics between those patients developing a SSI and those not developing a SSI are listed in Tables 4 and 5 respectively.

Table 4: Comparison of Demographic and Hospitalization Characteristics for Patients With and Without Infection

Patient Characteristics	Non Infection (N= 661)	Infection (N=22)	T-test or Chi-square
Age, mean (SD)	52.3 (20.2)	48.8 (21.9)	p=0.419
Gender (%)			p=0.861
Male	47.4	45.5	
Female	52.7	54.6	
Race (%)			p=0.723
Caucasian	86.5	90.9	
African-American	7.7	4.6	
Hispanic	2.6	4.6	
Other	3.18	0	
Adult Body Mass Index, mean (SD) <sup>1</sup>	31.2 (7.2)	31.6 (8.4)	p=0.802
Adult BMI group (%) <sup>1</sup>			p=0.269
Normal ( $\leq 25$ kg/m <sup>2</sup> )	19.7	27.8	
Overweight ( $>25$ and $<30$ kg/m <sup>2</sup> )	28.4	11.1	
Obese ( $\geq 30$ and $\leq 35$ kg/m <sup>2</sup> )	25.6	22.2	
Morbidly obese ( $>35$ kg/m <sup>2</sup> )	26.3	38.9	
Co-morbidities (%)			
Diabetes <sup>2</sup>	16.2	27.3	p=0.237
Cardiovascular Disease <sup>2</sup>	15.6	1.9	p=0.556
Respiratory Disease <sup>2</sup>	16.1	13.6	p=1.000
Hypertension <sup>2</sup>	54.6	49.2	p=0.620
Mean ASA Grade (SD) <sup>3</sup>	2.5 (0.6)	2.9 (0.5)	p=0.007
History of Surgical Site Infection (%) <sup>4</sup>	2.3	18.2	p=0.002
Current Cigarette Use at Time of Surgery (%) <sup>4</sup>	6.1	4.6	p=1.000
Alcohol Use (%) <sup>4</sup>	31.5	18.2	p=0.244
Mean Number of Days Hospitalized Until Discharge or SSI (SD)	6.0 (4.4)	7.7 (4.4)	p=0.072
Insurance Type (%) <sup>5</sup>			p=0.726
Commercial	44.9	36.4	
Medicare	30.9	36.4	
Medicaid	9.6	13.6	
Workmen's Comp	14.7	13.6	
Discharge Location (%)			p=0.083
Home	86.1	77.3	
Inpatient Rehabilitation	10.0	9.1	
Skilled Nursing Facility	3.9	13.6	

<sup>1</sup>No infection group N=574, Infection group N=18, <sup>2</sup>No infection group N=659  
<sup>3</sup>No infection group N=654, Infection group N=21, <sup>4</sup>No infection group N=658  
<sup>5</sup>No infection group N=660

Table 5: Comparison of Operative Characteristics for Patients With and Without Infection				
Patient Characteristics		Non Infection (N= 661)	Infection (N=22)	T-test or Chi-square
Diagnosis (%)				
	Spinal Stenosis	48.9	36.4	p=0.248
	Spondylolisthesis	42.4	36.4	p=0.575
	Degenerative Disc Disease/Herniated Disc	16.3	9.1	p=0.556
	Scoliosis	12.9	18.2	p=0.514
	Pseudoarthrosis	11.5	4.6	p=0.497
	Fracture	3.0	18.2	p=0.006
	Cancer	1.4	0.0	p=1.000
	Other	25.6	54.6	p=0.002
Blood Transfusion (%) <sup>1</sup>		30.8	57.1	p=0.010
Mean Number of Orthopedic Residents Involved in the Surgery (SD)		0.88 (0.4)	0.95 (0.2)	p=0.153
Mean Estimated Blood Loss in mL (SD) <sup>2</sup>		621 (764)	765 (674)	p=0.394
Mean Length of Surgery in minutes (SD) <sup>3</sup>		303 (126)	366 (147)	p=0.024
Mean Number of Levels Instrumented (SD)		3.6 (3.9)	5.5 (5.7)	p=0.134
Mean Number of Levels Fused (SD)		3.3 (3.7)	4.8 (5.2)	p=0.195
Associated Anterior Approach (%)		21.8	27.3	p=0.600
Decompression (%)		79.3	72.7	p=0.431
Pelvic Fixation (%)		12.1	36.4	p=0.004
Operative Levels (%)				p=0.115
	Cervical	6.4	4.6	
	Thoracic	2.7	0.0	
	Thoraco-lumbar	22.7	45.5	
	Lumbar	68.2	50.0	
Previous Surgery (%) <sup>4</sup>		44.6	54.6	p=0.356
Hemovac Drain Used (%)		92.4	95.5	p=1.000
Hair Removal (%) <sup>3</sup>				p=0.111
	Clippers	95.9	90.0	
	Razor	0.5	5.0	
	None	3.6	5.0	
Intrawound Vancomycin Use (%)		50.7	31.8	p=0.082

<sup>1</sup>No infection group N=657, Infection group N=21, <sup>2</sup>No infection group N=643, Infection group N=21  
<sup>3</sup>No infection group N=653, Infection group N=21, <sup>4</sup>No infection group N=657

In the multi-variable logistic regression model (N=673) we included intrawound vancomycin powder use, pelvic fixation, length of surgery, blood transfusion, diagnosis of fracture, discharge location, history of SSI, age and gender. Our model was significant (likelihood ratio chi-square = 35.2, p<0.001), and well fit (Hosmer-Lemeshow chi-square = 10.1, p=0.259). Regression results are displayed in Table 6. Intrawound vancomycin was negatively

associated with SSI (AOR= 0.479), however this was not significant (95% CI, 0.164-1.284; p=0.154). Operations that included a pelvic fixation (AOR= 4.194; 95% CI, 1.051-18.63; p=0.049), a diagnosis of fracture (AOR= 8.642; 95% CI, 1.865-35.81; p=0.004), an elevated ASA grade (AOR= 3.914; 95% CI, 1.324-13.975; p=0.021) or a discharge to a skilled nursing facility (AOR= 5.815; 95% CI, 1.084-25.666; p=0.025) had higher risk of developing a SSI.

Table 6: Multi-variable Logistic Regression Analysis of Any Surgical Site Infection					
Variable	Adjusted Odds Ratio			p-value	
	Estimate	95% CI			
Intrawound Vancomycin	0.479	0.164	1.284	0.154	
Pelvic Fixation	4.194	1.051	18.63	0.049	
Length of Surgery	1.001	0.996	1.005	0.662	
Blood Transfusion	0.515	0.122	1.998	0.349	
Diagnosis of Fracture	8.642	1.865	35.81	0.004	
Discharged to Inpatient Rehab	0.862	0.123	3.685	0.857	
Discharged to Skilled Nursing Facility	5.815	1.084	25.666	0.025	
History of Surgical Site Infection	4.244	0.718	19.145	0.077	
ASA Grade	3.914	1.324	13.975	0.021	

Model N=673, (21 with infections), Likelihood ratio chi-square= 35.2 (p<0.001), c-statistic= 0.804, and Hosmer-Lemeshow chi-square =10.1 (p=0.259)  
 Model included all variables listed as well as age and gender  
 ASA = American Society of Anesthesiologists

We used a power analysis for independent proportions to calculate the power of this study. Given a 4.4% rate of SSI for the Historical cohort and a 2.1% rate of SSI for the Vanco cohort, an alpha of 0.05 and 341 patients per group the power of our study was calculated to be 39.5%. The number of patients needed to reach a power of 80% is 932 per group. We would have to add over 500 additional cases per study group achieve a power of 80%.

## Discussion

The purpose of this study was to determine if the addition of intrawound vancomycin powder to the operative AMP regimen has decreased the rate of acute SSIs in our Vanco cohort compared to a Historical control cohort. We did not find a statistically significant decrease ( $p=0.082$ ) in the rate of total SSIs in the Vanco cohort (2.1%) compared to our Historical cohort (4.4%), because our study was underpowered at 39.5% to do so. Even so, we found a near 50% reduction in infections between the two groups and with a 91.8% chance that this finding is not random, this is certainly clinically significant.

Although our study was underpowered and the sample size was relatively small compared to recent national studies which have identified risk factors for SSI in spinal surgeries, our multiple-variable regression analysis identified pelvic fixation (AOR 4.19; 95% CI, 1.05-18.63), a fracture diagnosis (AOR 8.64; 95% CI, 1.87-35.81), discharge to a skilled nursing facility compared to being discharged home (AOR 5.82; 95% CI, 1.08-25.67) and ASA grade (AOR 3.91; 95% CI, 1.32-13.98) to be independent risk factors for developing a SSI. Length of surgery and having received a blood transfusion during or after the operation were included in the model but were not independently associated with increased infection risk after adjusting for the other variables. These two variables are likely inter-related with each other, as a longer surgery is likely to have greater blood loss which results in a blood transfusion.

Pelvic fixation is similarly associated with increased length of surgery and also blood transfusion, yet remained an independent risk factor with a four times greater risk for SSI in the adjusted model. Perry et al analyzed 238 posterior instrumented arthrodesis surgeries and identified operations with pelvic fixation as being a risk factor for SSI and postulated that using pelvic fixations extends the incision closer to the anus which predisposes for gastrointestinal bacterial infections<sup>39</sup>. Of those eight patients with pelvic fixation that developed a SSI in our



study population, only three of them developed enteric related bacterial infections, which may not support the incision-anus-proximity theory. However, those patients with pelvic fixation and SSI did have complicated diagnoses (neuromuscular scoliosis, Duchenne's muscular dystrophy, cerebral palsy, scoliosis, and fracture) and the severity of their diagnoses and the complexity of the operation to correct their deformities is likely responsible for their increased risk for SSIs. A multi-center retrospective study of 210 patients undergoing spinal surgery for neuromuscular scoliosis identified allograft use and mental retardation as risk factors for infection, but did not include pelvic fixation in their analysis<sup>40</sup>.

A diagnosis of fracture had an almost nine times higher risk of developing a SSI in our study. Our study included not only trauma fractures but also pathologic and osteoporotic fractures. Olsen et al identified fracture diagnosis as a risk factor for SSI in a univariate analysis of 2,316 patients undergoing laminectomy, discectomy and/or arthrodeses, but they did not report fracture as an independent risk factor in their multiple regression analysis<sup>18</sup>. Our findings are also supported by a case-series published by Rehtine et al that reported a SSI rate of 10% in 112 patients with lumbar and thoracic fractures treated with instrumentation which was higher than national average rates<sup>26</sup>.

The ASA grade is a measure of systemic disease and serves as a proxy for comorbidities and overall health in the patients undergoing surgery. American Society of Anesthesiologists grade of 3 or greater has previously been identified as a risk factor for SSI<sup>41</sup>, and this is reasonable given these patient's increased burden of disease. We also found that being diagnosed to a skilled nursing facility versus being discharged home was an independent risk factor for infection. Two explanations for this finding are suboptimal postoperative wound care at the skilled nursing facility or increased inherent risk in patients being discharged to the skilled

nursing facility. The later is more likely the case. Patients that are discharged to the skilled nursing facility instead of an inpatient rehab or to their home likely have a greater burden of illness and more comorbidities than those patients not going to skilled nursing facilities. This would agree with our finding that ASA grade is associated with increased risk for SSI.

Having a previous history of any SSI, orthopedic or otherwise, was associated with infection in the univariate analysis but not the adjusted analysis. According to a recent review by Pull ter Gunne et al, a prior history of SSI was associated with developing an SSI more often in the literature than not<sup>42</sup>. That this variable was not significantly associated with infection in our adjusted analysis (AOR 4.24; 95% CI, 0.718-19.145) is probably due to our study's sample size. Even so, this variable's association is an interesting finding because it is the only modifiable risk factor identified as significant in our study. While we cannot modify that these patients have previously had a SSI, we can modify how we approach prophylaxis for these patients and further research needs to be undertaken to determine how to treat this population prophylactically.

Intrawound vancomycin was the only other modifiable risk factor analyzed (AOR 0.479; 95% CI 0.164-1.284) but was not significantly associated with a decreased risk in SSI in the adjusted model. Although this study lacked sufficient power to detect a statistically significant difference in the total number of SSIs, we did find a statistically significant decrease in acute, deep *Staphylococcus* infections between our groups. There were seven such *S. aureus* or *S. epidermidis* infections (2.05%) in the Historical cohort compared to zero such infections in the Vanco cohort (p=0.008). This outcome was not analyzed with multiple logistic regression due to the small number of events.

Our results are similar to those published by Sweet et al last year, which is the most definitive work to date on the effectiveness of intrawound vancomycin powder use to prevent

SSIs in spine surgery. In their prospective cohort study, 911 of 1,732 consecutive posterior instrumented thoracic and lumbar spinal arthrodeses from 2000 to 2006 had 2 g of intrawound vancomycin powder added as prophylaxis<sup>25</sup>. They had a deep infection rate of 2.6% in the 821 patients not receiving the vancomycin powder compared to 0.2% in the group receiving the vancomycin powder<sup>25</sup>. The reduction was statistically significant ( $p < 0.0001$ ). Similar to our study they found 71% of their infections in the non-vancomycin group to be *Staphylococcus* compared to no deep *Staphylococcus* infections in the vancomycin group<sup>25</sup>.

O'Neill et al published a study on the effectiveness of intrawound vancomycin powder to prevent infections following spinal surgery in a trauma population<sup>27</sup>. They compared 54 control patients not receiving the vancomycin powder to 56 patients receiving the powder over a two year period<sup>27</sup>. They found seven infections (13%) in the group not receiving vancomycin and no infections in the vancomycin group ( $p = 0.02$ )<sup>27</sup>. Again these are similar findings to our study.

Finally, in a case series report, Molinari et al added 1 g of vancomycin powder to the operative site prior to closure in all of their spinal surgeries from 2005 to 2010<sup>43</sup>. They report a 0.99% rate of deep wound infections and suggested that their low rate of deep wound infections is associated with the use of vancomycin powder<sup>43</sup>. With the addition of our study to these previous three studies, adding vancomycin powder to the operative site is clearly associated with a reduced deep infection rate in instrumented spinal surgeries.

The exact mechanism by which vancomycin prevents infection when used in this manner is not fully understood, however Sweet et al also gathered prospective serum and surgical drain fluid levels of vancomycin from their study patients up to post-op day three and found that 80% of their patients receiving intrawound vancomycin had serum levels less than 0.6 µg/ml post-op day one<sup>25</sup>. Of the 20% of those patients that did have serum vancomycin levels greater than 0.6

µg/ml, the average level was 1.6 µg/ml and only 6% had detectable serum levels of vancomycin after post-op day one. However, the concentrations of vancomycin collected from the wound drain were 1,457 µg/ml on average on post-op day zero, and diminished over the next three days to an average of 128 µg/ml<sup>25</sup>. Sweet et al have shown that applying vancomycin powder to the surgical wound results in high doses of vancomycin in the surgical wound where prophylaxis is desired without appreciable systemic distribution of the antibiotic.

O'Neill et al have suggested the intrawound vancomycin powder is effective at preventing infection via a post-antibiotic effect (PAE)<sup>27</sup>. Gram-positive bacteria utilize a thick peptidoglycan (PG) cell wall as a main defense against hostile environments, including the human immune system. An integral part of the structure of the PG cell wall is the cross-linking of peptide chain subunits via transpeptidation. Vancomycin binds a precursor molecule in the extracellular space preventing PG synthesis and is bactericidal<sup>44</sup>. Vancomycin is concentration-independent, however, the PAE of the drug is concentration-dependent<sup>45</sup>. After being exposed to high concentrations of the drug the bacteria are inhibited even after the removal of the drug<sup>45</sup>. This PAE may partly explain the drug's effectiveness within the wound, as Sweet et al have shown concentrations extend well beyond the mean inhibitory concentration (MIC) for up to three days at least<sup>25</sup>. Delivering antibiotic locally is not a new concept in orthopedic surgery<sup>46,47</sup>, and is ideal because it decreases the systemic toxicities of IV drugs<sup>48</sup>; this is especially true with vancomycin, which is not readily absorbed. Further research is warranted to elucidate the exact mechanism by which vancomycin powder is preventing infection inside the wound.

Our study is limited in that it is retrospective and limited to data recorded in medical records. This study is dependent on the validity of that data. Although tobacco use is a possible risk factor for infection and other negative operative outcomes<sup>49</sup> we were not able to reliably

assess tobacco use in this study. All of Dr. Burton's elective procedures are required to be nicotine free before surgery, which accounts for the low smoking rates observed in this study. We were not able to assess the rate of smoking resumption following surgery; however, Dr. Burton has previously shown that up to 36% of his patients who have stopped smoking for surgery continue to cease smoking postoperatively at the one-year mark (personal communication, June 20, 2012). The strengths of this study are our relatively large sample size, consistency among operative characteristics between study groups, and the diversity of spinal procedures, diagnoses, and spinal levels included. All procedures are performed by a single surgeon, which limits variability within surgical technique. Although we did not use the CDC definitions for defining our infections, our definition required a positive tissue culture which is a less subjective definition.

There are many facets of intrawound vancomycin powder use that need to be further elucidated. As previously stated, the exact antimicrobial mechanisms of this mode of local administration of vancomycin are unknown and warrant further research. The benefits of using intrawound vancomycin powder to treat current spinal SSIs needs to be studied. Exact dosing optimization studies need to be undertaken to determine the proper amount of vancomycin powder to use. Finally, further research on how to best approach patients with a history of surgical site infections prior to spinal surgery is also necessary. This may be the only risk factor for SSI in our patient population that we can alter.

## **Conclusion**

In conclusion, while we did not find a statistically significant decrease in total deep infections, as Sweet et al<sup>25</sup> reported, we did find a statistically significant difference in deep *Staphylococcus* infections. *Staphylococcus* and *S. aureus* in particular are the most common

types of bacteria causing SSIs in posterior spinal surgery. The purpose of adding a gram positive covering antibiotic like vancyomycin to the prophylaxis regimen in posterior instrumented spinal arthrodeses would be to prevent *Staphylococcus* infection. This study shows that adding intrawound vancomycin powder to the prophylactic regimen accomplishes this.

## References

1. Martone WJ, Nichols RL. Recognition, Prevention, Surveillance, and Management of Surgical Site Infections: Introduction to the Problem and Symposium Overview. *Clinical Infectious Diseases*. Sept 2001;33(Supplement 2):S67-S68.
2. Klevens RM, Edwards JR, Richards CL, Jr., et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep*. 2007;122(2):160-166.
3. de Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: Incidence and impact on hospital utilization and treatment costs. *American Journal of Infection Control*. 2009;37(5):387-397.
4. Kathryn B. Kirkland MD, Briggs JPBSN, Sharon L. Trivette RN, William E. Wilkinson P, Daniel J. Sexton MD. The Impact of Surgical-Site Infections in the 1990s: Attributable Mortality, Excess Length of Hospitalization, and Extra Costs • *Infection Control and Hospital Epidemiology*. 1999;20(11):725-730.
5. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol*. Apr 1999;20(4):250-278; quiz 279-280.
6. Anderson DJ, Kaye KS. Staphylococcal surgical site infections. *Infect Dis Clin North Am*. Mar 2009;23(1):53-72.
7. Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with Staphylococcus aureus surgical site infection. *Clin Infect Dis*. Mar 2003;36(5):592-598.
8. Gaynes RP, Culver DH, Horan TC, et al. Surgical Site Infection (SSI) Rates in the United States, 1992–1998: The National Nosocomial Infections Surveillance System Basic SSI Risk Index. *Clinical Infectious Diseases*. Sept 2001;33(Supplement 2):S69-S77.
9. Olsen MA, Mayfield J, Laurysen C, et al. Risk factors for surgical site infection in spinal surgery. *J Neurosurg*. Mar 2003;98(2 Suppl):149-155.
10. Kirby JP, Mazuski JE. Prevention of surgical site infection. *Surg Clin North Am*. 2009;89(2):365-389, viii.
11. Altemeier WA, Culbertson WR, Hummel RP. Surgical considerations of endogenous infections--sources, types, and methods of control. *Surg Clin North Am*. Feb 1968;48(1):227-240.
12. Noskin GA, Rubin RJ, Schentag JJ, et al. National Trends in Staphylococcus aureus Infection Rates: Impact on Economic Burden and Mortality over a 6-Year Period (1998–2003). *Clinical Infectious Diseases*. Nov 2007 2007;45(9):1132-1140.
13. Anderson DJ, Kaye KS, Chen LF, et al. Clinical and financial outcomes due to methicillin resistant Staphylococcus aureus surgical site infection: a multi-center matched outcomes study. *PLoS One*. 2009;4(12):e8305.
14. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible Staphylococcus aureus bacteremia: a meta-analysis. *Clin Infect Dis*. Jan 2003;36(1):53-59.
15. Pull ter Gunne AF, Cohen DB. Incidence, prevalence, and analysis of risk factors for surgical site infection following adult spinal surgery. *Spine (Phila Pa 1976)*. Jun 2009;34(13):1422-1428.

16. Massie JB, Heller JG, Abitbol JJ, McPherson D, Garfin SR. Postoperative posterior spinal wound infections. *Clin Orthop Relat Res*. Nov 1992(284):99-108.
17. Thalgott JS, Cotler HB, Sasso RC, LaRocca H, Gardner V. Postoperative infections in spinal implants. Classification and analysis--a multicenter study. *Spine (Phila Pa 1976)*. Aug 1991;16(8):981-984.
18. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*. Jan 2008;90(1):62-69.
19. Kalmeijer MDM, Nieuwland-Bollen EvICP, Bogaers-Hofman DICP, Baere GAJdMD, Kluytmans JAJWP. Nasal Carriage of Staphylococcus aureus Is a Major Risk Factor for Surgical-Site Infections in Orthopedic Surgery • *Infection Control and Hospital Epidemiology*. 2000;21(5):319-323.
20. Campbell Jr DA, Henderson WG, Englesbe MJ, et al. Surgical Site Infection Prevention: The Importance of Operative Duration and Blood Transfusion--Results of the First American College of Surgeons-National Surgical Quality Improvement Program Best Practices Initiative. *Journal of the American College of Surgeons*. 2008;207(6):810-820.
21. Levi AD, Dickman CA, Sonntag VK. Management of postoperative infections after spinal instrumentation. *J Neurosurg*. Jun 1997;86(6):975-980.
22. Pull ter Gunne AF, van Laarhoven CJ, Cohen DB. Incidence of surgical site infection following adult spinal deformity surgery: an analysis of patient risk. *Eur Spine J*. 2010;19(6):982-988. Epub 2010 Jan 2012.
23. Gruskay J, Kepler C, Smith J, Radcliff K, Vaccaro A. Is surgical case order associated with increased infection rate after spine surgery? *Spine (Phila Pa 1976)*. Jun 2012;37(13):1170-1174.
24. Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. *Infect Control Hosp Epidemiol*. Oct 2008;29 Suppl 1:S51-61.
25. Sweet FAMD, Roh MMD, Sliva CMD. Intra-wound Application of Vancomycin for Prophylaxis In Instrumented Thoracolumbar Fusions: Efficacy, Drug Levels, and Patient Outcomes. *Spine (Phila Pa 1976)*. Nov 2011;36(24):2084-8.
26. Rehtine GR, Bono PL, Cahill D, Bolesta MJ, Chrin AM. Postoperative wound infection after instrumentation of thoracic and lumbar fractures. *J Orthop Trauma*. 2001;15(8):566-569.
27. O'Neill KR, Smith JG, Abtahi AM, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. *The Spine Journal*. Jul 2011;11(7):641-6.
28. Pahys J, Pahys J, Cho S, et al. Methods to decrease post-operative infections following posterior cervical spine surgery. *AAOS*. San Francisco, CA 2011.
29. Cheng MT, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. *Spine (Phila Pa 1976)*. Aug 2005;30(15):1689-1693.
30. Rao N, Cannella BA, Crossett LS, Yates Jr AJ, McGough Iii RL, Hamilton CW. Preoperative Screening/Decolonization for Staphylococcus aureus to Prevent Orthopedic Surgical Site Infection: Prospective Cohort Study With 2-Year Follow-Up. *The Journal of Arthroplasty*. Dec 2011;26(8):1501-7.
31. Webster J, Osborne S. Meta-analysis of preoperative antiseptic bathing in the prevention of surgical site infection. *British Journal of Surgery*. 2006;93(11):1335-1341.



32. Bailey RR, Stuckey DR, Norman BA, et al. Economic value of dispensing home-based preoperative chlorhexidine bathing cloths to prevent surgical site infection. *Infect Control Hosp Epidemiol*. May 2011;32(5):465-471.
33. Perl TM. Prevention of Staphylococcus aureus infections among surgical patients: Beyond traditional perioperative prophylaxis. *Surgery*. 2003;134(5, Supplement 1):S10-S17.
34. Harbarth S, Fankhauser C, Schrenzel J, et al. Universal Screening for Methicillin-Resistant Staphylococcus aureus at Hospital Admission and Nosocomial Infection in Surgical Patients. *JAMA: The Journal of the American Medical Association*. Mar 2008;299(10):1149-1157.
35. Wilcox MH, Hall J, Pike H, et al. Use of perioperative mupirocin to prevent methicillin-resistant Staphylococcus aureus (MRSA) orthopaedic surgical site infections. *Journal of Hospital Infection*. 2003;54(3):196-201.
36. Jones JC, Rogers TJ, Brookmeyer P, et al. Mupirocin Resistance in Patients Colonized with Methicillin-Resistant Staphylococcus aureus in a Surgical Intensive Care Unit. *Clinical Infectious Diseases*. Sept 2007;45(5):541-547.
37. Bolon MK, Morlote M, Weber SG, Koplan B, Carmeli Y, Wright SB. Glycopeptides are no more effective than beta-lactam agents for prevention of surgical site infection after cardiac surgery: a meta-analysis. *Clin Infect Dis*. May 2004;38(10):1357-1363.
38. Finkelstein R, Rabino G, Mashiah T, et al. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thorac Cardiovasc Surg*. Feb 2002;123(2):326-332.
39. Perry JW, Montgomerie JZ, Swank S, Gilmore DS, Maeder K. Wound Infections Following Spinal Fusion with Posterior Segmental Spinal Instrumentation. *Clinical Infectious Diseases*. Apr 1997 1997;24(4):558-561.
40. Sponseller PD, LaPorte DM, Hungerford MW, Eck K, Bridwell KH, Lenke LG. Deep Wound Infections After Neuromuscular Scoliosis Surgery: A Multicenter Study of Risk Factors and Treatment Outcomes. *Spine*. 2000;25(19):2461-2466.
41. Linam WMMD, Margolis Peter AMD, Staat Mary AMD, et al. Risk Factors Associated With Surgical Site Infection After Pediatric Posterior Spinal Fusion Procedure • *Infection Control and Hospital Epidemiology*. 2009;30(2):109-116.
42. Pull Ter Gunne DA, Hosman DA, Cohen DD, et al. A Methodological Systematic Review on Surgical Site Infections Following Spinal Surgery. Part 1: Risk factors. *Spine (Phila Pa 1976)*. May 2012.
43. Molinari WJ, Khera O, Molinari RW. Prophylactic Operative Site Powdered Vancomycin and Postoperative Deep Spinal Wound Infection: 1,512 Consecutive Surgical Cases during a Six-Year Period: PAPER #37. *Spine Journal Meeting Abstracts*. 2011:73-74.
44. Courvalin P. Vancomycin Resistance in Gram-Positive Cocci. *Clinical Infectious Diseases*. Jan 2006 2006;42(Supplement 1):S25-S34.
45. Rybak MJ. The Pharmacokinetic and Pharmacodynamic Properties of Vancomycin. *Clinical Infectious Diseases*. Jan 2006 2006;42(Supplement 1):S35-S39.
46. Stall AC, Becker E, Ludwig SC, Gelb D, Poelstra KA. Reduction of postoperative spinal implant infection using gentamicin microspheres. *Spine (Phila Pa 1976)*. Mar 2009;34(5):479-483.

47. Ostermann PA, Seligson D, Henry SL. Local antibiotic therapy for severe open fractures. A review of 1085 consecutive cases. *J Bone Joint Surg Br.* Jan 1995;77(1):93-97.
48. Hanssen AD, Osmon DR, Patel R. Local antibiotic delivery systems: where are we and where are we going? *Clin Orthop Relat Res.* Aug 2005(437):111-114.
49. Møller AM, Pedersen T, Villebro N, Munksgaard A. Effect of smoking on early complications after elective orthopaedic surgery. *Journal of Bone & Joint Surgery, British Volume.* Mar 2003;85-B(2):178-181.

Appendix Table A: Variable definitions and chart locations		
Variable	Definition	Location in Chart
Age	Age in years at date of surgery. Date of surgery-DOB	Patient admission document
Gender	Male or Female	Patient admission document
Race	Caucasian, African-American, Hispanic, or other	Patient admission document
Body mass index	Calculated from height in inches and weight in pounds	Height and weight found in pre-anesthesia testing document, ortho H&P or hospital admission patient profile
Insurance type	Categorized as Private, Medicare, Medicaid, or Workmen's compensation. Private includes commercial HMO and PPO	Patient admission document or hospital admission patient profile
American Society of Anesthesiologists grade	Grade recorded as 1,2,3, 4, or 5	Pre-anesthesia testing document, anesthesia OR form, or nursing OR flowsheet
History of surgical site infection	Yes or No	Pre-anesthesia testing document or ortho H&P
Current cigarette use	Yes or No	Pre-anesthesia testing and ortho H&P
Number of smoking pack years	Number of packs per day multiplied by the number of years smoked	Ortho H&P, or pre-anesthesia testing document
Smoking quit date	Date quit smoking	Ortho H&P, pre-anesthesia testing or hospital admission patient profile
Alcohol use	Yes or No. Yes for any alcohol use.	Pre-anesthesia testing, ortho H&P
Illicit drug use	Yes or No. Yes for any illicit drugs including marijuana	Pre-anesthesia testing, ortho H&P
Previous spinal surgeries	Yes or No. Yes if surgery is in the same spinal area as current surgery.	Ortho H&P, pre-anesthesia testing document.
Length of stay	Date of discharge - date of surgery	Discharge date taken from discharge summary document

Discharge location	Home, Inpatient Rehab, Skilled nursing facility, inpatient psych	Discharge summary document
Number of days of follow-up	Date of most recent follow-up in clinic with Dr. Burton – Date of surgery	Dr. Burton’s clinic notes.
Diagnosis	Up to 3 diagnoses listed on the OR Operative report	Dr. Burton’s OR operative report
Blood transfusion	Recorded as intraoperative if packed red blood cells were given during the operative time period, or post operative if given after the operative time period, or No if none given.	PACU document, anesthesia record, and discharge summary document
Number of residents	The number of ortho residents assisting	OR operative report, OR nursing flowsheet
Estimated blood loss	Volume of blood lost in milliliters	Anesthesia record, PACU document
Length of surgery	Incision time-closure time, documented in military time	OR Nursing flowsheet
Number of levels instrumented	Number of levels receiving instrumentation (e.g. L5-S1 is one level)	OR operative report
Number of levels fused	Number of levels being fused (e.g. L5-S1 is one level)	OR operative report
Associated anterior approach	Recorded as Same-Day-Front-Back, Same-Day-Back-Front, Staged-Front-Back, or Staged-Back-Front, depending on when the anterior approach was performed. Anterior approached occurring within 90 days of the posterior approaches were considered associated	OR operative reports, discharge summary documents, and Ortho clinic notes

Decompression	Yes or No. Yes if laminectomy, laminoforaminotomy, foraminotomy, or any osteotomy	OR operative report
Pelvic fixation	Yes or No. Yes if instrumentation was applied to the pelvis	OR operative report
Operative levels	Categorized as Cervical, Thoracic, Thoracolumbar, or Lumbar	OR operative report
Hemovac drain use	Yes or No. Yes if any surgical drain was placed	OR operative report, OR nursing flowsheet
Hair removal method	Clippers, Razor, or none	OR nursing flowsheet
Preoperative Antibiotic given	Quantity and type of antibiotic given IV (e.g. 1GANCEF is one gram of ancef)	Anesthesia record, PACU document
Time of first dose of prophylactic antibiotic	Time first dose was delivered, recorded in military time	Anesthesia record, OR nursing flowsheet, PACU document
Co-morbidities	Up to 10 comorbidities were recorded. This variable is the sum number of those	Ortho H&P and the pre-anesthesia testing document
Hypertension	Yes if patient had hypertension listed a comorbidity, else No	Variable was recoded from Co-morbidities
Cardiac disease	Yes if arrhythmia, atrial fibrillation, coronary artery disease, congestive heart failure or myocardial infarction history were listed in comorbidities, else No	Variable was recoded from Co-morbidities
Diabetes mellitus	Yes if insulin dependent diabetes mellitus, non-insulin dependent diabetes mellitus or diet controlled diabetes mellitus were listed as comorbidities, else No	Variable was recoded from Co-morbidities

Cerebral Palsy	Yes if cerebral palsy listed in comorbidities, else No	Variable was recoded from Comorbidities
Respiratory Disease	Yes if asthma, COPD, emphysema, chronic bronchitis, or other lung disease were listed in comorbidities, else No	Variable was recoded from Comorbidities
Renal disease	Yes if history of kidney stones or renal insufficiency listed in comorbidities, else No	Variable was recoded from Comorbidities
Cancer	Yes if history of any cancer listed in comorbidities (prostate, breast, GI, renal, etc.), else No	Variable was recoded from Comorbidities
Psychiatric Disease	Yes if depression, anxiety, bi-polar disorder listed in comorbidities, else No	Variable was recoded from Comorbidities
Surgical Complications	Complication associated with surgical hospital stay (e.g. UTI, pneumonia, dural tear, vertebroplasty, wound dehiscence, hematoma, etc.)	Discharge summary, consultation reports
Intrawound Vancomycin	Yes or No	OR operative report, OR nursing flowsheet
Surgical site infection	Yes or No. Yes if required operation and had a positive tissue culture, within 90 days of index surgery	OR operative reports, microbiology lab report, infectious disease consultation reports
Infection depth	Deep or Superficial. Deep if deep tissue culture was positive	OR operative reports, microbiology lab report, infectious disease consultation reports
Staphylococcus	Yes if deep or superficial culture was positive for Staphylococcus aureus or coagulase negative staphylococcus, else No	Microbiology lab reports

Deep Staphylococcus	Yes if deep culture was positive for Staphylococcus aureus or coagulase negative staphylococcus, else No	Microbiology lab reports
Staphylococcus aureus	Yes if deep or superficial culture positive for MSSA or MRSA, else No	Microbiology lab reports
Deep Staphylococcus aureus	Yes if deep culture positive for MSSA or MRSA	Microbiology lab reports
Superficial mixed culture	Yes if superficial infection contained more than one bacteria, else No	Microbiology lab reports
Deep mixed culture	Yes if deep infection contained more than one bacteria, else No	Microbiology lab reports
E. coli	Yes if deep or superficial infection was positive for E. coli, else No	Microbiology lab reports
Other deep	Yes if deep infection was something other than Staph or E.coli	Microbiology lab reports
Other superficial	Yes if superficial infection was something other than Staph or E.coli	Microbiology lab reports
Number of days post op for infection	Date of operation for infection – date of index surgery	OR operative reports
Number of operations for infection	Number of operations patient had to treat the surgical site infection	OR operative reports
Number of hospital days for infection treatment	Sum of days hospitalized for infection treatment	Discharge summary,
Infection occurred during index hospitalization	Yes if surgical site infection diagnosed during index surgery hospital stay, else No	Discharge summary
Number of readmissions for infection treatment	Number of time the patient was hospitalized for infection treatment	Discharge summary, infectious disease consultation reports, OR operative report

IV antibiotics used to treat surgical site infection	Yes or No	Discharge summary, infectious disease consultation report
Intrawound vancomycin used for surgical site infection treatment	Yes or No	OR operative reports, OR nursing flowsheet
Wound vac use for infection treatment	Yes or No	Operative report, discharge summary, infectious disease summary



Appendix B: Infections Data

Age	Gender	Diagnosis	Intrawound Vancomycin	Number of days postop	Superficial Bacteria	Deep Bacteria	Number of operations for SSI	Number of Days Hospitalized for SSI
53	Female	Spondylolisthesis	No	9	Moderate growth MSSA	Nine colonies of MSSA	10	43
19	Female	Neuromuscular scoliosis	No	9	Light growth Pseudomonas aeruginosa, One colony coagulase negative Staphylococcus	None	1	25
58	Female	Post-op fracture	No	10	Light growth MSSA	None	1	4
44	Female	Fracture dislocation	No	12	Light growth coagulase negative Staphylococcus, at iliac crest graft site	None	1	13
69	Female	Spondylolisthesis, radiculopathy, sacral insufficiency fractures	No	14	Light growth Klebsiella pneumoniae, Streptococcus agalactiae, and MSSA	Light growth Enterococcus	5	20
10	Male	Neuromuscular scoliosis, Myelomeningocele	No	15	One colony beta lactamase positive Prevotella Denticola, light growth Escherichia coli, Corynebacterium, Pseudomonas aeruginosa, and Enterococcus	None	1	5
50	Female	Spinal stenosis, degenerative disc disease	No	20	Moderate growth MRSA	Two colonies MRSA	2	6
67	Male	Spinal stenosis	No	21	Moderate growth MRSA	Moderate growth MRSA	4	21
55	Male	Spinal stenosis, spondylolisthesis	No	23	Light growth MRSA	Light growth MRSA	1	4

Appendix B: Infections Data

Age	Gender	Diagnosis	Intrawound Vancomycin	Number of days postop	Superficial Bacteria	Deep Bacteria	Number of operations for SSI	Number of Days Hospitalized for SSI
55	Female	Idiopathic scoliosis, spinal stenosis	No	27	Light growth MRSA	Light growth MRSA	2	15
24	Male	Painful implant, severe arthrosis	No	28	Light growth MSSA, Streptococcus agalactiae, and Corynebacterium	Moderate growth MSSA, and subsequent Light growth MRSA	7	30
63	Male	Degenerative disc disease, radiculopathy	No	30	Heavy growth MSSA	None	1	2
38	Female	Coronal imbalance, pseudoarthrosis, implant fracture	No	37	Heavy growth MSSA	None	1	5
84	Female	Fracture, radiculopathy, spondylolisthesis	No	43	Escherichia coli (from outside facility)	None	1	9
33	Male	Charcot spine	No	58	Coagulase negative Staphylococcus	Coagulase negative Staphylococcus	2	58
11	Male	Duchenne muscular dystrophy, myopathic scoliosis	Yes	6	Two colonies Pseudomonas aeruginosa, three colonies Escherichia coli	Two colonies Escherichia coli	2	6
51	Male	Cervical radiculopathy	Yes	10	Light growth Escherichia coli, and three colonies coagulase negative Staphylococcus	Light growth Escherichia coli and two colonies Propionibacterium acnes	1	3
57	Female	Spinal stenosis, spondylolisthesis	Yes	17	Moderate growth MSSA	None	1	5
57	Female	Spinal stenosis, instability	Yes	21	One colony Proteus mirabilis	Four colonies of Klebsiella oxytoca	1	14

Appendix B: Infections Data

Age	Gender	Diagnosis	Intrawound Vancomycin	Number of days postop	Superficial Bacteria	Deep Bacteria	Number of operations for SSI	Number of Days Hospitalized for SSI
13	Male	Spondylolisthesis, radiculopathy	Yes	28	Light growth MSSA	None	1	1
75	Female	Degenerative scoliosis, spinal stenosis, spondylolisthesis	Yes	34	E.coli, Streptococcus agalactiae, Anaerobic (Prevotella/corporis, Fusobacterium nucleatum)	One colony Streptococcus agalactiae	1	12
77	Male	Spinal stenosis, spondylolisthesis	Yes	36	Moderate growth Escherichia coli, and MRSA	None	1	3