Timing of Antimicrobial Prophylaxis and the Risk of Surgical Site Infections

Results From the Trial to Reduce Antimicrobial Prophylaxis Errors

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Objective: The objective of this study is to determine the optimal timing for surgical antimicrobial prophylaxis (AMP).

Summary Background Data: National AMP guidelines should be supported by evidence from large contemporary data sets.

Methods: Twenty-nine hospitals prospectively obtained information on AMP from 4472 randomly selected cardiac, hip/knee arthroplasty, and hysterectomy cases. Surgical site infections (SSIs) were ascertained through routine surveillance, using National Nosocomial Infections Surveillance system methodology. The association between the prophylaxis timing and the occurrence of SSI was assessed using conditional logistic regression (conditioning on hospital).

Results: One-hundred thirteen SSI were detected in 109 patients. SSI risk increased incrementally as the interval of time between antibiotic infusion and the incision increased (overall association between timing and infection risk $P = 0.04$). When antibiotics requiring long infusion times (vancomycin and fluoroquinolones) were excluded, the infection risk following administration of antibiotic within 30 minutes prior to incision was 1.6% compared with 2.4% associated with administration of antibiotic between 31 to 60 minutes prior to surgery (OR: 1.74; 95% confidence interval, 0.98–3.04). The infection risk increased as the time interval between preoperative antibiotic and incision increased or if the antibiotic was first infused after incision. Intraoperative redosing (performed in only 21% of long operations) appeared to reduce SSI risk in operations lasting more than 4 hours (OR of 3.08 with no redosing; 95% confidence interval 0.74–12.90), but only when the preoperative dose was given correctly.

Conclusions: These data from a large multicenter collaborative study confirm and extend previous observations and show a consistent relationship between the timing of AMP and SSI risk with a trend toward lower risk occurring when AMP with cephalosporins and other antibiotics with short infusion times were given within 30 minutes prior to incision.

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Antimicrobial prophylaxis can reduce the risk of surgical site infection (SSI) following many operations. Animal and clinical studies conducted over the past 3 decades ago suggest that antimicrobials should be given prior to the incision and that efficacy diminishes or disappears if the antibiotic is given either too early or after incision.[1–3] Despite general acceptance of these concepts and the existence of guidelines, wide variation in perioperative antibiotic administration practices have been reported in the United States.[4] To encourage appropriate antimicrobial prophylaxis, the Centers for Medicare and Medicaid Services and the Joint Commission have recently adopted performance measures specifying the choice of antimicrobial agent and the timing and duration of surgical prophylaxis.[5] Adherence to these measures is assuming increasing importance; and facility specific compliance is now publicly reported at http://www.hospitalcompare.hhs.gov/.

Current guidelines and performance measures for timing of perioperative antibiotics (parenteral antimicrobial prophylaxis initiated within 1 hour before incision or within 2 hours for vancomycin or fluoroquinolones) are based on data from clinical trials and pharmacokinetic data.[1–3,6,7] However, the studies on which the performance measures are based were not designed to determine the optimal timing of the initial preoperative dose. The seminal article addressing timing of surgical prophylaxis, an observational study conducted at one hospital, involved 2847 patients undergoing a wide variety of surgical procedures.[8] This study was conducted in 1985–1986, an era when there was considerable variation in the timing of prophylactic antibiotics; only 35% of patients received surgical antimicrobial prophylaxis meeting the contemporary standard of less than 1 hour prior to incision. Although this study elegantly showed the relationship between timing of antibiotics and risk of SSI, it did not find a significant difference in SSI rates when antibiotics were administered within 1 or 2 hours prior to incision compared with antibiotics administered 0 to 3 hours postoperatively.

In this article, we report the findings of a multicenter study with the goal of further exploring the relationships between timing, duration, and intraoperative redosing of surgical antimicrobial prophylaxis and the risk of SSI.

METHODS

The current study is an ancillary study to the multisite Trial to Reduce Antimicrobial Prophylaxis Errors (TRAPE). The parent TRAPE study was a trial including 44 hospitals designed to evaluate interventions to improve antibiotic prophylaxis. Hospitals for the parent TRAPE study were recruited through a mailing to Society for Healthcare Epidemiology of America membership in 2002. All TRAPE participating hospitals measured antibiotic prophylaxis performance in 100 randomly selected surgical cases in two 6 month periods from June to November 2003 (baseline) and February to July 2005 (remeasurement). The surgical procedures included car-

diac surgery, hysterectomy, and hip and knee arthroplasty, selected because there were prophylaxis guidelines in place at the inception of the study.[9]

After completion of the antimicrobial prophylaxis data collection, all TRAPE hospitals were invited to participate in this ancillary study provided that they (1) used the National Nosocomial Infections Surveillance (NNIS) system definitions of SSI and NNIS risk stratification as part of their routine SSI surveillance methodology[10] and (2) were able to link cases sampled for the parent study to SSI surveillance data.

Data Collection

Hospitals used a customized data entry system to collect data on the AMP process on randomly selected cases. Based on anticipated surgical volumes, the data entry system directed the hospital to collect information on every Nth surgical case after a random start at the beginning of every month with adjustments for the number of cases still needed for completion. For sampled cases that met the study inclusion criteria (no evidence of infection preoperatively, surgical start times documented, prophylaxis timing documented if AMP given), personnel at the hospital collected data on day and time of surgical incision, surgical close and the timing, drug, route and dose of all antibiotics given before surgery and after surgery up to 8 total doses. De-identified data were transmitted to the coordinating center at the Joint Commission.

To identify SSIs among the sampled surgical cases, infection control personnel at each hospital retrospectively matched the listing of cases for which AMP data were obtained with their record of previously identified SSIs. The SSI surveillance was conducted at each participating hospital as part of their routine infection control practices. All participating hospitals used NNIS definitions and risk stratification; postdischarge surveillance practices were not standardized among the hospitals. A survey was conducted to determine how each site defined and completed surveillance. The results of the survey are provided in Appendix A. Within hospitals, there were no changes in the definitions and methodologies used between baseline and remeasurement. When an infected case was identified, a standardized, de-identified case report form was completed.

The TRAPE study was funded by a grant from the Agency for Healthcare Research and Quality (R01 HS11331). Representatives from the funding source were not involved in any phases of the project. The protocol was approved by institutional review boards affiliated with the participating hospitals, the University of Tennessee at Memphis, Wake Forest University, CDC, and the Joint Commission. Data use agreements were established with each site to ensure compliance with HIPAA requirements.

Statistical Analysis

The study cohort was composed of all cases in the TRAPE database for which SSI outcome data would have been available had an SSI occurred. Infection risk is defined as the proportion of patients undergoing surgery who developed an infection.

The antimicrobial dose given prior to and closest to the time of incision was considered to be for prophylaxis. When more than 1 preoperative antibiotic was given, timing was based on the antibiotic given closest to the time of incision. If no antibiotic was given before incision, the timing was based on the dose given closest to the incision time after incision. When a preoperative antibiotic was given more than 3 hours before incision and a postoperative dose was given within an hour of incision, the postoperative dose was taken to be the prophylactic dose. The timing interval was calculated by subtracting the starting time for administration of the prophylaxis dose from the time of surgical incision. Because of sparse numbers, some of these timing categories were collapsed for various analyses. In surgical cases lasting more than 4 hours, antibiotics delivered after 4 hours but before the end of surgery were taken to be intraoperative redosing. Because vancomycin and fluoroquinolones require long infusion times and, per current guidelines, can be administered within 2 hours prior to incision, analyses were rerun omitting patients who received these antibiotic either preoperatively or up to 180 minutes postincision.

The relationship between timing and infection risk was assessed using the χ^2 distribution and Fisher exact test when indicated and Cochran-Mantel-Haenszel method for analyses stratified by hospital. We used conditional logistic regression to relate timing to the log-odds of infection conditioned on hospital. Conditional logistic regression was also used to examine the effect of potential confounding factors such as period of measurement, group status, procedure type, procedure duration, and ASA score of the patient undergoing the procedure. All analyses were done using SAS version 9.1 (Cary, NC). An alpha level of 0.05 was used as the nominal Type I error rate for all analyses.

RESULTS

Of 44 hospitals in the parent TRAPE study, 29 volunteered to participate in the SSI ancillary study and met the inclusion criteria described in Methods; 25 hospitals contributed data from both measurement periods; the remaining 4 hospitals contributed data from 1 measurement period. Characteristics of the 29 participating hospitals are shown in Table 1. Most hospitals were teaching hospitals, with approximately 55% having fewer than 250 beds. Table 1 also shows the distribution of surgical procedures included in the database.

Antimicrobial prophylaxis data were collected for 4472 surgical cases. Regarding prophylaxis received either preoperatively or postoperatively, 3405 received only cephalosporins or other antibiotics designated by the Surgical Care Improvement Project (SCIP) to be administered within 60 minutes of incision,[7] 575 received cephalosporins plus vancomycin, 218 received vancomycin only, 240 received fluoroquinolones with or without other agents, and 34 had no documented antimicrobial prophylaxis. Antibiotic selection met the SCIP antibiotic selection indicator in 90% of cases.

TABLE 1. Characteristics of Hospitals and Surgical Cases in the TRAPE Surgical Site Infection Study

Characteristics	Percentage of Hospitals (N)	Percentage of Surgical Cases (N)
Teaching hospital		
No	20.7 (6)	23.0 (1029)
Yes	79.3 (23)	77.0 (3443)
Hospital bed size		
<250	55.2 (16)	52.6 (2351)
>250	44.8. (13)	47.4 (2121)
Treatment group		
Feedback only	48.3 (14)	52.7 (2355)
Intervention group	51.7 (15)	47.3 (2117)
Collection period		
Baseline	89.6 (26)	47.4 (2121)
Follow-up	96.6 (28)	52.6 (2351)
Procedures selected for surveillance		
Cardiac	82.7 (24)	43.6 (1949)
Hip/knee arthroplasty	72.4 (21)	38.8 (1735)
Hysterectomy	44.8. (13)	17.6 (788)

One-hundred thirteen infections were detected in 109 patients. In 4 patients with multiple infections, the first identified infection was included in the analysis. Thirty-one infections were diagnosed during the hospital admission at which the index procedure was done. Of the 78 infections diagnosed after initial hospital discharge, 6 infections were diagnosed greater than 30 days postprocedure. The median day of diagnosis was 14 days postprocedure with the longest interval between procedure and infection diagnosis being 73 days (on 2 occasions). Sixty-three infections were superficial, 32 were organ space, and 14 were deep incisional. In all but 1 case, a culture report was found. Six (5.5%) cultured infections failed to grow microbial species. The most common bacterial species were methicillin-sensitive *Staphylococcus aureus* 17 (15.6%), methicillin-resistant *S. aureus* 17 (15.6%), and coagulase negative staphylococci 17 (15.6%), and gram negative bacteria 16 (14.7%).

Table 2 shows the association between hospital and patient characteristics and infection risk. The infection risk was lower at nonteaching hospitals than at teaching hospitals. Infection rates by procedure were 1.1% for joint arthroplasty, 3.1% for cardiac, and 3.8% for hysterectomy. Infections rates did not differ by hospital size, treatment group, or time of measurement. There was a tendency for infection rates to be higher in patients with higher ASA scores. Longer duration of surgery and teaching hospitals were associated with higher infection risk.

TABLE 2. Association Between Hospital and Patient Characteristics and Infection Risk

Characteristic	Infection/N-at-Risk (Percent)	Relative Risk (95% CI)
Teaching hospital		
No	16/1029 (1.6)	0.58 (0.34, 0.97)
Yes	93/3443 (2.7)	$P = 0.04$
Hospital bed size		
<250	57/2351 (2.4)	0.99 (0.68, 1.43)
>250	52/2121 (2.4)	$P = 0.95$
Treatment group		
Feedback only	64/2355 (2.7)	1.28 (0.88, 1.86)
Intervention group	45/2117 (2.1)	$P = 0.20$
Collection period		
Baseline	53/2121 (2.5)	0.98 (0.67, 1.43)*
Follow-up	56/2351 (2.4)	$P = 0.94$
Procedures selected for surveillance		
Cardiac	60/1949 (3.1)	Reference group*
Hip/knee arthroplasty	19/1735 (1.1)	0.45 (0.24, 0.83), $P = 0.009$
Hysterectomy	30/788 (3.8)	0.91 (0.55, 1.52), $P = 0.72$
ASA score		
One	3/146 (2.0)	Reference group*
Two	21 /1426 (1.5)	0.64 (0.19, 2.14), $P = 0.47$
Three	36/1281 (2.8)	1.20 (0.37, 3.83), $P = 0.76$
Four/five	48/1555 (3.1)	1.85 (0.52, 6.57), $P = 0.33$
(Missing = 64)		
Duration of surgery		
Up to 4 h	55/3395 (1.6)	Reference group*
4–7 h	51/988 (5.2)	2.75 (1.82, 4.10), $P < 0.001$
7 or more h	3/74 (4.0)	3.18 (1.00, 10.08), $P = 0.045$
(Missing = 15)		

*Relative risks, confidence intervals and *P* values based on an analysis stratified by hospital.

Table 3 presents the association between timing and infection risk for all cases. To account for the longer administration times of vancomycin and fluoroquinolones, we combined antibiotics and categorized administration into 4 groups, the first 2 of which are compliant with the SCIP timing indicator: Group 1—cephalosporins (and other antibiotics with short infusion times) within 30 minutes or vancomycin/fluoroquinolones within one hour prior to incision, Group 2—cephalosporins within 31 to 60 minutes or vancomycin/fluoroquinolones within 61–120 minutes prior to incision, Group 3—antibiotics given earlier than the guideline recommendations, and Group 4—initial antibiotic dose given postincision. The overall association between timing and infection risk was statistically significant ($P = 0.04$). Infection risk was lowest in Group 1, those with administration times closest to the incision (2.1%). Infection risk was somewhat higher with early antibiotic administration, but only postincision administration was associated with a statistically significant increased risk ($P = 0.02$). Eighty-one percent of cases were in compliance with the SCIP timing indicator.

Table 4 and Figure 1 present the relationship between timing interval and infection risk in patients whose preoperative regimen consisted of only cephalosporin or other antibiotics that, per current guidelines, should be administered within 60 minutes of incision (n = 3656). Cases that received preoperative fluoroquinolones or vancomycin or either drug up to 3 hours postincision are excluded (n=816). The infection risk with antibiotic administered within 30 minutes of incision was 1.6% compared with 2.4% when antibiotics were administered between 31 to 60 minutes prior to surgery with a conditional OR of 1.74, (95% CI: 0.98, 3.08), adjusting for procedure type and duration. The infection risk increased as the time interval between preoperative antibiotic and incision increased or if the antibiotic was first infused after incision. These results changed little after further adjusting for measurement period, randomization group, or ASA score.

Among patients who received both vancomycin and at least one other antibiotic preoperatively, the SSI risk was 3.5% (15 infections out of 433 patients). The SSI rate when vancomycin was used exclusively was 2.0%. The sample size was insufficient to examine timing in this subset.

Intraoperative Dosing

In 1062 (24%) cases, the surgical procedure lasted for at least 4 hours. Because of long half-lives and the reduced need for redosing, cases that received vancomycin or fluoroquinolones were excluded from the analysis of the impact of intraoperative redosing on infection risk (n = 372). Intraoperative redosing was given in 21% of 690 of these long operations. The data in Table 5 suggest that intraoperative redosing was associated with a lower infection risk only when the preoperative antibiotic was given in the recommended time frame. However, due to smaller samples sizes the estimates of effect are relatively imprecise.

Duration of Prophylaxis

We also examined the relationship between the duration of prophylaxis after the completion of surgery and risk of SSI in the 4472 surgical cases. Most patients in the study received postsurgical antibiotics for up to 24 (47.6%) or 48 hours (25.6%) after the end of surgery; only 12.7% received no doses following the end of surgery. The crude analysis indicates that not receiving any postoperative dose is associated with increased infection risk compared with patients receiving antibiotics up to 24 hours post surgery (24/567 [4.2%] and 49/2131 [2.3%], respectively; relative risk = 1.84; 95%CI: 1.14, 2.97). Procedure type and hospital however confounded this relationship. Patients receiving a hip/knee arthroplasty were more likely to receive a postsurgical antibiotic (98.1%) compared with patients undergoing the other 2 procedure types (80.5%).

TABLE 3. Association Between Timing of Prophylaxis and Infection Risk

Timing Interval Relative to Incision	Infection/N-at-Risk	Infection Risk*	Unadjusted Relative Risk of Infection (95% CI)	Adjusted Risk Odds Ratio for Infection From Conditional Logistic Regression (95% CI)†
Group 1: Vancomycin/fluoroquinolones within 60 min or cephalosporins‡ within 30 min before incision	38/1844	2.1%	Referent Group	Referent Group
Group 2: Vancomycin/fluoroquinolones 61–120 min or cephalosporins‡ 31–60 min before incision	43/1796	2.4%	1.16 (0.75, 1.79), $P = 0.50$	1.48 (0.92, 2.38), $P = 0.06$
Group 3: Any other preincision administration regimen	18/644	2.8%	1.36 (0.78, 2.36), $P = 0.28$	1.30 (0.70, 2.41), $P = 0.39$
Group 4: Post-incision	10/188	5.3%	2.58 (1.31, 5.10), $P = 0.005$	2.20 (1.03, 4.66), $P = 0.02$

*Test for overall association between timing and infection risk, $P = 0.04$.
†Adjusted for duration of surgery and procedure type.
‡Non cephalosporin antibiotics compromised <5% of those designated to be given with short infusion times and are included.

TABLE 4. The Association Between Timing Interval and Infection for Antimicrobial Prophylaxis, Using Cephalosporins or Other Antibiotics Designated to be Given Within 60 Minutes of Incision*

Timing Interval Relative to Incision	Infection/ N-at-Risk	Infection Risk	Unadjusted Relative Risk of Infection (95% CI)	Adjusted Risk Odds Ratio for Infection From Conditional Logistic Regression (95% CI)†
>120 min before incision or prophylaxis not given	4/96	4.7%	2.54 (0.89, 7.21), $P = 0.07$	2.11 (0.68, 6.59)
61–120 min before incision	12/489	2.4%	1.49 (0.74, 3.00), $P = 0.26$	1.25 (0.57, 2.76)
31–60 min before incision	38/1558	2.4%	1.48 (0.88, 2.50), $P = 0.13$	1.74 (0.98, 3.08)
0–30 min before incision	22/1339	1.6%	Reference group	Reference group
1–30 min after incision	4/100	4.0%	2.44 (0.86, 6.93), $P = 0.09$	1.96 (0.65, 5.95)
>31 min after incision	5/74	6.8%	4.12 (1.60, 10.53), $P = 0.002$	4.18 (1.37, 12.75)

*Cases receiving vancomycin or fluoroquinolones alone or in combination with cephalosporins either pre-operatively or within 3 hours postoperatively with another drug were excluded from this analysis.
†Adjusted for duration of surgery and procedure type.

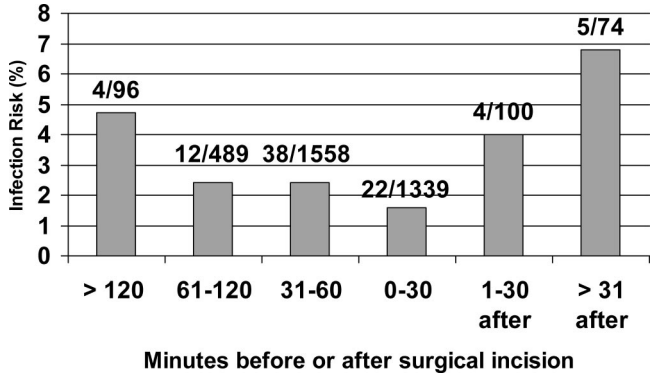

FIGURE 1. Surgical site infection risk based on timing of perioperative antibiotic dose, omitting vancomycin and fluoroquinolones. Annotation shows number of infections/number of operations for each time interval.

The arthroplasty patients also had a significantly lower infection rate (Table 2). After adjustment, there was no evidence that patients who did not receive postsurgical prophylaxis had higher infection rates (adjusted risk odds: 1.01; 95% CI: 0.56, 1.82) Overall, there were no statistically significant differences for any of the patterns of postsurgical antibiotic administration compared with doses given in the first 24 hours following the end of surgery.

DISCUSSION

In this prospective multicentered study of antimicrobial prophylaxis and surgical site infection risk, we found a consistent relationship between antimicrobial prophylaxis timing and infection risk with a trend toward lower risk when cephalosporin and other short infusion-time antibiotics were administered within 30 minutes prior to incision. Although our data suggest that the optimal timing is closer to incision than the national performance goal allows, these data can not exclude the possibility that the observed difference between the 1 to 30 minutes and 31 to 60 minutes was due to chance alone. Thus our data do not on their own support moving the national performance goal for most antibiotics from 60 minutes to 30 minutes, as advocated by some European guidelines.[11] However, the lower infection rate seen in the group closest to incision does allay concerns that antibiotics can be administered too close to incision.[12]

To our knowledge this is the largest observational study examining the relationship between antibiotic timing and SSI risk. In addition to being larger than the pivotal study by Classen et al,[8] data for this study were generated almost 2 decades later, during a period of increased national emphasis on antimicrobial prophylaxis performance measures. Antibiotics (excluding vancomycin and fluoroquinolones) were administered within one hour before incision in about 80% of cases in this study compared with 35% in the Classen study. The increased number of observations within one hour prior to incision in the current study (2897 compared with 1009) contributes to our ability to discriminate difference in infection risk closer

TABLE 5. Infection Risk and Intraoperative Dosing in Surgeries Lasting at Least 4 Hours*

Intraoperative Redosing in Surgeries Lasting >4 h	Infection/N-at-Risk	Infection Risk	Risk Odds Ratio for Infection From Conditional Logistic Regression (95% CI)
Recommended preoperative timing†			
Redosing	2/112	1.8%	Referent Group
No redosing	22/400	5.5%	3.08 (0.74, 12.90), $P = 0.06$
Suboptimal preoperative timing			
Redosing	2/35	5.6%	Referent Group
No redosing	8/143	5.7%	0.98 (0.22, 4.41), $P = 0.98$

*Excluding cases receiving vancomycin/fluoroquinolones.
†Recommended was defined as within 60 min prior to incision according to the guidelines.

to the incision. Still, the overall low incidence of infection and the relatively small differences in infection risk mean that even larger investigations will be required to definitively address the timing issue. In a recent observational study from the Netherlands assessing risk factors for postoperative infection, 87% of 1922 cases received antibiotics within one hour prior to incision. That study, although smaller is size and restricted to one surgical procedure (total hip arthroplasty), found results similar to ours with a decreasing rate of infections in those who received prophylaxis within 30 minutes prior to incision.[13] Another consequence of the high proportion of cases that received a nonvancomycin/fluoroquinolone antibiotic within one hour of surgery was the low number of cases that received the preoperative antibiotic earlier than one hour and which, thereby, limited our ability to test for the statistical significance of the higher infection rate seen with early administration.

Strengths of this study include the use of standardized surveillance definitions for SSI (NNIS) and the inclusion of a large number of hospitals. Also, the timing of antibiotic administration was recorded with precision and over 90% of cases received appropriate antibiotics according to national guidelines. Our findings are consistent with previous research showing an increased risk of infection with higher ASA scores and longer surgical duration.[14] The infection rates by surgery type in this study are very similar to the rates reported by NNIS for cardiac surgery and joint replacements; when combined, these procedures comprised 82% of cases in this study.[15] Although the infection rate for hysterectomy in this study is somewhat higher than rates reported by NNIS, the denominator for hysterectomy was only 778. Overall, infection rates by surgery type suggest that our participating hospitals are fairly representative.

There were several limitations to this study. Although this is the largest observational study looking at the association between antibiotic timing and infection, the number of events was small. Although the low absolute risk of surgical site infections is encouraging, the low number of cases limits statistical power. Although all hospitals used NNIS definitions, there were some differences among the hospitals in postdischarge surveillance methodologies and protocols related to long-term follow-up in patients with sternal wires. Our use of conditional logistic regression controls for potential confounders associated with hospitals themselves. Conditional logistic regression calculates the odds ratio of infection associated with poor timing within each hospital and then calculates a summary odds ratio across all hospitals. SSI surveillance, according to NNIS should be continued for 1 year in patients with implanted prosthetic material. Because of TRAPE study timing, the duration of follow-up in the remeasurement period was truncated at 3 to 9 months. This could lead to underascertainment of cases lowering statistical power. If there is a different association between prophylaxis and the time of infection occurrence, the lack of long-term follow-up could lead to bias in the estimation of effect. Even though the pattern of association was consistent with an effect of prophylaxis timing on infection risk, it is possible that prophylaxis timing was confounded by other infection control practices (such as aseptic procedures, glucose control, temperature control, and hair removal practice). All hospitals were volunteers; most were teaching hospitals that may not be representative of hospitals performing these surgical procedures. However, we would expect this to affect the overall infection risk and not the relative impact of prophylaxis timing on infection risk. Finally, the number of observations using vancomycin was too small to assess optimal timing for vancomycin.

Intraoperative redosing appeared to reduce the infection risk in operations lasting more than 4 hours, a finding consistent with other studies.[16,17] Higher infection rates with longer procedures is well established and is one of the 3 risk stratification variables used by NNIS.[13] How much of this increased rate can be influenced by antibiotic administration, is unclear. While preoperative dosing was appropriately timed in 81% of cases, intraoperative redosing was given in less than 1 in 4 cases in these highly motivated hospitals participating in a multicenter study. Although intraoperative redosing is not one of the indicators that is publicly reported, there are opportunities for considerable improvement in performance of this measure which could decrease infection rates.

These data are consistent with previous studies that show no impact of prolonging prophylaxis past 24 hours following the operation and infection risk.[18] Despite guidelines and a systematic review supporting no postoperative dosing,[7,18,19] only 12.7% received no doses following the end of surgery.

In conclusion, these findings confirm and extend the results previous studies that show a consistent relationship between timing of prophylactic antibiotics and infection risk and show a trend toward lower risk when prophylaxis with cephalosporins and other antibiotics with short infusion times was given within 30 minutes prior to incision. While full compliance with SCIP measures will reduce infection rates, focus on existing SCIP measures should not distract efforts to improve compliance with intraoperative redosing during long surgeries, an under-recognized cause of antimicrobial prophylaxis errors.

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REFERENCES

1. Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery*. 1961;50:161–168.
2. Polk HC Jr, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery*. 1969;66:97–103.
3. Stone HH, Hooper CA, Kolb LD, et al. Antibiotic prophylaxis in gastric, biliary and colonic surgery. *Ann Surg*. 1976;184:443–452.
4. Bratzler DW, Houck PM, Richards C, et al. Use of antimicrobial prophylaxis for major surgery: baseline results from the National Surgical Infection Prevention Project [comment]. *Arch Surg*. 2005;140:174–182.
5. Surgical Care Improvement Project Core Measure Set. Available at: http://www.jointcommission.org/PerformanceMeasurement/PerformanceMeasurement/SCIP+Core+Measure+Set.htm. Accessed October 6, 2008.
6. DiPiro JT, Vallner JJ, Bowden TA Jr, et al. Intraoperative serum and tissue activity of cefazolin and cefoxitin. *Arch Surg*. 1985;120:829–832.
7. Bratzler DW, Houck PM; Surgical Infection Prevention Guidelines Writers Workgroup, et al. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project [see comment]. *Clin Infect Dis.* 2004;38:1706–1715.
8. Classen DC, Evans RS, Pestotnik SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection [comment]. *N Engl J Med*. 1992;326:281–286.
9. Kritchevsky SB, Braun BI, Bush AJ, et al. The Effect of a quality improvement collaborative to improve antimicrobial prophylaxis in surgical patients. *Ann Intern Med*. 2008;149:472–480.
10. 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. *Clin Infect Dis*. 2001;33(suppl 2):S69–S77.
11. van Kasteren ME, Gyssens IC, Kullberg BJ, et al. Optimizing antibiotics policy in the Netherlands. V. SWAB guidelines for perioperative antibiotic prophylaxis. Foundation Antibiotics Policy Team [erratum in *Ned Tijdschr Geneeskd.* 2001;145:112] [in Dutch]. *Ned Tijdschr Geneeskd*. 2000;144:2049–2055.
12. Dellinger EP. Prophylactic antibiotics: administration and timing before operation are more important than administration after operation [comment]. *Clin Infect Dis*. 2007;44:928–930.
13. van Kasteren ME, Mannien J, Ott A, et al. Antibiotic prophylaxis and the risk of surgical site infections following total hip arthroplasty: timely administration is the most important factor [comment]. *Clin Infect Dis*. 2007;44:921–927.
14. Culver DH, Horan TC, Gaynes RP, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med*. 1991;91:152S–157S.
15. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control.* 2004;32:470–485.
16. Zanetti G, Giardina R, Platt R. Intraoperative redosing of cefazolin and risk for surgical site infection in cardiac surgery. *Emerg Infect Dis*. 2001;7:828–831.
17. Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. *Am Surg*. 1997;63:59–62.
18. McDonald M, Grabsch E, Marshall C, et al. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review [comment]. *Aust NZ J Surg*. 1998;68:388–396.
19. Antimicrobial prophylaxis for surgery. *Treat Guidel Med Lett.* 2006;4:83–88.

APPENDIX A. SSI Surveillance Definitions and Methods

	N (%)
SSI definition	
Followed the NNIS/NHSN definitions exactly	29 (100)
Followed the NNIS/NHSN definitions with modification	0
Followed definitions other than NNIS/NHSN	0
Timeframe for including SSI follow-up when sternal wires used	
Within 30 d of the surgery	7 (24.1)
Up to 1 yr after the surgery	18 (62.1)
Don't know	0
Not applicable	4 (13.8)
How SSI's are identified during the admission (check all that apply)	
Notification from nursing staff	20 (69.0)
Notification from physician or surgeon	22 (75.9)
Direct observation of wound by ICP	2 (6.9)
Review of microbiology reports	28 (96.6)
Review of surgical log/case records	15 (51.7)
Review of pharmacy department antibiotic records	4 (13.8)
Don't know	0
Other: describe	5 (17.2)
How SSI's are identified after discharge (check all that apply)	
Surgeon surveys via telephone or mail	9 (31.0)
Patient surveys via telephone or mail	1 (3.4)
Review of out-patient microbiology reports	19 (65.5)
Notification from ICP (or other staff) at another healthcare facility	15 (51.7)
Notification from home health nurse	9 (31.0)
Review of out-patient or emergency department records	11 (37.9)
Review of surgical log/case records	9 (31.0)
Review of pharmacy department antibiotic records	1 (3.4)
No post-discharge surveillance was done	3 (10.3)
Do not know	0
Other: describe	2 (6.9)
How SSI's are identified upon readmission (check all that apply)	
Notification from nursing staff	15 (51.7)
Notification from physician or surgeon	17 (58.6)
Direct observation of wound by ICP	2 (6.9)
Review of microbiology reports	27 (93.1)
Review of surgical log/case records	12 (41.3)
Review of pharmacy department antibiotic records	4 (13.8)
Review of admitting diagnoses	21 (72.4)
Do not know	0
Other: describe	6 (20.7)