

## NATIONAL QUALITY FORUM—Evidence (subcriterion 1a)

**Measure Number** (if previously endorsed): #0264

**Measure Title:** Prophylactic Intravenous (IV) Antibiotic Timing

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Not a component in a composite performance measure

**Date of Submission:** 3/17/2014

### Instructions

- For composite performance measures:
  - A separate evidence form is required for each component measure unless several components were studied together.
  - If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.
- Respond to all questions as instructed with answers immediately following the question. All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of supplemental materials may be submitted, but there is no guarantee it will be reviewed.
- If you are unable to check a box, please highlight or shade the box for your response.
- Maximum of 10 pages (includes questions/instructions; minimum font size 11 pt; do not change margins).  
**Contact NQF staff if more pages are needed.**
- Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](#).

**Note:** The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF's evaluation criteria.

### 1a. Evidence to Support the Measure Focus

The measure focus is evidence-based, demonstrated as follows:

- **Health outcome:** <sup>3</sup> a rationale supports the relationship of the health outcome to processes or structures of care. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior.
- **Intermediate clinical outcome:** a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence <sup>4</sup> that the measured intermediate clinical outcome leads to a desired health outcome.
- **Process:** <sup>5</sup> a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence <sup>4</sup> that the measured process leads to a desired health outcome.
- **Structure:** a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence <sup>4</sup> that the measured structure leads to a desired health outcome.
- **Efficiency:** <sup>6</sup> evidence not required for the resource use component.

### Notes

3. Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.
4. The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) [grading definitions](#) and [methods](#), or Grading of Recommendations, Assessment, Development and Evaluation ([GRADE](#)) [guidelines](#).
5. Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.
6. Measures of efficiency combine the concepts of resource use and quality (see NQF's [Measurement Framework: Evaluating Efficiency Across Episodes of Care](#); [AQA Principles of Efficiency Measures](#)).

**1a.1. This is a measure of:** (should be consistent with type of measure entered in De.1)

Outcome

- ☐ Health outcome: Click here to name the health outcome
- ☐ Patient-reported outcome (PRO): Click here to name the PRO  
*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors*
- ☐ Intermediate clinical outcome (e.g., lab value): Click here to name the intermediate outcome
- ☒ Process: [Timely administration of intravenous antibiotics for the prophylaxis of surgical site infection.](#)
- ☐ Structure: Click here to name the structure
- ☐ Other: Click here to name what is being measured

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**HEALTH OUTCOME/PRO PERFORMANCE MEASURE** *If not a health outcome or PRO, skip to 1a.3*

**1a.2.** Briefly state or diagram the path between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.

**1a.2.1.** State the rationale supporting the relationship between the health outcome (or PRO) to at least one healthcare structure, process, intervention, or service (i.e., influence on outcome/PRO).

*Note: For health outcome/PRO performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.*

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**INTERMEDIATE OUTCOME, PROCESS, OR STRUCTURE PERFORMANCE MEASURE**

**1a.3.** Briefly state or diagram the path between structure, process, intermediate outcome, and health outcomes. Include all the steps between the measure focus and the health outcome.

1. Timely administration of intravenous antimicrobial prophylaxis prior to surgery
2. Surgical intervention
3. Surgical recovery with or without the development of a surgical site infection

**1a.3.1.** What is the source of the systematic review of the body of evidence that supports the performance measure?

- ☒ Clinical Practice Guideline recommendation – **complete sections 1a.4, and 1a.7**
- ☐ US Preventive Services Task Force Recommendation – **complete sections 1a.5 and 1a.7**
- ☐ Other systematic review and grading of the body of evidence (e.g., Cochrane Collaboration, AHRQ Evidence Practice Center) – **complete sections 1a.6 and 1a.7**
- ☐ Other – **complete section 1a.8**

*Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.*

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**1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION**

**1a.4.1.** Guideline citation (including date) and URL for guideline (if available online):

Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm.* 2013 Feb 1;70(3):195-283. doi: 10.2146/ajhp120568.

URL for guideline: <http://www.ajhp.org/content/70/3/195.long>

**1a.4.2. Identify guideline recommendation number and/or page number and quote verbatim, the specific guideline recommendation.**

Page 197 states as follows:

*“Preoperative-dose timing.* The optimal time for administration of preoperative doses is within 60 minutes before surgical incision. This is a more specific time frame than the previously recommended time, which was “at induction of anesthesia.” Some agents, such as fluoroquinolones and vancomycin, require administration over one to two hours; therefore, the administration of these agents should begin within 120 minutes before surgical incision.”

**1a.4.3. Grade assigned to the quoted recommendation with definition of the grade:**

No grade is assigned to the quoted recommendation.

**1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system.** (Note: If separate grades for the strength of the evidence, report them in section 1a.7.)

The guideline assigns grades to recommendations for the use of antimicrobial prophylaxis are provided and graded according to the strength of evidence available. Studies supporting the recommendations were classified as follows:

Level I (evidence from large, well- conducted, randomized, controlled clinical trials or a meta-analysis),

Level II (evidence from small, well- conducted, randomized, controlled clinical trials),

Level III (evidence from well- conducted cohort studies),

Level IV (evidence from well- conducted case–control studies),

Level V (studies that were not well conducted),

Level VI (conflicting evidence that tends to favor the recommendation), or

Level VII (expert opinion or data extrapolated from evidence for general principles and other procedures).

Each recommendation was categorized according to the strength of evidence that supports the use or nonuse of antimicrobial prophylaxis as category A (levels I–III), category B (levels IV–VI), or category C (level VII). However, as stated above the guideline does not specifically grade the recommendation for the timing of the pre-operative dosing of the recommended antibiotic(s).

**1a.4.5. Citation and URL for methodology for grading recommendations** (if different from 1a.4.1):

Same as the URL for the guideline: <http://www.ajhp.org/content/70/3/195.long>

**1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?**

☐ Yes → complete section 1a.7

☐ No → report on another systematic review of the evidence in sections 1a.6 and 1a.7; if another review does not exist, provide what is known from the guideline review of evidence in 1a.7

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**1a.5. UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

**1a.5.1. Recommendation citation** (including date) and **URL for recommendation** (if available online):

**1a.5.2.** Identify recommendation number and/or page number and quote verbatim, the specific recommendation.

**1a.5.3.** Grade assigned to the quoted recommendation with definition of the grade:

**1a.5.4.** Provide all other grades and associated definitions for recommendations in the grading system. (Note: the grading system for the evidence should be reported in section 1a.7.)

**1a.5.5.** Citation and URL for methodology for grading recommendations (if different from 1a.5.1):

**Complete section 1a.7**

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#### **1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE**

**1a.6.1.** Citation (including date) and URL (if available online):

**1a.6.2.** Citation and URL for methodology for evidence review and grading (if different from 1a.6.1):

**Complete section 1a.7**

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#### **1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE SUPPORTING THE MEASURE**

*If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.*

**1a.7.1. What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?** The quoted guideline discusses antimicrobial administration and the timing of the initial dose. Please see pages 207 through 208 of the guideline for a summary of the evidence review for the timing of administration.

**1a.7.2. Grade assigned for the quality of the quoted evidence with definition of the grade:** No grade was assigned.

**1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.** Please see 1a.4.4. for the system applied to other recommendations within the guideline.

**1a.7.4. What is the time period covered by the body of evidence? (provide the date range, e.g., 1990-2010).** **Date range:** The earliest study quoted in the section on the guideline that reviewed the evidence for the timing of the initial dose of antimicrobial prophylaxis was published in 1985; the latest study quoted was performed in 2009. The guideline authors state that the review of evidence was through 2010.

#### **QUANTITY AND QUALITY OF BODY OF EVIDENCE**

**1a.7.5. How many and what type of study designs are included in the body of evidence? (e.g., 3 randomized controlled trials and 1 observational study)** The clinical studies referenced in the guideline discussion of the body of evidence were all prospective studies. Six were large

observational studies and two were small. Three were randomized controlled trials (two were presented together in one report).

**1a.7.6. What is the overall quality of evidence across studies in the body of evidence?** (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*) The overall quality of the evidence is good, but several of the studies were limited to selected types of operations (e.g., knee arthroplasty, total hip arthroplasty, cardiac surgery), which could limit the ability to extrapolate results to all surgical interventions.

#### **ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE**

**1a.7.7. What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence?** (*e.g., ranges of percentages or odds ratios for improvement/decline across studies, results of meta-analysis, and statistical significance*) The studies consistently suggest that timely administration of antimicrobial prophylaxis results in fewer surgical site infections, but the magnitude of the effect was variable and is difficult to compare across studies due to different methodologies and different approaches to timing.

**1a.7.8. What harms were studied and how do they affect the net benefit (benefits over harms)?**  
Harms were not studied.

#### **UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE**

**1a.7.9. If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review.**

There have been many new studies published since the guideline review. Major studies are summarized below. Most, but not all, suggest a reduction in surgical site infection when antimicrobial administration is timely, and many suggest that timeframes closer to incision further reduce the risk of subsequent surgical site infection.

Ho VP, Barie PS, Stein SL, Trencheva K, Milsom JW, Lee SW, Sonoda T. Antibiotic regimen and the timing of prophylaxis are important for reducing surgical site infection after elective abdominal colorectal surgery. *Surg Infect (Larchmt)*. 2011 Aug;12(4):255-60. doi: 10.1089/sur.2010.073. Epub 2011 Jul 26. Retrospective review from a prospective database of a random sample of patients undergoing elective abdominal colorectal procedures with anastomosis. Antibiotic regimens, initial dose timing (IDT), and re-dosing were evaluated. Appropriate regimens covered gram-positive cocci, gram-negative bacilli, and anaerobes. The IDT was considered proper if completed within 30 min prior to incision; re-dosing parameters were determined pharmacokinetically for each agent. The main outcome was SSI. Sequential logistic models were generated: Model 1 assessed antibiotic administration factors, whereas Model 2 controlled for patient and clinical factors, including disease process, patient characteristics, intra-operative factors, and post-operative factors. RESULTS: Six hundred five patients were included. The most common diagnoses were cancer (38.8%) and inflammatory bowel disease (22.0%). Seventy-six patients (12.6%) had superficial or deep incisional SSI, and 54 (8.9%) had organ/space SSI. Regimens included cefazolin + metronidazole for 219 patients (36.2%), cefoxitin for 214 (35.4%), and levofloxacin + metronidazole for 48 (7.9%). One hundred fourteen patients (18.8%) received other/nonstandard regimens, and ten had no documented antibiotic prophylaxis. Fifty-five patients (9.1%) received insufficient coverage, whereas 361 patients (59.7%) had proper IDT, and 401 regimens (66.3%) were re-dosed properly. In Model 1, the use of other/nonstandard regimens (odds ratio [OR] 2.069; 95%

confidence interval [CI] 1.078-1.868) and early administration of the initial prophylaxis dose (OR 1.725; 95% CI 1.147-2.596) were associated with greater odds of SSI. After adding clinical factors in Model 2, both of these factors remained significant (OR 2.505; 95% CI 1.066-5.886 and OR 1.733; 95% CI 1.017-2.954, respectively). CONCLUSIONS: Appropriate antibiotic selection and timing of administration for prophylaxis are crucial to reduce the likelihood of SSI after elective colorectal surgery with intestinal anastomosis.

Koch CG, Nowicki ER, Rajeswaran J, Gordon SM, Sabik JF 3rd, Blackstone EH. When the timing is right: Antibiotic timing and infection after cardiac surgery. *J Thorac Cardiovasc Surg.* 2012 Oct;144(4):931-937.e4. doi: 10.1016/j.jtcvs.2012.01.087. Epub 2012 May 16. From 1/1/1995-1/1/2008, 28,250 patients underwent 28,702 cardiac surgical procedures involving a median sternotomy; 85% received only cefuroxime and 15% received only vancomycin prophylaxis. Multivariable analysis identified factors associated with infection within each phase, and risk-adjusted optimal timing was determined using patient data, risk variables, and hypothetical values of antibiotic timing. RESULTS: Prevalence of sternal wound infection was 2.0% (489 patients) for cefuroxime and 2.3% (101 patients) for vancomycin. Minimum prevalence for infection was 1.8% observed when cefuroxime was administered 15 minutes before incision; risk increased to 2.2% with administration more than 45 minutes before incision and to 2.8% at 60 minutes before incision. Minimum prevalence of infection in patients who received vancomycin was 1.8% observed with initiation 32 minutes before incision; risk increased to 2.2% for administration 45 minutes before incision and 3.2% with administration 60 minutes before incision. Simulation for optimal timing found that it was influenced by phase-specific risk factors. CONCLUSIONS: Refining current antibiotic prophylaxis guidelines may lower sternal wound infections. Antibiotic administration timing resulting in lowest likelihood for infection varied with antibiotic and patient-specific factors. Optimal risk-adjusted timing could potentially reduce infections by 9%-31%.

Hawn MT, Richman JS, Vick CC, Deierhoi RJ, Graham LA, Henderson WG, Itani KM. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. *JAMA Surg.* 2013 Jul;148(7):649-57. doi: 10.1001/jamasurg.2013.134. Retrospective cohort study using national Veterans Affairs patient-level data on prophylactic antibiotic timing for orthopedic, colorectal, vascular, and gynecologic procedures from 2005 through 2009. RESULTS: Of the 32,459 operations, prophylactic antibiotics were administered at a median of 28 minutes (interquartile range, 17-39 minutes) prior to surgical incision, and 1497 cases (4.6%) developed an SSI. Compared with procedures with antibiotic administration within 60 minutes prior to incision, higher SSI rates were observed for timing more than 60 minutes prior to incision (unadjusted odds ratio [OR] = 1.34; 95% CI, 1.08-1.66) but not after incision (unadjusted OR = 1.26; 95% CI, 0.92-1.72). In unadjusted generalized additive models, we observed a significant nonlinear relationship between prophylactic antibiotic timing and SSI when considering timing as a continuous variable ( $P = .01$ ). In generalized additive models adjusted for patient, procedure, and antibiotic variables, no significant association between prophylactic antibiotic timing and SSI was observed. Vancomycin hydrochloride was associated with higher SSI occurrence for orthopedic procedures (adjusted OR = 1.75; 95% CI, 1.16-2.65). Cefazolin sodium and quinolone in combination with an anaerobic agent were associated with fewer SSI events (cefazolin: adjusted OR = 0.49; 95% CI, 0.34-0.71; quinolone: adjusted OR = 0.55; 95% CI, 0.35-0.87) for colorectal procedures. CONCLUSIONS: The SSI risk varies by patient and procedure factors as well as antibiotic properties but is not significantly associated with prophylactic antibiotic timing. While adherence to the timely prophylactic antibiotic measure is not bad care, there is little evidence to suggest that it is better care.

Koch CG, Li L, Hixson E, Tang A, Gordon S, Longworth D, Phillips S, Blackstone E, Henderson JM. Is it time to refine? An exploration and simulation of optimal antibiotic timing in general surgery. *J Am Coll Surg.*

2013 Oct;217(4):628-35. doi: 10.1016/j.jamcollsurg.2013.05.024. Epub 2013 Jul 10. The population consisted of 6,731 patients who underwent 7,095 general surgery procedures between January 5, 2006 and June 25, 2012. Patients with pre-existing infections, such as pneumonia and sepsis, and patients with no recorded use of antibiotics were excluded, as were patients on vancomycin and surgical procedures longer than 4 hours in duration. The final analysis dataset included 4,453 patients. The National Surgical Quality Improvement Program was used for perioperative variables and outcomes. The end point was a composite of wound disruption; superficial, deep, organ space, surgical site infections; and sepsis. Semi-parametric logistic regression was used to study the association between antibiotic timing and infection. RESULTS: There were 444 (10%) patients with a primary end point of infectious complication. A nonlinear "bowl-shaped" relationship between duration of interval from antibiotic administration and surgical incision and infection was observed; lowest risk corresponding to administration time close to incision was 4 minutes before incision (95% one-sided CI, 0-18 minutes). The model suggested optimal timing would result in an 11.3% reduction in the primary infection end point. CONCLUSIONS: Risk of infectious complications decreased as antibiotic administration moved closer to incision time. These data suggest an opportunity to reduce infections by 11.3% by targeting initial antibiotic administration closer to incision.

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#### **1a.8 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

##### **1a.8.1 What process was used to identify the evidence?**

##### **1a.8.2. Provide the citation and summary for each piece of evidence.**