

## Prolonged Perioperative Antibiotics: Not Worth the Risk

### Introduction

Surgical site infections (SSI) place a significant burden on patients, providers, and the healthcare system and are a primary focus of infection prevention and antimicrobial stewardship programs. We previously reviewed the World Health Organization (WHO), American College of Surgeons (ACS), and Centers for Disease Control and Prevention (CDC) guidelines for the prevention of SSI (See prior [August 2017 DASON](#) and [January 2017 DICON](#) newsletters).

Each SSI guideline provides slightly different recommendations for timing of antibiotic discontinuation. For example, the CDC recommends discontinuation of prophylactic antibiotics in all clean and clean-contaminated surgeries immediately after incisional closure. The ACS states the “optimal duration of antibiotic therapy remains unknown”<sup>1,2</sup> for certain clean procedures including joint arthroplasty, and cardiac procedures. Several studies suggest that continuation of perioperative antibiotics beyond 24 hours offers no improvement in SSI rates, but the adverse effects of continued prophylaxis have not been well characterized.<sup>3-5</sup> In the July 2019 issue of *JAMA Surgery*, Branch-Elliman and colleagues published a large, retrospective study across the national Veterans Affairs (VA) health care system evaluating the unintended consequences of prolonged surgical antibiotic prophylaxis (AMP).<sup>6</sup> This newsletter will provide a summarized review and commentary of their findings.

### The Study

Branch-Elliman et al. retrospectively reviewed all patients who underwent cardiac, orthopedic joint, colorectal, and vascular surgeries in the VA healthcare

system from October 2008 through September 2013. Subjects were only excluded if SSI outcomes data was unavailable, resulting in an ultimate review of 79,058 surgical procedures. The outcome variables measured were development of SSI at 30 days, 7-day incidence of acute kidney injury (AKI) and 90-day incidence of *C. difficile* infection. Exposure variables measured were duration of AMP, and choice of AMP, classified as beta-lactam, vancomycin, aminoglycoside, other antibiotic, or combination therapy. Covariates identified *a priori* to adjust for confounding included both patient (age, sex, race, tobacco use one year prior to surgery, history of diabetes, ASA score, prior receipt of NSAIDs or PPIs, MRSA colonization status, mupirocin administration) and surgical (anesthesia type, cardiopulmonary bypass time, and intraoperative blood loss requiring transfusion) factors.

### The Results

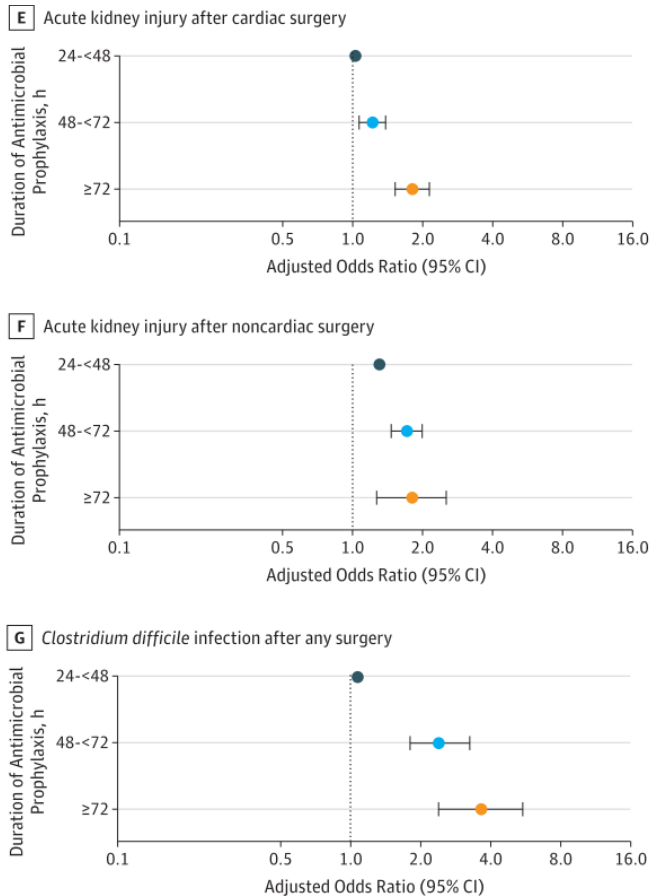
Patients primarily received either a beta-lactam or vancomycin for surgical prophylaxis (93.9% of regimens administered) for a median duration of 18.5 hours after skin closure. However, 21,212 patients received greater than 24 hours of prophylaxis (26.9%) with 886 patients receiving over 72 hours of prophylaxis (1.1%).

In adjusted analysis, patients were stratified into categories by duration of antibiotic therapy by days (i.e., <24 h, 24-<48 h, 48-<72 h, and > 72 h). Accounting for confounders identified *a priori*, prolonged antibiotic prophylaxis after 24 hours did not improve rates of SSI.

**The study’s main finding was that AMP greater than 24 hours was associated with increased risk of AKI and *C. difficile* infection.** These risks increased with each additional day of antibiotic delivery up to 72 hours or more, highlighting a dose-dependent effect. At greater than 72 hours of AMP, the adjusted odds ratio (aOR) of AKI for patients undergoing cardiac surgery was 1.82 (95% CI, 1.54 – 2.16). For patients undergoing noncardiac surgery, the aOR was 1.79 (95% CI, 1.79 – 2.53). For all

surgeries, the aOR of *C. difficile* infection after 72 hours of AMP was measured at 3.65 (95% CI, 2.40 – 5.55). These findings are represented visually in Figure 1.

**Figure 1.** Risk of AKI and *C. difficile* infection with Antibiotic Duration



Furthermore, usage of vancomycin for any length of duration appeared to increase risk of postoperative AKI in both cardiac and noncardiac surgeries. Usage of combination AMP in cardiac surgery correlated with increased risk of AKI, although combination vancomycin and beta-lactam therapy in cardiac surgery was associated with a modest decrease in SSI, with an absolute risk reduction of 0.6%.

The numbers need to harm for AKI were nine, six, and four, and for *C. difficile* infection, 2000, 90, and 50 for each additional day of prophylaxis after 24 hours, respectively. For a busy surgeon’s practice, these numbers are quite significant! This study provides stewards with important data to use in educating

surgeons and other staff about the importance of limiting AMP durations in the perioperative period.

## Limitations

There are several limitations to note with this study. First, its retrospective, observational design limits the ability to adjust for effects of unmeasured confounders on the observed outcome. There may have been selection bias with more complex patients receiving prolonged antibiotic courses. Additional confounding risk factors for *C. difficile* infection, such as concurrent antibiotic usage and length of stay, were not measured. This study also has limited generalizability: the vast majority of participants were male (96.33%) and all received care within the VA healthcare system. Patients who potentially sought treatment for SSI, AKI, or *C. difficile* infection following surgery outside the VA system may have been missed in review. Furthermore, roughly 16% of the initially identified cohort were excluded from analysis for missing SSI outcome data, which potentially may have affected the outcome. Despite these limitations, Branch-Elliman and colleagues present a strong argument for limiting surgical antimicrobial prophylaxis to 24 hours after incision.

## Key Points:

- Among a large cohort of patients undergoing cardiac, orthopedic, colorectal, and vascular surgeries, AMP greater than 24 hours provided **no benefit** with regard to SSI risk, and instead **increased risk of AKI and *C. difficile* infection**.
- Each additional day of antibiotic therapy increased the risk of AKI and *C. difficile*, with the number needed to harm as low as nine patients for just one additional day of therapy.
- In the vast majority of surgical procedures, no antibiotics are needed after surgical closure. In most cardiac, orthopedic, colorectal, and vascular surgeries where antibiotics are continued, the duration should be limited to no more than 24 hours after incision.
- Antibiotic stewards and infection preventionists can use these data to educate perioperative staff about the little benefit and real harm associated with prolonged antimicrobial prophylaxis.

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## References

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