MEDICAL UNIVERSITY OF SOUTH CAROLINA
VALUE INSTITUTE
Evidence-Based Practice Brief
Cardiac Rhythm Device SSI Prevention in Adults

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**ASK THE QUESTION**

**Question:** In adult patients with cardiac arrhythmias requiring implantation of a cardiac rhythm management device, how effective is prophylactic use of cefazolin for decreasing device infection rates compared to vancomycin?

**SEARCH FOR EVIDENCE**

**Databases:** PubMed, Scopus

**PubMed search strategy:** ("Anti-Bacterial Agents"[Mesh] OR antibacterial OR antibiotics OR antimicrobial) AND (prophyla* OR prevent* OR empiric) AND ("Pacemaker, Artificial"[Mesh] OR cardiac resynchronization therapy devices OR cardiac rhythm device implantation OR cardiac implantable electronic device OR CIED)

**Filters:** Humans, English, Published last 5 years

**CRITICALLY ANALYZE THE EVIDENCE**

### Existing External Guidelines

<table>
<thead>
<tr>
<th>Title</th>
<th>Organization and Author</th>
<th>Date</th>
<th>Evidence Evaluation</th>
</tr>
</thead>
</table>
| Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection | British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE) (Sandoe et al.) | 2015 | A: high-quality RCTs and meta-analysis of RCTs  
B: observational data and non-randomized trials  
C: expert opinion or working party consensus |

This published clinical guideline has been evaluated for this review using the University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale. The scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

- Intravenous antimicrobials should be administered within 1 h prior to skin incision. [A]
- Repeat dosing of antimicrobials is not recommended after skin closure. [A]
- The choice of prophylactic agent should cover the most likely pathogens in cardiac implantable electronic device infection. [C]
- A glycopeptide (e.g. intravenous teicoplanin, according to local dosing protocols) is the current preferred agent (with or without gentamicin depending on local Gram-negative infection rates). [C]

There were also four primary research articles found indirectly addressing the prophylactic use of specific antimicrobials for decreasing infection rates in adult patients requiring implantation of a cardiac rhythm management device. Two systematic reviews and meta-analyses (Ali et al., 2017; Koerber et al., 2018) evaluated the role of antibiotic envelopes to decrease cardiac implantable electronic device (CIED) infection. Both meta-analyses found that CIED infection rates were lowered by using antibiotic envelopes, with Ali et al. (2017) reporting a 71% reduction in odds of infection with the use of the TYRX envelope and Koerber et al. (2018) reporting a 69% reduction in infection risk with the use of an antibiotic envelope (both absorbable and non-resorbable). A systematic review and meta-analysis by Kang et al. (2017) evaluated the effectiveness of pocket irrigation with antimicrobial agents for reducing CIED pocket infection. They found that medicated pocket irrigation reduced the odds of infection by 56%, with antibiotics, rather than antiseptics, exerting the protection. Finally, a prospective observational study by Lee et al. (2017) compared the use of preoperative antibiotics only to pre- and postoperative antibiotics for reducing CIED infection. IV cefazolin was the predominant antibiotic used in both groups (98.2% and 93.8%). Their findings are congruent with previous studies that found no additional benefit for the use of postoperative antibiotics (p=0.624).

PICO Question: In adult patients with cardiac arrhythmias requiring implantation of a cardiac rhythm management device, how effective is prophylactic use of cefazolin for decreasing device infection rates compared to vancomycin?

<table>
<thead>
<tr>
<th>Author/Date/ Journal</th>
<th>Purpose of Study</th>
<th>Study Design</th>
<th>Sample &amp; Setting</th>
<th>Outcomes</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ali et al., 2017,</td>
<td>To assess the</td>
<td>Systematic</td>
<td>5 cohort studies (4779)</td>
<td>Odds of CIED infection was 71% lower in</td>
<td>Study Limitations =</td>
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</table>

See Appendix A for full description of the Trustworthy Guideline grading system.
<p>| Therapeutic Advances in Infectious Disease | role of TYRX antibiotic envelope for the prevention of cardiac implantable electronic device (CIED) infection | review &amp; meta-analysis | patients) with a control&lt;br&gt;-4 retrospective, 1 prospective&lt;br&gt;-TYRX: n= 2214&lt;br&gt;-control: n= 2565&lt;br&gt;Only compared the individuals from control and intervention groups who had the most comparable baseline risk factor profile as determined by each study&lt;br&gt;- TYRX: 14 cases of CIED infection&lt;br&gt;- Control: 60 cases of CIED infection&lt;br&gt;Included studies comparing event rates between two or more groups with complete information&lt;br&gt;No evidence of publication bias based on funnel plot analysis&lt;br&gt;the TYRX group (pooled OR 0.29, 95% CI 0.09–0.94; p &lt; 0.004, I²=58%)&lt;br&gt;Sensitivity analysis did not result in statistically significant differences&lt;br&gt;-excluding retrospective: OR 0.20 (95% CI 0.07-0.58); p=0.701&lt;br&gt;-excluding studies with ≤ 6 mo F/U: OR 0.40 (95% CI 0.05-3.25) p=0.809 |
| Koerber et al., 2018, Journal of Cardiovascular Electrophysiology | To compare cardiac implantable electronic device (CIED) infection rates with and without use of an antibiotic envelope | Systematic review &amp; meta-analysis | 5 cohort studies (4490 patients) with a control&lt;br&gt;- antibiotic envelope: n=1798&lt;br&gt;-control: n=2692&lt;br&gt;Excluded studies without a control arm&lt;br&gt;-included a variety of device types, procedures, and risk factors&lt;br&gt;-both absorbable and non-resorbable envelopes&lt;br&gt;CIED infection events:&lt;br&gt;-envelope: n= 13&lt;br&gt;-control: n= 56&lt;br&gt;Use of the antibiotic envelope was associated with a 69% relative risk reduction in CIED infection (pooled RR 0.31, 95% CI 0.17-0.58; p = 0.0002, I²=64%)&lt;br&gt;Propensity matched cohort: use of an antibiotic envelope was associated with an 86% reduction (OR 0.14, 95% CI 0.05-0.41, p = 0.0003, I²=0%) in the odds of a CIED infection&lt;br&gt;Study Limitations = None Systematic Review&lt;br&gt;Review did not address focused clinical question&lt;br&gt;Search was not detailed or exhaustive&lt;br&gt;Quality of the studies was not appraised or studies were of low quality&lt;br&gt;Methods and/or results were inconsistent across studies |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Study Design</th>
<th>Results</th>
<th>Study Limitations</th>
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<tr>
<td>Kang et al., 2017, BMC Cardiovascular Disorders</td>
<td>To evaluate the effectiveness of pocket irrigation with antimicrobial agents for reducing pocket infection during cardiac implantable electronic device (CIED) implantation</td>
<td>Systematic review &amp; meta-analysis</td>
<td>Propensity-matched data from 3 studies based on risk factors (1909 patients) -envelope: n= 956 -control: n= 953</td>
<td>None</td>
</tr>
<tr>
<td>Lee et al., 2017, Clinical Cardiology</td>
<td>To investigate the efficacy of postoperative antibiotics in patients undergoing cardiac implantable electronic device (CIED) implantation</td>
<td>Prospective observational (with control)</td>
<td>Medicated pocket irrigation (antibiotic/antiseptic) reduced the odds of infection by 56% (OR 0.44, 95% CI 0.31-0.63, I² = 32.7%) - subgroup analysis showed that antibiotics, rather antiseptic exerted the protection</td>
<td>None</td>
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**REFERENCES**


### Appendix A. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

#### 1. Transparency

| A | Guideline development methods are fully disclosed. |
| B | Guideline development methods are partially disclosed. |
| C | Guideline development methods are not disclosed. |

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:

- Who wrote the initial draft
- How the committee voted on or otherwise approved recommendations

Evidence review, external review and methods used for updating are not addressed in this standard.
2. Conflict of interest

A
Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members.

B
Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.

C
Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.

NR
Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

A
Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.

B
Guideline development group includes one of the above, but not both.

C
Guideline developers all from one specialty or organization, and no methodologists.

NR
Affiliations of guideline developers not reported.

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

A
Guideline includes a systematic review of the evidence or links to a current review.

B
Guideline is based on a review which may or may not meet systematic review criteria.

C
Guideline is not based on a review of the evidence.

In order to qualify as a systematic review, the review must do all of the following:
Describe itself as systematic or report search strategies using multiple databases
Define the scope of the review (including key questions and the applicable population)
Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

A
Specific supporting evidence (or lack thereof) for each recommendation is cited and graded.
Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded. Recommendations are not supported by specific evidence.

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

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<tbody>
<tr>
<td>A</td>
<td>Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.</td>
</tr>
<tr>
<td>B</td>
<td>Either one or the other of the above criteria is met.</td>
</tr>
<tr>
<td>C</td>
<td>Neither of the above criteria are met</td>
</tr>
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In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

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<tbody>
<tr>
<td>A</td>
<td>Guideline was made available to external groups for review.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline was reviewed by members of the sponsoring body only.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline was not externally reviewed.</td>
</tr>
<tr>
<td>NR</td>
<td>No external review process is described.</td>
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8. Updating and currency of guideline

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<tr>
<td>A</td>
<td>Guideline is current and an expiration date or update process is specified.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline is current but no expiration date or update process is specified.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline is outdated.</td>
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A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.