ASK THE QUESTION

Question: In patients undergoing elective colorectal surgery, is the use of povidone-iodine nasal swabs effective in preventing surgical site infections caused by *Staphylococcus aureus*?

SEARCH FOR EVIDENCE

Databases: PubMed, Scopus

**PubMed search strategy:**

("Surgical Wound Infection"[Mesh] OR "surgical site infection" OR SSI) AND ("Povidone-Iodine"[Mesh] OR povidone-iodine) AND prevent* AND (nasal OR nare)

**Keywords:** surgical wound infection, surgical site infection, SSI, povidone-iodine, nasal, nare*

CRITICALLY ANALYZE THE EVIDENCE

There were 5 studies found addressing the use of povidone-iodine nasal swabs effective in preventing surgical site infections (SSI) caused by *Staphylococcus aureus*. None of the studies were completed in patients undergoing elective colorectal surgery, and publication bias was suspected.

Three of the studies (Bebko et al., 2014; Phillips et al., 2014; Torres et al., 2016) evaluated the use of povidone-iodine nasal swabs in elective orthopedic surgery populations. Bebko et al. (2014) studied the effect of a decontamination protocol that included the following: 1) chlorhexidine washcloth (2%) night before & morning of surgery; 2) chlorhexidine oral rinse (0.12%) night before & morning of surgery; and 3) intranasal povidone-iodine swab (5%) morning of surgery on SSI rates. When comparing SSI rates before and after implementation of the protocol, Bebko and colleagues found that use of the decontamination protocol before surgery was independently associated with a 76% decrease in the odds of SSI within 30 days after surgery (OR 0.24, 95% CI 0.08-0.77). Phillips et al. (2014) compared the use of nasal mupirocin in the 5 days prior to surgery to povidone-iodine application in the 2hr before surgery. Intent to treat analysis showed SSI rates were not significantly different between the two groups (p=0.1), however in patients that were compliant with all components of the protocol (chlorhexidine bath, nasal swab application, prophylactic antibiotics) there was a significant decrease in *S. aureus* SSI development when using povidone-iodine (5 with mupirocin vs 0 with povidone-iodine; p=0.03). Torres et al. (2016) assessed for SSI rates following a protocol change from MRSA screening & treatment to
universal application of povidone-iodine nasal swab 1 hour before surgery and found that SSI rates were similar (0.8% vs 0.8%, p=.10). Cost analysis of the protocol change found a significant decrease in the cost per patient ($121.16+26.18 for the MRSA screening group vs $27.21+0 for the povidone-iodine nasal swab antiseptic group; p ≤ .01).

Anderson et al. (2015) was a laboratory study that showed a marked reduction in S. aureus nasal flora following the application of povidone-iodine versus saline at 1, 6 and 12 hours following application. The ex vivo study also found that 5% povidone-iodine skin & nasal prep decreased MRSA CFUs more effectively than 2% mupirocin and control saline. These findings indicate that povidone-iodine application can minimize MRSA colonization during the hours before surgery, versus multiple applications over a few days like with 2% mupirocin.

An indirectly related systematic review and meta-analysis by Levy et al. (2013) found a marked increase in risk of surgical site infection in cases of nasal carriage of S. aureus (OR 5.92, 95% CI 1.15—30.39; p = 0.033; I²=90%). These findings promote the need for an effective strategy for preventing S. aureus-related SSI, of which povidone-iodine nasal swabs is one viable option.

### PICO Question: In patients undergoing elective colorectal surgery, is the use of povidone-iodine nasal swabs effective in preventing surgical site infections caused by *Staphylococcus aureus*?

<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>Levy et al., 2013, Orthopaedics and Traumatology: Surgery and Research</td>
<td>To assess the relationship between nasal carriage of S. aureus and the development of osteoarticular infection and secondly current methods of decolonization</td>
<td>Systematic review &amp; meta-analysis</td>
<td>Relationship: 5 studies (8337 patients) Methods of decolonization: Mupirocin: 6 studies (5376 patients)</td>
<td>There is a markedly increased risk of surgical site infection in case of nasal carriage of S. aureus (OR 5.92, 95% CI 1.15—30.39; p = 0.033; I²=90%) There was a non-significant trend for intranasal mupirocin to reduce S. aureus SSI: (OR 0.60, 95% CI 0.34—1.06; p = 0.08)</td>
<td>Study Limitations = None Systematic Review = None Review did not address focused clinical question Search was not detailed or exhaustive Quality of the studies was not appraised or studies were of low quality Methods and/or results were inconsistent across studies</td>
</tr>
<tr>
<td>Anderson et al., 2015, Antimicrobial Agents and Chemotherapy</td>
<td>To demonstrate that povidone-iodine skin and nasal prep is effective for preventing of methicillin-resistant S. aureus (MRSA) infections ex vivo, to show its efficacy versus mupirocin in a</td>
<td>Prospective observational (Laboratory)</td>
<td>Nasal flora samples (n=70) with baseline levels of &gt;5 x 10³ CFU/swab -povidone iodine (n=13-18) -saline (n=7-9) Applied povidone-iodine or saline to nostrils for 30s x 2 (1min per nare)</td>
<td>At all three time points, the S. aureus log₁₀ reduction from the baseline level in povidone-iodine skin &amp; nasal prep treated subjects was significantly greater than that observed in the saline control subjects: -0.86 ±0.73 versus 2.3±1.68 at 1 h -0.76±0.58 versus 2.79±1.52 at 6 h -0.6±0.9 versus 2.37±1.77 at</td>
<td>Study Limitations = None Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey) Insufficient sample size Sample not representative of patients in the population as a whole Variables (confounders, exposures, predictors) were not described Outcome criteria not objective or consistent across studies</td>
</tr>
</tbody>
</table>
| Medical University of South Carolina | **novel ex vivo human skin MRSA infection model, and to validate MRSA reduction in the anterior nares of human subjects** | **Flora assessed at:**  
- baseline  
- 1hr post  
- 6hr post  
- 12hr post  
  *Used MRSA-infected porcine vaginal mucosa samples to assess for prevention of infection with povidone-iodine skin & nasal prep vs mupirocin (1hr incubation)* | **12 h [all values are log$_{10}$ CFU])**  
**MRSA CFU recovered from:**  
- untreated controls: log$_{10}$ 4.19±0.12 CFU/sample  
-2% mupirocin-treated: log$_{10}$ 4.53±0.05 CFU/sample  
-5% povidone-iodine skin & nasal prep: log$_{10}$ 0.00±0.00 CFU/sample  
*were not applied in blind fashion*  
☐ Insufficient follow-up, if applicable  
☐ For prognostic study, sample not defined at common point in course of disease/condition  
☐ For diagnostic study, gold standard not applied to all patients  
☐ For diagnostic study, no independent, blind comparison between index test and gold standard | **Bebko et al., 2014, JAMA Surgery**  
**To examine the effect of a MRSA decontamination protocol on SSIs in patients undergoing elective orthopedic surgery with hardware implantation** | **Retrospective observational study (Pre-post intervention)**  
723 patients undergoing elective orthopedic surgery  
Prem: n=344  
Post: n=365  
VA hospital new standard of care (2013):  
- chlorhexidine washcloth (2%) night before & morning of surgery  
- chlorhexidine oral rinse (0.12%) night before & morning of surgery  
- intranasal povidone-iodine swab (5%) morning of surgery  
-MRSA nasal colonization re-assessed in patient admitted 24hr  
- English only, 18+ yr with clinic visit 5 days before surgery | **MRSA nasal carriage on day of admission was not significantly different pre and post intervention (5.7% vs 2.2%, p=0.05)**  
Use of the decontamination protocol before surgery (OR 0.24, 95% CI 0.08-0.77) provided a significant protective effect against the development of an SSI within 30 days after surgery | **Study Limitations =**  
☐ None  
☐ Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey)  
☐ Insufficient sample size  
☒ Sample not representative of patients in the population as a whole  
☐ Variables (confounders, exposures, predictors) were not described  
☐ Outcome criteria not objective or were not applied in blind fashion  
☐ Insufficient follow-up, if applicable  
☐ For prognostic study, sample not defined at common point in course of disease/condition  
☐ For diagnostic study, gold standard not applied to all patients  
☐ For diagnostic study, no independent, blind comparison between index test and gold standard | **Increase Quality Rating if:**  
☐ Large Effect  
☐ Very Low  
☐ Level of evidence for studies as a whole:  
☒ High  
☐ Moderate  
☐ Low  
☐ Very Low  
*company sponsors study on effectiveness of drug*
| Phillips et al., 2014, Infection Control and Hospital Epidemiology | To determine whether a one-time application of nasal povidone-iodine just before surgery would be as effective as twice daily application of nasal mupirocin during the 5 days before surgery in preventing SSI and would provide a more convenient option for patients at a lower cost | RCT | 1697 patients undergoing arthroplastic or spine fusion surgery - Mupirocin (2%): in each nostril 2x daily for 5 days (n=855 ITT; n=763 per protocol) - Povidone-iodine (5%): 2x per nostril within 2hr of surgery (n=842 ITT; n=776 per protocol) Protocol: decontamination with topical chlorhexidine wipes and appropriate antibiotic prophylaxis - Excluded if no FU within 30 days post-surgery or if chronic bone/joint infection at surgical site occurred | Deep SSI within 3 months post-surgery: - Intent to treat analysis was not significantly different (14 SSI with mupirocin vs 6 SSI with povidone-iodine; p=0.1) - Per protocol analysis showed a significant decrease in *S. aureus* SSI development when using povidone-iodine (5 with mupirocin vs 0 with povidone-iodine; p=0.03) | Study Limitations = |
| --- | --- | --- | --- | --- |
| None | RCT & Quasi-Experimental Studies | Insufficient sample size | None | None |
| Lack of randomization | Lack of blinding | Stopped early for benefit | Lack of allocation concealment | Large losses to F/U |
| Lack of blinding | Lack of allocation concealment | Selective reporting of measures | None | Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey) |

<table>
<thead>
<tr>
<th>Torres et al., 2016, Journal of Arthroplasty</th>
<th>To assess rates of SSI within 90 days of surgery after povidone-iodine nasal swab implementation and perform cost analysis comparing povidone-iodine to former mupirocin protocol</th>
<th>Retrospective observational study (Pre-post intervention)</th>
<th>2853 THA/TKA patients - MRSA screening and treatment (n=849) - Povidone-iodine nasal swab (n=1004) Protocol change: MRSA screening &amp; treatment to universal application of povidone-iodine</th>
<th>There were no differences in SSI rates for the groups, with 0.8% of patients in the MRSA screening group and 0.8% of patients in the povidone-iodine nasal swab group experiencing SSI (p=1.0) <strong>The mean cost per case (including chlorhexidine baths) for the MRSA screening group was significantly higher</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Limitations =</td>
<td>None</td>
<td>Insufficient sample size</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Sample not representative of patients in the population as a whole</td>
<td>Variables (confounders, exposures, predictors) were not described</td>
<td>Outcome criteria not objective or meaningful</td>
<td>None</td>
<td>Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey)</td>
</tr>
</tbody>
</table>
nasal swab 1 hour before surgery
All patients were instructed to take chlorhexidine bath for 5 days prior to surgery

$121.16 + 26.18 vs the povidone-iodine nasal swab antiseptic group $27.21 + 0 (p ≤ .01).

were not applied in blind fashion
☐ Insufficient follow-up, if applicable
☐ For prognostic study, sample not defined at common point in course of disease/condition
☐ For diagnostic study, gold standard not applied to all patients
☐ For diagnostic study, no independent, blind comparison between index test and gold standard

REFERENCES


Appendix A: GRADE criteria for rating a body of evidence on an intervention
Developed by the GRADE Working Group

Grades and interpretations:
High: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low: Any estimate of effect is very uncertain.

Type of evidence and starting level
Randomized trial–high
Observational study–low
Any other evidence–very low

Criteria for increasing or decreasing level
Reductions
Study quality has serious (−1) or very serious (−2) problems
Important inconsistency in evidence (−1)
Directness is somewhat (−1) or seriously (−2) uncertain
Sparse or imprecise data (−1)
Reporting bias highly probable (−1)

**Increases**
- Evidence of association† strong (+1) or very strong (+2)
- Dose-response gradient evident (+1)
- All plausible confounders would reduce the effect (+1)

†Strong association defined as significant relative risk (factor of 2) based on consistent evidence from two or more studies with no plausible confounders. Very strong association defined as significant relative risk (factor of 5) based on direct evidence with no threats to validity.

**Appendix B. 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**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline development methods are fully disclosed.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline development methods are partially disclosed.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline development methods are not disclosed.</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>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).</td>
</tr>
<tr>
<td>B</td>
<td>Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.</td>
</tr>
</tbody>
</table>
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

B  Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.

C  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

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<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>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

8. Updating and currency of guideline

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<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>
</tr>
</tbody>
</table>

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.