MEDICAL UNIVERSITY OF SOUTH CAROLINA
VALUE INSTITUTE
Evidence-Based Practice Brief
Appropriate Clinical Indications for Urine Culture in Suspected CAUTI

Author(s): Amanda Davis, MPH, RD, CHES; Emily Brennan, MLIS

ASK THE QUESTION

Question: In patients with a Foley catheter, what are the appropriate clinical indications for urine culture in suspected CAUTI?

SEARCH FOR EVIDENCE

Databases: PubMed, CINAHL, Scopus


Filters: English, Published last 10 years

CRITICALLY ANALYZE THE EVIDENCE

A comprehensive review by Garcia et al. (2017) was published with the goal of consolidating the published evidence on the influence of inappropriate ordering of urine specimens and subsequent treatment of asymptomatic bacteriuria (ASB) and associated adverse effects; review research on bacterial contamination and preservation; and delineate best practices in the collection, handling, and testing of urine specimens for culture or for biochemical analysis in both catheterized and non-catheterized patients. The Centers for Disease Control and Prevention define symptomatic UTI as highlighted below:
Additionally, Garcia and colleagues (2017) consolidated multiple guidelines to indicate the appropriate indications for urine cultures, including catheterized patients, as shown below:

Table 2
Appropriate and inappropriate indications for urine cultures (UC) in asymptomatic and symptomatic patients

<table>
<thead>
<tr>
<th>Asymptomatic patients to screen for bacteriuria</th>
<th>Symptomatic patients to screen for a UTI</th>
<th>Asymptomatic patients to avoid screening for bacteriuria</th>
<th>Avoid UC collection or antimicrobial treatment if basing decision solely on 1 or more of the following findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Pyuria</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Odorous urine</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Cloudy urine</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Change in color</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Sediments</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Turbidity</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Screening urine cultures such as on admission</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Standing orders for urinalysis or urine culture without an appropriate indication</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Panculturing</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Repeat urine culture to document clearing of bacteriuria</td>
</tr>
<tr>
<td>Before transurethral resection of the prostate</td>
<td>Before urologic procedures for which mucosal bleeding is anticipated</td>
<td>Pregnant women</td>
<td>Upon routine catheter insertion</td>
</tr>
</tbody>
</table>

UTI, urinary tract infection.
They further note that for urine culture collection “when a patient with an indwelling urinary catheter develops symptoms of UTI, the old catheter should be removed, and the sample obtained from a newly inserted catheter; if catheter removed, obtain a voided mid-stream urine sample or from or intermittent catheter” as supported by both the American Society for Microbiology (2009) and IDSA (2010) evidence-based guidelines.

There were also six research studies found addressing appropriate clinical indications for urine culture for suspected CAUTI. Three of these studies (Gralton et al., 2017; Sarg et al., 2016; Shirley et al., 2017) were quasi-experimental studies evaluating interventions to improve the clinical appropriateness of urine specimen culture in hospitalized patients with urinary catheters. Gralton et al. (2017) evaluated a decision support tool created to minimize the volume of urine specimens from acute aged care patients (≥ 65 yo) with indwelling urinary catheters at a hospital in Australia. As a result of this intervention, the total number of catheter urine specimens decreased significantly (p=0.02) while the proportion of specimens from catheters was not significantly different (p=0.26) between the two time periods. Sarg et al. (2016) evaluated antimicrobial utilization before and after implementation of a reflexive urine culture only if there was evidence of pyuria. They found a 30% decrease in the rate of urine cultures performed immediately following the intervention (p<0.001), followed by a 6% relative decrease in the month-to-month trend over 12 months (p<0.05). The proportion of patients started on antimicrobials based on the result of the index urine-culture order was also significantly lower (pre: 41% vs post: 23%). Shirley et al. (2017) used a pilot study to evaluate the impact of an EMR-anchored intervention, based on an institutional appropriateness guideline, to reduce unnecessary urine cultures in two critical care units at an academic medical center. After implementation and minor updates to the intervention based on feedback, there was a significant downward trend in urine cultures ordered for catheterized patients (1.3 orders per 1,000 catheter days; p = .031) after 2 months.

There were also three observational studies (Drekonja et al., 2014; Hartley et al., 2013; Jones et al., 2016) that evaluated physician and nursing knowledge and use of urine culture for suspected CAUTI compared to evidence-based guidelines. Drekonja et al. (2014) evaluated the appropriateness of urine culture ordering and associated antimicrobial use in hospitalized patients at a VA hospital. They found that while 69% urine culture orders were appropriate, only 13% of appropriate cultures were obtained for dysuria or frequency. In the study, 63% of appropriate urine cultures were obtained for non-specific clinical manifestations, usually presence of 2+ SIRS criteria, although the majority of these patients had a known or suspected non-UTI condition that could explain these clinical manifestations. Jones et al. (2016) evaluated 394 nurses’ knowledge regarding appropriate reasons and methods to obtain urine culture specimens in patients with urinary catheters. Overall, these nurses tended to agree with obtaining a urine culture based on smell, color, and consistency of urine, none of which are supported by clinical guidelines. Hartley et al. (2013) retrospectively reviewed the documented indications for urine culture in 208 randomly sampled adult inpatients at a hospital in the University of Michigan Health System and compared them to multiple evidence-based guidelines (e.g., IDSA, CDC, National Institute on Disability and Rehabilitation). This study, which included inpatients with and without urinary catheters, found that 57.7% of patients did NOT meet guideline-based criteria for a urine culture.

<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>Gralton et al., 2017, Infection, Disease and Health</td>
<td>To test the effect and practicality of a decision support tool to inform clinically appropriate urine specimen collection and culture for patients with urinary catheters</td>
<td>Quasi-experimental (before/after)</td>
<td>Patients (65 years and older) in an acute aged care ward of a major tertiary hospital in Australia</td>
<td>Total number of urine specimens collected decreased significantly (pre: 81 vs post: 52; p=0.005) -total number of catheter urine specimens decreased significantly (pre: 26 vs post: 12; p=0.02) while the proportion of specimens from catheters was not significantly different (p=0.26)</td>
<td>Study Limitations = None</td>
</tr>
</tbody>
</table>

## PICO Question

<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>Gralton et al., 2017, Infection, Disease and Health</td>
<td>To test the effect and practicality of a decision support tool to inform clinically appropriate urine specimen collection and culture for patients with urinary catheters</td>
<td>Quasi-experimental (before/after)</td>
<td>Patients (65 years and older) in an acute aged care ward of a major tertiary hospital in Australia</td>
<td>Total number of urine specimens collected decreased significantly (pre: 81 vs post: 52; p=0.005) -total number of catheter urine specimens decreased significantly (pre: 26 vs post: 12; p=0.02) while the proportion of specimens from catheters was not significantly different (p=0.26)</td>
<td>Study Limitations = None</td>
</tr>
</tbody>
</table>

### Study Limitations

- High risk of bias (When design limitations for one or more criteria impact the quality of studies sufficiently enough to lower confidence in the estimate of effect)
- Studies inconsistent

© 2017 MUSC Value Institute Quality Management/Library, Medical University of South Carolina
**Sarg et al., 2016 Infection Control and Hospital Epidemiology**

**Objective:** To assess antimicrobial utilization before and after a change in urine culture ordering practice in adult ICUs.

**Design:** Quasi-experimental (before/after)

**Participants:** Patients in 7 adult ICUs at a single academic medical center (2012 vs 2013)

**Intervention:** New urine-culture ordering practice known as reflex urine culture was introduced: urinalysis was performed first and urine culture was performed reflexively only if there was evidence of pyuria (i.e., urine WBC count > 10 per high power field [hpf]).

**Analysis:**
- Population level:
  - There was a 30% decrease in the rate of urine cultures performed immediately following the intervention (p<0.001), followed by a 6% relative decrease in the month-to-month trend over 12 months (p<0.05)
  - No significant change in the antimicrobial utilization rate either immediately following the intervention or in the relative month-to-month trend over 12 months

- Patient level:
  - Pre-intervention 100% were ordered as regular urine cultures; post-intervention 30% were ordered as regular urine cultures, 70% ordered as reflex cultures
  - Proportion of patients detected to have bacteriuria was significantly less in the post-intervention group (pre-intervention 31%; post-intervention 16%; p<.05)
  - Proportion of patients (not previously on antimicrobials) started on a new antimicrobial based on the result of the index urine-culture order was significantly lower (post-intervention 23%; pre-intervention 41%, p = 0.002)

**Study Limitations:**
- None

---

**Shirley et al., 2016 Quaternary Care**

**Objective:** To examine the change in urine culture ordering practice in 2 critical care units.

**Design:** Quasi-experimental

**Participants:** There was a non-significant decrease in urine specimens for culture were being collected at a more appropriate frequency after implementation of the new tool.

**Study Limitations:**
- None

---

**RCT & Quasi-Experimental Studies**

- Insufficient sample size
- Lack of randomization
- Lack of blinding
- Stopped early for benefit
- Lack of allocation concealment
- Selective reporting of measures
- Large losses to F/U

---

**Publication Bias**

- E.g., pharmaceutical company sponsors study on effectiveness of drug

---

**Increase Quality Rating if:**

- Large effect (When the relative risk of association between two factors is large or very large)

---

**Dose response**

- When the dose-response relationship increases the confidence that an effect is real and substantial

---

**Plausible confounders**

- When plausible residual confounding is directly impacting the magnitude of effect
<table>
<thead>
<tr>
<th>Year</th>
<th>Study Title</th>
<th>Study Design</th>
<th>Study Details</th>
<th>Findings</th>
<th>Level of evidence for studies as a whole</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Infection Control and Hospital Epidemiology</td>
<td>Impact of an EMR-anchored intervention to reduce unnecessary urine cultures</td>
<td>Experimental (before/after)</td>
<td>at an academic medical center over 4 months -Pre: 2 months (1115 catheter days) -Post 1: 2 months (1086 catheter days); updates were made based on feedback -Post 2: 2 months (1113 catheter days) Necessity based on an institutional guideline regarding urine culture indications (see table below) -embedded into the EMR urine culture order and visible to all providers</td>
<td>Urine cultures (UCs) ordered during post-intervention Period 1 and 34% fewer UCs were ordered for catheterized patients during post-intervention Period 2 (pre: 62, post 1: 48, post 2: 41; p=0.049) -there was a significant downward trend in UCs ordered for catheterized patients (1.3 orders per 1,000 catheter days; p = .031) There was no significant difference in the number of UAs or UCs ordered in patients with urinary catheters in other critical care units during the same time period The most commonly selected indication for UC in patients with urinary catheters was fever, followed by anticipated urologic surgery and suprapubic pain or tenderness</td>
</tr>
<tr>
<td>2014</td>
<td>Drekonja et al.</td>
<td>To evaluate the appropriateness of urine culture ordering and associated antimicrobial use in hospitalized patients</td>
<td>Prospective cohort</td>
<td>496 urine cultures from 351 inpatients at Minneapolis Veterans Affairs medical center over 3 months (97% male) -indwelling or condom catheters (33%) -high count growth (&gt;100,000 CFU/mL)</td>
<td>Appropriateness of culture: -69% urine culture (UC) orders were appropriate -15% were inappropriate -16% were indeterminate Only 13% of the presumably appropriate cultures were obtained for dysuria or frequency -63% of UCs were obtained for non-specific clinical manifestations, usually presence of 2 or more SIRS criteria -in 65% of the appropriate UCs, the patient had a known or suspected non-UTI condition that could explain the clinical manifestation(s) that prompted the culture High-count growth was more common with inappropriate (27%) or indeterminate (21%) cultures compared with appropriate cultures (15%; p = 0.04) -high-count growth was strongly predictive of antimicrobial therapy (OR</td>
</tr>
</tbody>
</table>

**Study Limitations =**
- None

**RCT & Quasi-Experimental Studies**
- Insufficient sample size
- Lack of randomization
- Lack of blinding
- Stopped early for benefit
- Lack of allocation concealment
- Selective reporting of measures
- Large losses to F/U

**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 and accounted for
- 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
<table>
<thead>
<tr>
<th>Study Authors and Source</th>
<th>Study Design</th>
<th>Study Population</th>
<th>Study Methods</th>
<th>Results</th>
<th>Study Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hartley et al., 2013, Infection Control and Hospital Epidemiology</td>
<td>Retrospective chart review</td>
<td>208 randomly sampled adult inpatients at the University of Michigan Health System with a urine culture (2008-09)</td>
<td>-excluded if: previous renal transplant or urinary diversion surgery, urinary stents or nephrostomy tubes in place, admission to the ICU at the time of culture, pregnancy, treatment for UTI as an outpatient at the time of admission, receipt of empirical treatment for UTI for &gt; 48 hours before urine culture, and hospital discharge or death before urine culture results were reported</td>
<td>57.7% of patients did NOT meet guideline-based criteria for a urine culture -20% for screening before an orthopedic procedure -13.3% for altered mental status without a urinary catheter -37.5% had no documented reason for culture 84.6% had no growth, and this rate was similar regardless of the presence or absence of guideline-based criteria (84.1% vs 85.0%) Emergency department (p=0.01) and outpatient procedure area (p&lt;0.01) admissions were significantly more likely to order urine cultures for inappropriate indications There was excellent inter-rater agreement for appropriateness of obtaining culture (k=0.89)</td>
<td>Study Limitations = None</td>
</tr>
<tr>
<td>Jones et al., 2016, American Journal of Infection Control</td>
<td>Cross-sectional survey</td>
<td>Convenience sample of 384 nurses at 5 hospitals completed a 40-question survey regarding their self-reported CAUTI identification knowledge: 15.7% excellent 38.1% above average 43.1% average 3.0% below average</td>
<td></td>
<td></td>
<td>Study Limitations = None</td>
</tr>
</tbody>
</table>
| methods to obtain urine culture specimens in patients with urinary catheters | knowledge, training and practices of appropriate reasons for obtaining urine cultures  
- single health care system in SE Michigan  
- ICU and non-ICU settings  
Survey reviewed by nurses, infection preventionists and ID physicians before distribution  
- included 19 clinical scenarios (urine collection correct, incorrect or controversial) | 76.1% had received education regarding strategies to reduce CAUTI risk in the past 12 months  
- no difference between ICU and non-ICU nurses  
- no difference between hospitals  
- only 58.3% of ICU nurses and 54.3% of non-ICU nurses reported receiving education on how to correctly obtain a urine culture in the past 12 months  
- 92.9% of respondents said additional education about obtaining a urine culture was important  
83% of nurses surveyed reported that they never collect urine samples by draining directly from the drainage bag, but only 58.4% reported others to be fully compliant with that standard (p < .001)  
- 55.3% of nurses reported that PCTs collected specimens > 60% of the time  
- 78.9% reported they would obtain the specimen by aspirating from the sampling port either with a syringe or other access device designed to collect urine samples from an indwelling urinary catheter  
- 17% report that at one point they have collected a culture from a urine bag, and 41.6% of them have observed others doing the same  
Overall, respondents tended to agree with obtaining a urine culture based on smell, color, and consistency of urine, none of which are supported by clinical guidelines (See Table 1 below)  
- almost half of nurses surveyed would obtain urine cultures either at the time of urinary catheter placement (46.0%) or after being in place for >3 days (45.8%) | study/series, survey | □ Insufficient sample size  
☒ Sample not representative of patients in the population as a whole  
□ Variables (confounders, exposures, predictors) were not described and accounted for  
□ 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 |
Gralton et al. (2017)

Fig. 1 Decision support tool for improved appropriateness of specimen collection from patients with an IDC. Since the completion of this study this tool has been updated and can be downloaded from here: http://www.cec.health.nsw.gov.au/patient-safety-programs/adult-patient-safety/cauti-prevention/maintenance-and-care.
### Shirley et al. (2017)

**Table 1. Appropriate and Inappropriate Urine Culture Indications in Catheterized Patients**

<table>
<thead>
<tr>
<th>Indications for Urine Culture in Catheterized Patients</th>
<th>Inappropriate Indications for Urine Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Suprapubic pain/tenderness</td>
<td>• Abnormal urine quality</td>
</tr>
<tr>
<td>• Acute gross hematuria</td>
<td>• Routine component of “pan-culture” in fever evaluation until other etiologies have been excluded</td>
</tr>
<tr>
<td>• Costovertebral angle tenderness</td>
<td>• Asymptomatic pruria</td>
</tr>
<tr>
<td>• New fever/rigres with clinical assessment negative for more likely etiology</td>
<td>• Asymptomatic elderly, diabetic or institutionalized patient</td>
</tr>
<tr>
<td>• Acute alteration of mental status with clinical assessment negative for more likely etiology</td>
<td>• Routine documentation of bacteriuria clearance</td>
</tr>
<tr>
<td>• Alteration in medical condition with clinical assessment negative for more likely etiology in patient whom fever may not be a reliable sign</td>
<td></td>
</tr>
<tr>
<td>• Increased spasticity or autonomic dysreflexia in patients with altered neurologic sensation</td>
<td></td>
</tr>
</tbody>
</table>

### Jones et al. (2016)

Table 1

<table>
<thead>
<tr>
<th>Statement</th>
<th>Answered true</th>
<th>Answered false</th>
<th>Answered do not know</th>
<th>Statement is</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Foul-smelling urine</td>
<td>172/210 (82.5)</td>
<td>6/210 (2.8)</td>
<td>38/210 (1.8)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>2. Hematuria</td>
<td>208/204 (62.7)</td>
<td>91/204 (33.7)</td>
<td>25/204 (6.5)</td>
<td>Correct</td>
</tr>
<tr>
<td>3. Cloudy urine</td>
<td>272/201 (65.5)</td>
<td>12/201 (3.0)</td>
<td>5/201 (1.2)</td>
<td>Correct</td>
</tr>
<tr>
<td>4. Urine sediment</td>
<td>90/169 (52.8)</td>
<td>42/169 (25.1)</td>
<td>17/169 (10.1)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>5. Urine color becoming darker in color</td>
<td>269/282 (94.9)</td>
<td>140/282 (50.0)</td>
<td>35/282 (12.5)</td>
<td>Correct</td>
</tr>
<tr>
<td>6. Urgency (urgency to urinate)</td>
<td>50/385 (13.1)</td>
<td>80/385 (20.8)</td>
<td>10/385 (2.6)</td>
<td>Correct</td>
</tr>
<tr>
<td>7. Catheter insertion routinely</td>
<td>174/378 (46.0)</td>
<td>176/378 (46.6)</td>
<td>28/378 (7.4)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>8. Catheter present for ≥3 days</td>
<td>186/378 (49.3)</td>
<td>100/384 (26.4)</td>
<td>42/384 (10.9)</td>
<td>Correct</td>
</tr>
<tr>
<td>9. Chronic urinary catheter on admission</td>
<td>265/389 (68.4)</td>
<td>10/389 (2.6)</td>
<td>20/389 (5.1)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>10. New onset lower abdominal pain</td>
<td>297/385 (76.7)</td>
<td>54/385 (14.0)</td>
<td>34/385 (8.8)</td>
<td>Correct</td>
</tr>
<tr>
<td>11. New onset confusion in an elderly patient (&gt;65 y old)</td>
<td>381/391 (97.6)</td>
<td>23/391 (5.9)</td>
<td>7/391 (1.8)</td>
<td>Correct</td>
</tr>
<tr>
<td>12. Patient going for bladder tumor resection</td>
<td>194/386 (50.3)</td>
<td>84/386 (21.8)</td>
<td>100/386 (26)</td>
<td>Correct</td>
</tr>
<tr>
<td>13. Patient going for colon surgery</td>
<td>119/381 (31.2)</td>
<td>130/381 (34.3)</td>
<td>123/381 (32.5)</td>
<td>Correct</td>
</tr>
<tr>
<td>14. Temperature of 38°C (100.4°F) with stable blood pressure and heart rate without clear source</td>
<td>287/386 (74.4)</td>
<td>69/386 (17.9)</td>
<td>28/386 (7.2)</td>
<td>Correct</td>
</tr>
<tr>
<td>15. Temperature of 38°C (100.4°F) with hypotension without clear source</td>
<td>323/388 (85.0)</td>
<td>21/388 (6.7)</td>
<td>38/388 (9.8)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>16. Temperature of 38°C (100.4°F) with hypotension in a patient with pneumonia</td>
<td>185/383 (48.3)</td>
<td>124/383 (32)</td>
<td>64/383 (16.7)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>17. A urine WBC (un spun) of 25 cells</td>
<td>135/378 (35.6)</td>
<td>93/378 (24.7)</td>
<td>148/378 (39.4)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>18. A urine WBC (un spun) of 100 cells</td>
<td>226/378 (59.8)</td>
<td>22/378 (5.8)</td>
<td>130/378 (34.4)</td>
<td>Incorrect</td>
</tr>
<tr>
<td>19. A urine WBC (un spun) of 500 cells</td>
<td>265/384 (69)</td>
<td>12/384 (3.1)</td>
<td>107/384 (27.9)</td>
<td>Incorrect</td>
</tr>
</tbody>
</table>

*NOTE: Values are n/N (%) or as otherwise indicated.
WBC, white blood cells.*
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 (RR 2-5 or 0.5-0.2) based on consistent evidence from two or more studies with no plausible confounders;
Very strong association defined as significant relative risk (RR >5 or <0.2) based on direct evidence with no threats to validity