

**Summary Statement Title:**

**Antibiotic exposure and the risk of Methicillin-resistant *Staphylococcus aureus* (MRSA): Evidence and implications for public health**

**Quality Assessment Rating: 7 (moderate)**

**Review on which this summary statement is based:**

Tacconelli, E., De Angelis, G., Cataldo, M.A., Pozzi, E., & Cauda, R. (2008). **Does antibiotic exposure increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) isolation? A systematic review and meta-analysis.** *Journal of Antimicrobial Chemotherapy*, 61, 26-38.

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*This is a summary statement written to condense the work of the authors of this systematic review, referenced above. The intent of this summary is to provide an overview of the findings and implications of the full review. For more information on individual studies included in the review, please see the review itself.*

**Review Content Summary**

A systematic review and meta-analysis were performed to determine whether antibiotic exposure acts as a risk factor for the isolation of methicillin-resistant *Staphylococcus aureus* (MRSA). Studies were included if they presented data on the relationship between antibiotic use and MRSA colonization or infection in adult patients. Seventy-six studies (case-control studies, cohort studies, and prevalence surveys) met such inclusion criteria. Thirty-five studies included patients with healthcare-associated MRSA, 26 with community-acquired MRSA (CA-MRSA), and 15 with mixed isolation. Antibiotic therapy studied included beta-lactams, glycopeptides, macrolides and quinolones. Findings suggest that subjects who have been exposed to antibiotic therapy have an increased risk of acquiring MRSA as opposed to non-exposed subjects. Such findings will help inform policy on the appropriate management of antibiotic therapy, with the subsequent hope of decreasing the incidence of MRSA.

**Comments on this review's methodology**

This is a methodologically moderate systematic review. Using satisfactory inclusion criteria, the authors searched two electronic health databases from December 1976 to June 2007, and reviewed reference lists of retrieved articles. The search strategy could have been more comprehensive. The level of evidence of the primary studies included in the review was clearly outlined. The authors failed to assess the methodological quality of primary studies, but did independently extract data on various study characteristics (including research design and sample size). The authors detected significant heterogeneity among studies, and thus explored potential sources of heterogeneity through subgroup and sensitivity analyses. The authors then computed a summary relative risk (RR) of the effects with a 95% confidence interval (CI) using the inverse variance fixed effects method. Lastly, studies were weighted according to sample size.

**Why is this issue of interest to public health?**

While methicillin is effective in treating most *Staphylococcus aureus* infections, some bacteria have developed resistance to methicillin and can no longer be killed by this antibiotic.<sup>1</sup> In 2006, the Canadian Nosocomial Infection Surveillance Program identified 5787 new cases of MRSA.<sup>2</sup> Of this number, acute care hospitals and long-term care facilities accounted for 3561 and 452 cases respectively. CA-MRSA accounted for 893 cases and the remaining 404 cases were unknown.<sup>2</sup> The emergence and spread of MRSA is of concern for several reasons. MRSA may cause life-threatening infections in a substantial number of colonized patients.<sup>3</sup> MRSA is typically multi-drug resistant, and thus treatment options are limited. Vancomycin, a potentially more toxic and less effective antibiotic, is the current treatment of choice for serious MRSA infections.<sup>3</sup> However, MRSA strains with reduced susceptibility to vancomycin are now being reported.<sup>3</sup> Finally, patients harbouring MRSA require prolonged hospitalization, special control measures, costly treatments and extensive surveillance. It is suggested that the direct health care cost attributable to MRSA in Canada averaged \$82 million in 2004 and could reach \$129 million in 2010.<sup>3</sup> MRSA is a costly public health issue that needs to be tackled if the growing burden of this disease in Canadian hospitals, long-term care facilities, and communities is to be limited.<sup>3</sup>

## Evidence and implications

Evidence points are not weighted or ranked according to strength

What's the evidence?	Implications for practice and policy:
<p><b>1. Antibiotic use and MRSA isolation</b> (76 studies)</p> <p>1.1. Participants who were previously treated with antibiotic therapy were almost twice more likely to acquire MRSA (infection or colonization) than participants who did not receive antibiotics. The true risk ranged from 1.7 to 1.9 times more likely (RR 1.8, 95%CI 1.7 to 1.9, p&lt;0.001).</p> <p>1.2. For specific classes of antibiotics, (18 studies)</p> <p>1.2.1. <b>Quinolones</b> - Participants who were previously treated with quinolones were three times more likely to acquire MRSA than participants who did not receive antibiotics. The true risk ranged from 2.5 to 3.5 times more likely (RR 3, 95%CI 2.5 to 3.5).</p> <p>1.2.2. <b>Glycopeptides</b> - Participants who were previously treated with glycopeptides were almost three times more likely to acquire MRSA than participants who did not receive antibiotics. The true risk ranged from 2.4 to 3.5 times more likely (RR 2.9, 95%CI 2.4 to 3.5).</p> <p>1.2.3. <b>Cephalosporins</b> - Participants who were previously treated with cephalosporins were over twice as likely to acquire MRSA as participants who did not receive antibiotics. The true risk ranged from 1.7 times more likely to 2.9 times more likely (RR 2.2, 95%CI 1.7 to 2.9).</p> <p>1.2.4. <b>Other <math>\beta</math>-lactams</b> - Participants who were previously treated with other <math>\beta</math>-lactams were almost twice as likely to acquire MRSA as participants who did not receive antibiotics. The true risk ranged from 1.9 times more likely to 2.2 times more likely (RR 1.9, 95%CI 1.7 to 2.2).</p>	<p><b>1. Antibiotic use and MRSA isolation</b></p> <p>Public health organizations should collaborate with hospitals and community-based care providers that prescribe antibiotics to:</p> <p>1.1. inform health care providers and the general population of the clear association between exposure to antibiotics and isolation of MRSA (infection or colonization) and evidence-informed prevention strategies</p> <p>1.2. advocate for reductions in the use of antibiotics, especially quinolones and glycopeptides</p> <p>1.3. participate in a MRSA surveillance system to improve recognition of MRSA</p>
<p><b>2. Methodological issues of primary studies</b></p> <p>2.1. Varied control group definition</p> <p>2.2. Varied sampling sources</p> <p>2.3. Failure to state type of infection included</p> <p>2.4. Lack of data on antibiotic use and dosages</p> <p>2.5. Varied length of time in which antibiotic exposure was detected</p> <p>2.6. Failure to adjust for covariates</p>	<p><b>2. Program Evaluation and Research</b></p> <p>2.1. High quality research and rigorous program evaluations should be conducted to further investigate the association between antibiotic exposure and development of MRSA.</p>
<p><b>3. Cost benefit or cost-effectiveness information</b></p> <p>3.1. Cost benefit and cost-effectiveness information was not included in this review</p>	<p><b>3. Cost benefit or cost-effectiveness information</b></p> <p>3.1. Future research should include the cost-effectiveness of interventions.</p>
<p><b>General implications</b></p> <ul style="list-style-type: none"> <li>• There is a clear association between antibiotic use and MRSA isolation.</li> <li>• There is a role for public health in advocating for reduced antibiotic use among key stakeholder groups</li> </ul>	
<p><b>Legend:</b> CI – Confidence Interval; OR – Odds Ratio; RR – Relative Risk  **please see the <a href="http://www.health-evidence.ca/glossary-of-terms">health-evidence.ca glossary of terms</a> (found under 'How to Use This Site') for definitions</p>	

## References used to outline issue

1. Canadian Centre for Occupational Health & Safety. (2005). *Methicillin-resistant Staphylococcus aureus*. Retrieved from [http://www.ccohs.ca/oshanswers/biol\\_hazards/methicillin.html](http://www.ccohs.ca/oshanswers/biol_hazards/methicillin.html)
2. Public Health Agency of Canada. (2006). *The Canadian Nosocomial Infection Surveillance Program: Surveillance for methicillin-resistant Staphylococcus aureus (MRSA) 2006 results*. Retrieved from [http://www.phac-aspc.gc.ca/nois-sinp/projects/pdf/mrsa\\_report2006-eng.pdf](http://www.phac-aspc.gc.ca/nois-sinp/projects/pdf/mrsa_report2006-eng.pdf)
3. Goetghebeur, M. (2007). Methicillin-resistant Staphylococcus aureus: A public health issue with economic consequences. *Canadian Journal of Infectious Diseases and Medical Microbiology*, 18(1), 27-34.

## Other quality reviews on this topic

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- Arnold, S. R., & Straus, S. E. (2005) Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database of Systematic Reviews, Issue 4*, Art. No.: CD003539.
- Safdar, N., & Bradley, E. A. (2008). The risk of infection after nasal colonization with *Staphylococcus aureus*. *The American Journal of Medicine*, 121(4), 310-315N.

## Related links

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- Canadian Nosocomial Infection Surveillance Program <http://www.phac-aspc.gc.ca/nois-sinp/survprog-eng.php>
- Centers for Disease Control and Preventions <http://www.cdc.gov/>
- National Collaborating Centre for Infectious Diseases <http://www.nccid.ca/en/home>
- Antimicrobial Resistance and Nosocomial Infections Laboratory <http://www.nml-lnm.gc.ca/eb-be/ARNI-RAIN-eng.htm>
- Canadian Committee on Antibiotic Resistance <http://www.ccar-ccra.com/>
- Canadian Antimicrobial Resistance Alliance <http://www.can-r.com/>
- Canadian Integrated Program on Antimicrobial Resistance Surveillance <http://www.phac-aspc.gc.ca/cipars-picra/index-eng.php>
- Community Hospital and Infection Control Association <http://www.chica.org/>

## Suggested citation

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Bruinsma, K., Robeson, P., & Dobbins, M. (2010). Antibiotic exposure and the risk of methicillin-resistant *Staphylococcus aureus* (MRSA): Evidence and implications for public health. Hamilton, ON: McMaster University. Retrieved from [http://www.health-evidence.ca/documents/18757/Tacconelli\\_2008\\_Summary\\_Statement\\_-\\_English.pdf](http://www.health-evidence.ca/documents/18757/Tacconelli_2008_Summary_Statement_-_English.pdf)

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