# Cochrane for Clinicians

*Putting Evidence into Practice*

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

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## Calcium Supplementation for Preventing Hypertensive Disorders in Pregnancy

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### Clinical Question

Does calcium supplementation prevent hypertensive disorders in pregnancy?

### Evidence-Based Answer

High-dose calcium supplementation (i.e., at least 1,000 mg per day) during pregnancy reduces the risk of developing hypertension and preeclampsia. The most significant risk reduction occurs in women at risk of hypertensive disorders and those with low-calcium diets. (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

### Practice Pointers

Hypertensive disorders occur in up to 10% of pregnancies and are a major source of fetal and maternal morbidity and mortality.[1] Although early recognition and treatment have improved some outcomes, the pathogenesis of preeclampsia spectrum disorders is still not well understood. The incidence of all hypertensive disorders of pregnancy is increasing in the United States, making the need for prevention even greater. More than one-half of women of childbearing age do not have adequate calcium intake.[2]

The authors identified 13 randomized controlled trials (RCTs) comparing high-dose calcium supplementation (at least 1,000 mg per day) with placebo or no calcium in 15,730 women. Meta-analysis showed a risk reduction with calcium supplementation for hypertension (relative risk = 0.65; 95% confidence interval [CI], 0.53 to 0.81) and for preeclampsia (relative risk = 0.45; 95% CI, 0.31 to 0.65). Eight of the RCTs looked specifically at women with low-calcium diets (less than 900 mg per day). These trials included 10,678 women, and found even greater risk reduction for hypertensive disorders with calcium supplementation (relative risk = 0.36; 95% CI, 0.20 to 0.65). There was also a decrease in preterm births, but no difference in neonatal intensive care unit (NICU) admissions or stillbirths. Overall, the number needed to treat (NNT) to prevent one case of preeclampsia in the general population is 28, and in patients at high risk of preeclampsia, the NNT is 7.

The authors also examined 10 RCTs that evaluated low-dose calcium supplementation in 2,234 women. Although there were reductions in hypertension, preeclampsia, NICU admissions, and preterm birth, most of the participants were already at high risk of preeclampsia. Because of the high risk of bias and small sample size, more studies are needed to determine the effectiveness of recommending low-dose calcium supplementation.

In persons with low-calcium diets who are at high risk of hypertensive disorders, calcium supplementation could prevent the development of these disorders. Based in part on this Cochrane review, the World Health Organization recommends supplementing at-risk pregnant women with the equivalent of 1.5 to 2.0 g of elemental calcium daily (i.e., 3,750 to 5,000 mg of calcium carbonate daily).[3] Family physicians should consider calcium supplementation in conjunction with other recommendations for preventing pregnancy-related hypertensive disorders.

SOURCE: Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev.* 2014;(6):CD001059.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD001059.

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## Point-of-Care C-Reactive Protein Testing to Help Guide Treatment of Acute Respiratory Infections

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### Clinical Question

Does point-of-care measurement of C-reactive protein (CRP) reduce inappropriate antibiotic prescribing for patients with acute respiratory infections?

### Evidence-Based Answer

Point-of-care CRP testing used as an adjunct to a physician's clinical examination can modestly reduce antibiotic use. Measurement of CRP to guide antibiotic prescription does not appear to affect the duration of illness or recovery, although one study suggests that it increases the risk of hospitalization. The best algorithm is not known, although most state that a CRP level of less than 20 mg per L (190.5 nmol per L) suggests a viral infection. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

### Practice Pointers

Acute respiratory infections are among the most common symptomatic reasons for visits to family physicians.[1,2] These predominantly viral infections are the most common indication for an antibiotic prescription, despite a lack of benefit for most patients.[2-5] An estimated 41 million unnecessary antibiotic prescriptions are written at a cost of $1.1 billion per year for noninfluenza viral respiratory infections.[6] Guidelines already advocate the use of CRP to help determine the appropriateness of antibiotics in patients with lower respiratory infection.[7]

The authors of this Cochrane review examined the evidence for point-of-care biomarkers to guide antibiotic prescribing in primary care settings and found only studies of CRP. They identified six randomized controlled trials with 6,183 participants from primary care settings for this systematic review; the mean age of participants was 46 years, and 139 were children. CRP was generally not used if the clinician was confident about the decision to initiate or withhold antibiotic treatment. A variety of algorithms were used, with a CRP level of less than 20 mg per L suggesting a viral infection and no need for antibiotics. The studies were conducted in Europe and Russia between 1995 and 2013; two of the studies were directly supported by manufacturers of QuikRead CRP analyzers (Orion Diagnostica) and NycoCard Reader II (Nycomed Pharma). Overall the studies had a low to moderate risk of bias.

The primary outcome was the number of patients given an antibiotic prescription at the index consultation and at follow-up 28 days later. All studies showed a statistically significant reduction in the number of antibiotic prescriptions issued for acute respiratory infections when CRP was used to guide therapy (relative risk [RR] = 0.78; 95% confidence interval [CI], 0.66 to 0.92). Studies in which practices were randomized had a greater effect (number needed to treat = 6) than those in which individual patients were randomized (number needed to treat = 20), although there was significant variability between studies. The effect was maintained at day 28. No difference was found between groups for the number of patients with substantial improvement at day 7, and no deaths or serious complications were reported.

The number of patients in need of hospital admission at 28 days was based on a single study. Out of 30 hospitalizations in 4,264 patients, 22 hospitalizations occurred in the CRP groups vs. eight in the control group. The effect was no longer statistically significant after adjusting for whether patients or practices were randomized (RR = 2.45; 95% CI, 0.65 to 9.19). No data were available on which hospitalized patients did not initially receive antibiotic treatment or on their initial CRP levels. There were no differences in the number of patients requiring reconsultation at 28 days, the duration of acute respiratory infections, the number of satisfied patients, or the number of patients with substantial improvement at 28 days.

The meta-analysis did not identify an optimal algorithm and therefore should be considered proof of concept until further

research can be performed, including research in the U.S. population. This intervention promotes improved antimicrobial use by influencing prescribing practices consistent with the goal of antimicrobial stewardship. Current guidelines recommend a no-antibiotic prescribing policy with deference to case-by-case evaluation, and appropriate patient education for simple acute otitis media, sore throat, pharyngitis, tonsillitis, common cold, rhinosinusitis, and bronchitis.[3-5]

SOURCE: Aabenhus R, Jensen JU, Jørgensen KJ, Hróbjartsson A, Bjerrum L. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. *Cochrane Database Syst Rev.* 2014;(11):CD010130.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD010130.

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### GLOSSARY OF EVIDENCE-BASED MEDICINE AND STATISTICAL TERMS

| *Term* | *Abbreviation* | *Definition* |
|---|---|---|
| Sensitivity | Sn | Percentage of patients with disease who have a positive test for the disease in question |
| Specificity | Sp | Percentage of patients without disease who have a negative test for the disease in question |
| Predictive value (positive and negative) | PV+<br>PV- | Percentage of patients with a positive or negative test for a disease who do or do not have the disease in question |
| Pretest probability | | Probability of disease before a test is performed |
| Post-test probability | | Probability of disease after a test is performed |
| Likelihood ratio | LR | LR >1 indicates an increased likelihood of disease, LR <1 indicates a decreased likelihood of disease. The most helpful tests generally have a ratio of less than 0.2 or greater than 5. |
| Relative risk reduction | RRR | The percentage difference in risk or outcomes between treatment and control groups. Example: if mortality is 30 percent in controls and 20 percent with treatment, RRR is (30 - 20)/30 = 33 percent. |
| Absolute risk reduction | ARR | The arithmetic difference in risk or outcomes between treatment and control groups. Example: if mortality is 30 percent in controls and 20 percent with treatment, ARR is 30 - 20 = 10 percent. |
| Number needed to treat | NNT | The number of patients who need to receive an intervention instead of the alternative in order for one additional patient to benefit. The NNT is calculated as: 1/ARR. Example: if the ARR is 4 percent, the NNT = 1/4 percent = 1/0.04 = 25. |
| Number needed to harm | NNH | The number of patients who need to receive an intervention instead of the alternative in order for one additional patient to experience an adverse event. |
| 95 percent confidence interval | 95% CI | An estimate of certainty. It is 95% certain that the true value lies within the given range. A narrow CI is good. A CI that spans 1.0 calls into question the validity of the result. |
| Systematic review | | A type of review article that uses explicit methods to comprehensively analyze and qualitatively synthesize information from multiple studies |
| Meta-analysis | | A type of systematic review that uses rigorous statistical methods to quantitatively synthesize the results of multiple similar studies |