# POEMs

## *Patient-Oriented Evidence That Matters*

## Laboratory-Based Prediction Model Can Rule Out Serious Bacterial Infections in Febrile Infants

### Clinical Question

Can a laboratory-based prediction model rule out serious bacterial infections in infants?

### Bottom Line

In febrile infants up to 60 days of age, the combination of a normal urinalysis result, an absolute neutrophil count of less than 4,090 per mL ($4.1 \times 10^9$ per L), and a serum procalcitonin level of less than 1.71 ng per mL is accurate at ruling out serious bacterial infections. (Level of Evidence = 1b)

### Synopsis

Most of us believe that clinical signs are unreliable in identifying serious illness in febrile infants, which results in extensive and invasive septic work-ups. The authors recruited a convenience sample of febrile infants (rectal temperature of at least 100.4°F [38°C]) up to 60 days of age who showed up in emergency departments during times when research staff were available. They excluded infants who appeared critically ill, those born prematurely, and those with chronic conditions. All infants had standardized clinical assessments, and blood and urine cultures and lumbar punctures were done at the discretion of the treating physician. Of 3,230 eligible infants, 1,821 had a procalcitonin sample drawn. The presence of a serious bacterial infection, as defined by bacterial meningitis, bacteremia, or a urinary tract infection, was detected in 170 infants (9%). The researchers performed a variety of statistical gymnastics to derive a prediction model on a split sample of the infants and then validated the model on the rest. Using the validation sample, the combination of a negative urinalysis, an absolute neutrophil count less than 4,090 per mL, and a procalcitonin level of less than 1.71 ng per mL was accurate at ruling out serious infections: 97.7% sensitivity (95% CI, 91.3 to 99.6) and 60.0% specificity (56.6 to 63.3), with a positive likelihood ratio of 2.4 (2.1 to 2.7) and a negative likelihood ratio of 0.04 (0.006 to 0.15). The clinicians were asked to predict the likelihood of a serious infection and they were not particularly accurate.

**Study design:** Decision rule (validation)

**Funding source:** Government

**Setting:** Emergency department

**Reference:** *Kuppermann N, Dayan PS, Levine DA, et al.; Febrile Infant Working Group of the Pediatric Emergency Care Applied Research Network (PECARN). A clinical prediction rule to identify febrile infants 60 days and younger at low risk for serious bacterial infections.* JAMA Pediatr. *2019;173(4):342-351.*

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## Pneumatic Compression in Addition to Pharmacologic Thromboprophylaxis Does Not Further Reduce DVT Risk

### Clinical Question

Does the addition of intermittent pneumatic compression to pharmacologic thromboprophylaxis further decrease the risk of deep venous thrombosis (DVT) in critically ill patients?

### Bottom Line

This study found no benefit to the addition of intermittent pneumatic compression to pharmacologic anticoagulation for the prevention of proximal DVT in critically ill patients. Although this finding was consistent across per-protocol and sensitivity analyses, the study itself was

underpowered because of a low incidence of DVT in the control group. The possibility of a clinically important effect of the intervention, either benefit or harm, is not completely excluded. (Level of Evidence = 1b–)

### Synopsis

Current guidelines recommend pharmacologic thromboprophylaxis in all critically ill patients. In this international multicenter study, researchers investigated whether the addition of mechanical thromboprophylaxis with intermittent pneumatic compression would further reduce the risk of DVT in these patients. Adult patients expected to be in the intensive care unit (ICU) for at least 72 hours were randomized, using concealed allocation, to receive pneumatic compression (n = 991) or pharmacologic thromboprophylaxis alone (n = 1,012). Both groups received pharmacologic thromboprophylaxis with unfractionated heparin or low-molecular-weight heparin. In the pneumatic compression group, patients also received intermittent compression to both lower limbs for at least 18 hours per day. Although sequential compression devices with thigh-length sleeves were preferred, nonsequential devices and knee-length sleeves, as well as foot pumps, were permitted. In the control group, pneumatic compression was only permitted during times when pharmacologic thromboprophylaxis was interrupted. Proximal venous ultrasonography of the lower limbs was performed 48 hours after randomization and then twice weekly if DVT was clinically suspected. The two groups were balanced at baseline: the mean age was 58 years, almost 80% of patients were medical admissions to the ICU, and two-thirds were receiving mechanical ventilation. The primary outcome of new proximal lower limb DVT did not differ significantly between the two groups (3.9% in the pneumatic compression group vs. 4.2% in the control group; relative risk = 0.93; 95% CI, 0.60 to 1.44; $P$ = .74). There were no significant differences detected in any secondary outcomes, including pulmonary embolisms, death, or skin injuries related to pneumatic compression. Because the incidence of DVT in the control group was lower than an expected 7%, this trial was underpowered to detect a difference if it truly exists.

**Study design:** Randomized controlled trial (nonblinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Inpatient (ICU only)

**Reference:** *Arabi YM, Al-Hameed F, Burns KE, et al.; Saudi Critical Care Trials Group. Adjunctive intermittent pneumatic compression for venous thromboprophylaxis.* N Engl J Med. *2019;380(14):1305-1315.*

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## Oral Antibiotics Are Equal to IV Antibiotics for Serious Bone and Joint Infections

### Clinical Question

Is switching to oral antibiotics as safe and effective as at least six weeks of intravenous (IV) antibiotics for patients with bone and joint infections?

### Bottom Line

Oral antibiotics started within seven days of surgery for patients with a serious bone or joint infection are as safe and effective as six weeks of IV antibiotics. (Level of Evidence = 1b)

### Synopsis

Researchers identified adults with one of the following infections: osteomyelitis of the extra-axial skeleton, native joint infection requiring excision arthroplasty, infection of a prosthetic joint or orthopedic fixation device, or vertebral osteomyelitis. All patients would have typically been treated with IV antibiotics. They were randomized within seven days of surgery, or if no surgery, the start of antibiotic therapy, to receive IV or oral antibiotics. The antibiotics were selected on the basis of cultures, sensitivity, and other clinical factors by an infectious disease consultant. Of the 1,054 recruited patients, 39 had no end point data, so the modified intention-to-treat analysis includes 1,015 patients. The mean age of participants was 50 years, 64% were men, and all had some kind of surgical debridement or device removal. The most common identified organisms were *Staphylococcus aureus* (38%) and coagulase-negative staphylococci (27%). This was a noninferiority trial, which is appropriate because the goal was to evaluate the efficacy of a simpler, cheaper treatment option. Approximately 80% of patients in the IV group received six weeks of IV antibiotics; 90% of patients in the oral group received less than seven days of IV antibiotics. For the primary outcome of treatment failure, oral therapy was equivalent at one year to at least six weeks of IV therapy (14.6% in the IV group vs. 13.2% in the oral group; 95% CI for the difference, −4.9% to 2.2%). There was no difference in overall quality of life or in hip function scores, but knee function scores showed greater improvement in the oral treatment group. The length of hospital stay was three days longer in the IV treatment group. Although there were more catheter-related complications in the IV group, the overall rate of serious adverse events was similar between groups.

**Study design:** Randomized controlled trial (single-blinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Inpatient (any location) with outpatient follow-up

**Reference:** *Li HK, Rombach I, Zambellas R, et al.; OVIVA Trial Collaborators. Oral versus intravenous antibiotics for bone and joint infection.* N Engl J Med. *2019;380(5):425-436.*

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## e-Cigarettes More Effective Than Nicotine Replacement for Cessation of Tobacco Use in Adults

### Clinical Question

Are e-cigarettes an effective way to help patients quit smoking?

### Bottom Line

Among adults who smoked a median of 15 cigarettes per day, those who were randomized to receive e-cigarettes were more likely to be abstinent at one year than those who received nicotine replacement (number needed to treat [NNT] = 12). They also had less cough and phlegm production. (Level of Evidence = 1b)

### Synopsis

Many physicians have had patients who claimed to have stopped smoking by switching to e-cigarettes. But is this switch truly effective, and how durable are the effects? In this trial, adult smokers in the United Kingdom were recruited via social media and randomized to receive nicotine replacement or e-cigarettes. All participants were not currently using either approach and expressed no preference. Those randomized to use nicotine replacement could choose their preferred method, including nasal spray, inhaler, mouth spray, microtabs, gum, or patch. Those randomized to use e-cigarettes received a starter kit and were encouraged to experiment with different flavors and strengths of e-liquids. The median age of participants was 41 years, approximately one-half were women, and the median number of cigarettes smoked per day was 15. Groups were balanced at the beginning of the study, and a total of 884 patients were randomized. The primary outcome, evaluated using the intention-to-treat principle, was self-reported abstinence confirmed by a carbon monoxide level of less than 8 ppm at one year. This occurred for 18% in the e-cigarette group and 9.9% in the nicotine replacement group ($P < .05$; NNT = 12). Short-term abstinence at four weeks was also higher with the use of e-cigarettes (43.8% vs. 30.0%; $P < .05$; NNT = 7). Respiratory symptoms of cough and phlegm were somewhat less common among those in the e-cigarette group at 52 weeks. There was no difference in adverse events between groups, with nausea more common in the nicotine replacement group (number needed to treat to harm [NNTH] = 16) and throat irritation more common in the e-cigarette group (NNTH = 7). A total of 40% of the patients in the e-cigarette group were still using e-cigarettes at one year, so they were still hooked on nicotine, just not tobacco.

**Study design:** Randomized controlled trial (nonblinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Outpatient (any)

**Reference:** *Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of e-cigarettes versus nicotine-replacement therapy.* N Engl J Med. *2019;380(7):629-637.*

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**Editor's Note:** See related article and online comment from the author regarding recent adverse events related to e-cigarette use at https://www.aafp.org/afp/2019/0815/p227.html

Dr. Ebell is Deputy Editor for Evidence-Based Medicine for *AFP* and cofounder and Editor-in-Chief of Essential Evidence Plus, published by Wiley-Blackwell.■