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This series is coordinated by Sumi Sexton, MD, Associate Deputy Editor.

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Step-by-Step Approach to Ruling Out Infant Infection Is Accurate

Clinical Question

Is the Step-by-Step approach useful for ruling out systemic infection in young low-risk infants?

Bottom Line

The Step-by-Step approach, using a basic physical examination and readily available urine and blood tests (without lumbar puncture; see the Synopsis section), can successfully identify low-risk infants younger than 90 days who will not need empiric antibiotic treatment and lumbar puncture. However, this approach has not been studied (nor has any other approach, I believe) in a randomized controlled trial to see whether it is effective at decreasing lumbar punctures or hospital admissions. (Level of Evidence = 1a)

Synopsis

This study was conducted at 11 European pediatric emergency departments. The researchers enrolled 2,185 previously healthy term infants younger than 90 days with fever without source. The relatively new Step-by-Step approach was evaluated in comparison with the Rochester criteria or the Lab-score (*Arch Dis Child*. 2010;95(12):968-973), both methods of ruling out invasive bacterial infection. All infants were evaluated via urine dipstick, a urine culture, white blood

cell count, C-reactive protein level, procalcitonin, and blood culture. Eventually, 4% (n = 87) of the infants were given a diagnosis of systemic infection and approximately 45% (n = 991) were classified as low-risk using the Step-by-Step approach. Sensitivity and negative predictive value for ruling out infection were 92.0% and 99.3% for the Step-by-Step approach, 81.6% and 98.3% for the Rochester criteria, and 59.8% and 98.1% for the Lab-score. Seven of the 991 infants (0.7%) who were classified as low risk by the score were found to have a systemic infection using the Step-by-Step approach.

The Step-by-Step approach: Children at low risk of systemic infection have the following characteristics: not ill-appearing, younger than 21 days, no leukocyturia, procalcitonin level less than 0.5 ng per mL, C-reactive protein level less than 20 mg per L (190.5 nmol per L), and absolute neutrophil count less than 10,000 per mm³ (10.0 × 10⁹ per L).

Study design: Decision rule (validation)

Funding source: Self-funded or unfunded

Setting: Emergency department

Reference: Gomez B, Mintegi S, Bressan S, Dalt L, Gervais A, Lacroix L; European Group for Validation of the Step-by-Step Approach. Validation of the "Step-by-Step" approach in the management of young febrile infants. *Pediatrics*. 2016;138(2):e20154381.

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Cervical Treatment Associated with Adverse Obstetric Outcomes

Clinical Question

Is cervical treatment for preinvasive and early invasive disease associated with subsequent adverse obstetric outcomes?

Bottom Line

Cervical treatments for dysplasia and early cervical carcinoma are associated with subsequent risk of preterm birth. Excisional ►

treatments carry higher risk than ablative treatments, and multiple treatments carry higher risk than single treatments. The frequency and severity of prematurity-related outcomes increase with increasing cone depth and volume. (Level of Evidence = 2a)

Synopsis

This report is a meta-analysis of observational studies to assess the associations between local treatments for cervical intraepithelial neoplasia or early invasive carcinoma and subsequent obstetric outcomes. The authors included 71 studies (70 cohort, one case-control) with 65,082 treated women and 6,292,563 untreated women. Several types of untreated comparison groups were used, including a small subset in which women with high-grade lesions were not treated. The overall risk of premature birth (before 37 weeks' gestation) was higher among treated women than among untreated women (relative risk [RR] = 1.78; 95% confidence interval [CI], 1.60 to 1.98). It was also higher for severe prematurity (32 to 34 weeks' gestation) and extreme prematurity (28 to 30 weeks' gestation), with RRs of 2.40 (95% CI, 1.92 to 2.99) and 2.54 (95% CI, 1.77 to 3.63), respectively.

The magnitude of effect was higher for excision over ablative treatments (e.g., the RR of prematurity was 2.7 [95% CI, 2.14 to 3.40] with cold knife conization and 1.46 [95% CI, 1.27 to 1.66] for ablation not otherwise specified). Within excisional treatments, the magnitude of effect was greater with greater depth of cone (up to RR of 4.91 for 20 mm or more) and greater volume of excision (up to RR of 13.9 for 6 mL or more). Multiple treatments were associated with progressively greater risk (e.g., the RR for two excisional treatments was 5.48; 95% CI, 2.68 to 11.24). Subgroup analyses were performed on the different types of untreated comparison groups. The increase in risk of prematurity was attenuated when the untreated comparison group was composed of women who also had cervical intraepithelial neoplasia (RR = 1.27; 95% CI, 1.14 to 1.41), which implies an increase in baseline risk of prematurity due to the disease process itself in addition to the effects of cervical treatments. The risks of spontaneous

preterm labor and chorioamnionitis were also increased among treated women. Neonatal outcomes were as expected related to prematurity.

Study design: Meta-analysis

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: Kyrgiou M, Athanasiou A, Paraskevaïdi M, et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis. *BMJ*. 2016;354:i3633.

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Larger Bottles Associated with Greater Weight in Infants

Clinical Question

Is the size of the bottle used to feed infants associated with weight gain?

Bottom Line

In nonbreastfed infants, using large bottles (at least 6 oz [180 mL]) to feed infants two months of age was associated with greater weight gain by six months of age. The authors did not report adverse effects associated with bottle size. This is an interesting study that suggests that smaller bottles may prevent overfeeding. (Level of Evidence = 2b)

Synopsis

The data for this study were obtained from a study aimed at preventing childhood obesity. The U.S. authors identified 386 infants who were born at least 34 weeks' gestational age, weighed at least 1,500 g (3 lb, 5 oz), and were exclusively formula-fed. The infant population was 41% black, 35% Hispanic, and 23% white. At the two-month visit, parents of 44% of the infants reported using large (at least 6 oz) bottles. White parents and parents of boys were more likely to use larger bottles. All infants were examined again at six months. After adjustment for birth weight, time between visits, and other variables, infants fed with large bottles had 0.21 kg (95% confidence interval, 0.05 to 0.37) more weight change at the six-month visit. The study did not randomly assign bottle sizes

to children, and the authors did not report on children older than six months, although other studies have shown that weight gain between two and four months of age predicts the likelihood of being overweight at two years of age. This is a preliminary study that suggests that using smaller bottles at an early age might prevent overfeeding.

Study design: Cohort (prospective)

Funding source: Government

Setting: Outpatient (primary care)

Reference: Wood CT, Skinner AC, Yin HS, et al. *Bottle size and weight gain in formula-fed infants.* *Pediatrics.* 2016;138(1):e20154538.

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Lumbar Fusion No Better Than Exercise and Therapy in the Long Term

Clinical Question

Is lumbar fusion effective for patients with chronic low back pain?

Bottom Line

This trial is a good example of how to do just about everything wrong to get the results you want. The authors did not conceal allocation, did not mask anyone in the study, used an unvalidated and subjective primary outcome, and downplayed the intention-to-treat analysis. Funding for the original study came from industry, and the authors have numerous conflicts of interest. Two other trials in the United Kingdom and Norway found no benefit to lumbar fusion, and the results of this study are consistent with those findings, despite what the authors conclude. (Level of Evidence = 2b)

Synopsis

This is an important question—one not without controversy. This study reports a mean 12.8 years of follow-up from a trial that randomized 294 persons with severe chronic low back pain in a 3:1 ratio to lumbar fusion

or physical therapy. This report provides almost no detail about the authors' methods, but a look at their earlier publication reveals that outcome assessors (and, obviously, patients) were not masked to treatment assignment. The earlier report, after two years of follow-up, showed generally favorable results for surgery. Approximately 20% of patients in each group died or were lost to follow-up.

In the long-term results, using intention-to-treat analysis, there is no difference between groups for any outcome, including the patient's global assessment of back pain score, the Oswestry Disability Index score, a visual analog scale for pain score, pain medication use, pain frequency, or employment status. The authors also report an as-treated analysis, which counts the 19 of 72 patients who crossed over to surgery as if they had originally been assigned to surgery (they were not), and they report a per-protocol analysis, which ignores patients who crossed over or were lost to follow-up. Both of these analyses found an improvement in the patient's global assessment score with surgery but failed to find improvement in any other outcomes. On the basis of the single outcome of global assessment score in the more biased analyses, the authors' conclusion is that surgery should be considered effective. An accompanying editorial, which strongly disagrees with the authors, begins with the snide headline: Consensus at last... fusion is no better than nonoperative care in improving pain and disability in chronic low back pain.

Study design: Randomized controlled trial (nonblinded)

Funding source: Industry

Allocation: Unconcealed

Setting: Outpatient (specialty)

Reference: Hedlund R, Johansson C, Hagg O, Fritzell P, Tullberg T. *The long-term outcome of lumbar fusion in the Swedish lumbar spine study.* *Spine J.* 2016;16(5):579-587.

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