One of the most common management decisions pediatricians face involves early-onset sepsis (EOS). Which infants should be evaluated? Which infants should receive empiric antibiotics? If an infant is clinically ill, the decision is straightforward, as most pediatricians will treat empirically while they await the results of blood cultures or other diagnostic tests. However, in most cases the newborn is well appearing or only has minor physiologic disturbances (tachypnea, temperature instability). In general, the presence of risk factors such as group B Streptococcus (GBS), inadequate intrapartum antibiotic prophylaxis (IAP), maternal chorioamnionitis, and prolonged rupture of membranes (≥ 18 hours) has been used to decide which infants to evaluate with a blood culture and/or treat empirically with antibiotics. However, making a rational decision to evaluate or treat an infant should depend on the probability of infection as well as the cost-benefit relationship between unnecessarily treating uninfected infants and delaying antibiotic treatment in infected infants.

Widespread use of IAP has led to a sharp decline in EOS from GBS.1-4 The Centers for Disease Control and Prevention (CDC) reports that the rate of EOS secondary to GBS has decreased from 1.7 cases per 1,000 births (1993) to 0.28 cases per 1,000 births.5 During this time, the incidence of non-GBS EOS has declined as well.6,7 Although the population risk has declined, how do we determine an infant’s individual risk? The CDC 2002 (and revised 2010) guidelines for the prevention of neonatal GBS disease provide algorithms for the evaluation of infants at risk for GBS EOS.6,7 Presumably, infants with a higher probability of EOS should have an evaluation or empiric treatment recommended, but the algorithm neither gives an explicit risk nor specifies risk levels for evaluation or treatment. Although simple to use, the CDC algorithm has several drawbacks. Information is lost as continuous variables are dichotomized (that is, rupture of membranes ≥ 18 hours and gestational age < 37 weeks). Using chorioamnionitis, a clinical and thus less reliable predictor, is also problematic. In the current era, when internet access and smartphones are ubiquitous, more sophisticated, multivariate risk prediction models can be employed.

Under current CDC guidelines, the percentage of infants being treated with antibiotics is ~200-fold higher than the incidence of EOS. In 2008 and 2009, clinicians at Brigham and Women’s Hospital (Boston) treated 8% of well-appearing infants born at ≥ 34 weeks’ gestation with antibiotics, while the incidence of EOS among those infants was only 0.4 cases per 1,000 live births.8 Similarly, an internal review of births in Kaiser Permanente Northern California between 2010 and 2013 demonstrated that 15% of infants born ≥ 34 weeks’ gestation had blood cultures, and 5.4% received antibiotics, despite an incidence of EOS of only 0.3 cases per 1,000 live births.

Unnecessary evaluations and antibiotic treatment are not risk free. In the short term, obtaining blood cultures may result in infant discomfort and parental anxiety. Given the low incidence of EOS, false positive cultures will outnumber the true positive and inevitably lead to more laboratory tests and/or unnecessary antibiotic exposure. Infants receiving antibiotics are often admitted to a neonatal ICU for treatment; this may interrupt parental bonding and breastfeeding. Finally, an emerging literature suggests that early antibiotic exposure may be associated with diseases later in childhood. Studies have shown an association between early antibiotic exposure and asthma,9-16 allergic/autoimmune disease,17-21 and obesity.22-25 Additional studies are needed to delineate the relationship between early antibiotic exposure on the neonatal microbiome and later disease. Prudence should dictate a more conservative stance toward exposing large numbers of newborns to broad-spectrum antibiotics.

Our goal was to implement an evidence-based approach for the evaluation and management of newborns suspected of EOS. To achieve this goal, we adapted two predictive models...
developed by our research team for use in an integrated health care delivery system. In this article, we describe the strategy and the tools that we employed. The central component of our efforts was to take advantage of new technologies not used by the CDC guideline—Web-based analytic tools, smart phones, and an administrative infrastructure for establishing consensus across a network of 14 delivery hospitals.

**Tool Development and Description**

**EARLY-ONSET SEPSIS RISK PREDICTION MODEL**

In two recent reports, our team described the development and validation of two linked predictive models for EOS. These models employ a Bayesian approach. The first model establishes a newborn’s baseline probability of EOS entirely on the basis of the maternal risk factors (or EOS risk at birth). EOS risk at birth is calculated using gestational age and maternal variables that are available at the moment of birth (highest antepartum temperature, GBS carriage status, duration of rupture of membranes, and the nature and timing of IAP).

To maximize the reliability of the variables, we favored objective variables such as “highest maternal antepartum temperature” over more subjective variables such as “physician diagnosis of chorioamnionitis.” We used nonparametric smoothing methods to incorporate continuous variables. Thus, instead of dichotomizing continuous variables, as is done in the CDC algorithm, the relationship of each variable to the outcome was analyzed separately and then combined into a multivariate model.

**EARLY-ONSET SEPSIS CALCULATOR**

One difficulty with a multivariate risk prediction model is that it is not as simple to use as the CDC flow diagram. Expecting clinicians to manually calculate risk using regression model coefficients is unrealistic. To facilitate clinical adoption, we built Web-based calculators for desktop Web browsers and smartphones that allow clinicians to quickly enter patient-specific data and calculate individualized risk of EOS. Physicists determine sepsis risk using the calculator when admitting a patient and writing his or her history and physical (H&P). As had been done in the past under CDC guidelines, nursing staff alert pediatric providers of risk factors (GBS–positive status, maternal fever, obstetricians’ chorioamnionitis diagnoses), or clinical symptoms (tachypnea, increased work of breathing, fever), particularly in those instances in which a physician was not completing the H&P immediately. In those instances, pediatric providers calculate the initial sepsis risk and determine appropriate management.

**DISSEMINATION OF EARLY-ONSET SEPSIS CALCULATOR**

KPNC serves a population of 3.9 million members, which constitutes nearly 40% of the insured population in Northern California. Fourteen hospitals have obstetrical and neonatal services, which care for approximately 35,000 newborns each year. Newborn care is provided by a combination of hospital-based pediatricians, neonatal nurse practitioners, and neonatologists. Two of the facilities also have pediatric residents involved in the care of newborns. The EOS calculator and an explanation of the risk prediction model were presented to the neonatology chiefs with a “soft launch” (no guidance was given to staff with respect to intervention thresholds) in December 2012. This strategy permitted staff to familiarize themselves with the calculator and probability of EOS at birth.

Critical to the introduction of the EOS calculator was an administrative structure that has developed at KPNC during the past decade. Three key venues for the introduction of initiatives are the Perinatal Research Unit (PRU), the Neonatology Chiefs Group, and the electronic health record (EHR) (Kaiser Permanente HealthConnect [KPHC]) governance group. Often, an idea will be brought forward at the Chiefs group. A request goes out to the regionwide journal club for a review of the literature and to the PRU for analysis of internal data. After a consensus is built around a specific clinical practice, those ideas go back to the journal club for further vetting and then back to the Chiefs for endorsement. Whenever possible, tools are built into the EHR to support and reinforce that new practice.

**INTEGRATION OF CLINICAL PRESENTATION**

The second predictive model for EOS that we developed quantifies how the baseline risk is modified by the infant’s clinical examination. Using a variety of statistical and visualization techniques, our team analyzed newborn data to define a hierarchical classification scheme for a newborn’s evolving clinical examination in the first 12 hours of life. We defined three clinical-presentation categories (clinical illness, equivocal, and well appearing) and calculated likelihood ratios (LRs) for each. Through a combination of recursive partitioning (classification and regression trees) and logistic regression, we stratified infants on the basis of both their clinical presentation and the three levels of sepsis risk at birth (<0.65 cases/1,000 live births, 0.65–1.54 cases/1,000 live births, ≥1.54 cases/1,000 live births). On the basis of the posterior probability of EOS in these strata and estimated numbers needed to treat (NNT), management choices were suggested (continued observation, observe and evaluate, and treat empirically). In August 2013, at a regional KPNC journal club for neonatal staff, we formally introduced the EOS...
calculator, as well as thresholds for treatment based on this stratification scheme.

**Problems with Our Original Risk Stratification**

Our original stratification strategy suffered from several limitations. Collapsing EOS risk at birth into three categories results in significant information loss, which is most pronounced in the highest-risk group. Although the low (< 0.65 cases/1,000 live births) and medium (0.65–1.54/1,000 live births) EOS risk at birth groups had relatively narrow ranges of risk, a much broader range of risk is present in the high-risk (≥ 1.54 cases/1,000 live births) group. Therefore, information loss was particularly problematic among well-appearing infants in the highest-risk group. The mean posterior probability in this group was 6.74 cases/1,000 infants (NNT, 148). However, infants whose risk was close to the lower bound of the high-risk range would actually have a posterior probability of < 1 case/1,000 live births (NNT ≥ 1,000) when the LR for a normal exam is taken into account. In addition, the strata means were determined from the nested case-control study, not a population-based sample. Because the incidence of EOS is relatively rare, the nested-case control study with three controls for case, by design, results in an EOS–enriched cohort.

Consequently, we examined more recent data (KPNC 2010–2012 births) and calculated EOS risk at birth for all infants. We found a left-skewed risk distribution (Figure 1, right); that is, a large percentage of infants in our original high-risk stratum had a risk near the lower bound of the distribution. Thus, applying our initial stratification schema would result in the treatment of a large number of infants in the high-risk group who, if well appearing, would have a low individual risk.

**Determining Individual Risk of EOS (Incorporating the Clinical Presentation)**

To remedy this issue, we utilized Bayes’s theorem (prior odds multiplied by the LR equals the posterior odds) to calculate individual posterior probabilities for EOS risk for each infant. The LR equals the probability of a particular finding in individuals with disease divided by the probability of a particular finding in individuals without disease. We converted the probability of EOS risk at birth to odds to determine the prior odds (odds = probability / [1 – probability]). The finding of interest is the infant’s evolving clinical presentation after birth. We used LRs from our prior work as follows:

- Clinical illness, 14.5 (95% confidence interval [CI] 10.2–21.2)
- Equivocal presentation, 3.75 (95% CI 2.83–5.00)
- Well appearing, 0.36 (95% CI 0.31–0.41)

We wanted to give clinicians a single value for EOS risk rather than a range. However, because the LR estimate has an uncertainty bound, we reasoned that using the point estimate of the LR could be dangerous (and lead to underestimation of an infant’s risk). To be conservative and estimate the maximum EOS risk, we used the upper limit of the 95% confidence interval of the LR instead of the point estimate of the LR itself (21.20 for clinical illness, 5.00 for equivocal presentation, and 0.41 for well-appearing presentation). Figure 2 illustrates the effect of clinical presentation on the posterior probability of EOS for a given EOS risk at birth (prior probability). A well-appearing presentation will decrease the posterior probability, an equivocal presentation increases the posterior probability, and clinical illness greatly increases the posterior probability (and has the most dramatic effect).

**Setting Treatment Thresholds**

Now that we could determine an individual’s risk for EOS, we needed to define management thresholds. We decided to establish two: one for continued observation/blood culture and one for empiric antibiotics/blood culture. Unfortunately, there are no randomized controlled trials to inform the probability of infection at which the benefits of starting antibiotics immediately exceed the risk and costs of delaying treatment. It is important to remember that the treatment choice is not that of...
Effect of Clinical Presentation on Early-Onset Sepsis (EOS) Risk

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well Appearing</td>
<td>LR 0.41</td>
</tr>
<tr>
<td>Equivocal</td>
<td>LR 5.0</td>
</tr>
<tr>
<td>Clinical Illness</td>
<td>LR 21.2</td>
</tr>
</tbody>
</table>

Figure 2. The effect of likelihood ratios (LRs) for clinical presentation on the posterior probability of EOS is shown.

antibiotics versus no antibiotics but, rather, between (a) starting antibiotics empirically, (b) drawing a blood culture and waiting to start antibiotics if the infant becomes clinically ill or the blood culture becomes positive, or (c) observing the infant and waiting to start antibiotics if the infant becomes clinically ill. On September 4, 2012, we convened a one-day symposium of local experts in the San Francisco Bay Area and queried the KPNC chiefs of neonatology to help determine a risk threshold for intervention. We reached consensus for (a) posterior probability of EOS of ≥ 1/1,000 live births (NNT²⁹ 1,000) to obtain a blood culture, monitor vital signs every 4 hours in the mother-baby unit, and remain in the hospital until the culture was incubated for 24 hours, and (b) a posterior probability of EOS of ≥ 3/1,000 (NNT 333) to obtain a blood culture and start empiric antibiotics. We reasoned that these NNT were relatively conservative. For a comparison in perinatal medicine, the risk of uterine rupture complicating vaginal birth after cesarean section (VBAC) is ~1%, leading to death or severe neurologic injury in the infant in approximately 10% of those births.³⁰⁻³³ Thus, the risk of death or severe neurologic injury after VBAC is about 1/1,000 VBACs or a number needed to harm of 1,000.

Revisions to the Early-Onset Sepsis Calculator to Improve Clinical Acceptance

In July 2014 we added several enhancements to the calculator. We modified some of the specifications in our original papers to improve face validity and clinician acceptance. These modifications centered on the need to facilitate dissemination across 14 hospitals. To broaden the ability to apply the calculator to different populations, we added the ability to select the baseline prevalence of EOS in the population being managed. Because the predictive model was developed using data from the nested-case control study, its intercept term needs to be adjusted to reflect the prevalence of EOS in the population to which it is being applied.²⁶,³⁴

The original EOS calculator was adjusted for an EOS prevalence of 0.6 cases per 1,000 live births—the prevalence of the population from which the nested cases and controls were drawn.³⁵ However, in KPNC the current (2010–2012) prevalence of EOS was 0.3 cases per 1,000 live births. The revised calculator allows the user to select a baseline prevalence of 0.3–0.6/1,000 live births, in increments of 0.1.

The original risk prediction model used broad-spectrum antibiotics < 4 hours prior to delivery and GBS–specific antibiotics any time prior to delivery as predictors that reduced the probability of EOS. However, even with the large study population of 608,014, there were not enough cases for antibiotic administration to be included in the model as a continuous variable. Further, antibiotic timing as displayed in the calculator lacked face validity because clinical efficacy of antibiotics administered shortly before delivery was questioned. Consequently, we reviewed the IAP timing literature with respect to efficacy of preventing EOS. Evidence exists that IAP had some effect even if administered as little as 30 minutes prior to delivery, but the effectiveness of IAP in preventing GBS if given ≥ 2 hours was ≥ 89%.³⁵⁻³⁸ Therefore, we elected to be more conservative than the risk-prediction model by stipulating that antibiotic administration must occur at least 2 hours before delivery, which increased face validity and clinician acceptance. In deciding on adequate IAP for GBS, we instructed clinicians to include erythromycin and clindamycin as adequate prophylaxis only if GBS cultures had shown sensitivity to these antibiotics. We also modified the clinical presentation descriptions and timing specifications. Because infants often have transient respiratory distress transitioning to ex-utero life, we explicitly state that the need for respiratory support needed to occur beyond the delivery room. We added high-flow nasal cannula (which has become more widely used) to the list of respiratory support. We expanded the study criterion of seizure to the more inclusive criterion of encephalopathy. For the supplemental oxygen requirement, we added a caveat that supplemental oxygen needed to maintain pulse oximetry of > 90% for > 2 hours to avoid misclassification. For the equivocal presentation, we clarified time periods regarding vital signs abnormalities.

We expanded the time frame to identify clinical illness or equivocal presentation from 12 hours to 24 hours, which is
consistent with a more conservative stance. Table 1 (above) summarizes our modified criteria. The most notable enhancement was adding posterior probabilities for each of the three clinical exam categories. This provides the user with (a) the individual probability for EOS, incorporating both the EOS risk at birth and clinical presentation, and (b) a clinical recommendation based on it. The clinical recommendations play an important purpose, as we found that in the comment phase absent recommendations, physicians often set their own thresholds for intervention (rather than the consensus thresholds endorsed by the neonatology chiefs). One of the goals of the EOS calculator was to reduce practice variability so that the efficacy, as well as the safety, of the treatment thresholds can be evaluated. Although physicians remain free to do what they wish, it is much harder to stray from the recommendations if the calculator—whose output is visible to nurses and other physicians—gives a specific recommendation rather than just a number. Prior to developing the calculator, we saw tremendous variability between centers with regard to antibiotic usage. When a clinician enters in the maternal and infant data, the calculator produces the risk of EOS and clinical recommendations for all three clinical presentations. If an infant developed clinical symptoms several hours after birth, the physician would apply the clinical recommendation based on the new clinical presentation status. There is no need to reenter data into the calculator because it provides recommendations on all three clinical presentations.

Also, we introduced two additional safeguards into the calculator. Although the LR for clinical illness was high (21), it was theoretically possible to have an EOS risk at birth so low such that, when multiplied by 21, a posterior probability of < 3 cases/1,000 live births (clinical recommendation would be not to initiate antibiotics) would have resulted. We did not want physicians to withhold antibiotics in an infant with clinical illness, even if his or her posterior probability was below the consensus threshold. Therefore, the EOS calculator clinical recommendation for an infant with clinical illness and a posterior probability of < 3 cases/1,000 live births reads, “Strongly consider antibiotics.”

Finally, we recognized that a septic infant might appear well at birth and then develop symptoms later. Because a major component of the EOS calculator is clinical presentation and its effect on the posterior probability, we wanted to ensure that infants with a higher EOS risk at birth (≥ 1 case/1,000 live births) would not merely have their posterior probability reduced by a reassuring exam shortly after birth. The infant might then be placed in the newborn nursery under routine care and have the identification of clinical symptoms missed or delayed. As a result, we added an additional clinical recommendation on the basis of the EOS risk at birth: If the EOS risk at birth was ≥ 1 case/1,000 live births, the clinical recommendation is for vital signs every 4 hours for 24 hours to encourage more timely identification of any clinical symptoms that might arise.

**Use of the Early-Onset Sepsis Calculator**

In December 2012 we made the EOS calculator available in both a computer-formatted website ([http://www.kp.org/EOScalc](http://www.kp.org/EOScalc)) and a smartphone-formatted display ([http://www.Newbornsepsiscalculator.org](http://www.Newbornsepsiscalculator.org)). The computer-formatted website is shown in Figure 3 (page 237, also available in color in online article). Key issues surrounding implementation of the EOS calculator and their solutions are summarized in Table 2 (page 238).

The calculators are being used widely at KPNC. The calculator has been accessed by users in all 50 states, with 52% of page views by users in California, and by users in 124 other countries. Figure 4 (page 238) shows the monthly use of the desktop calculator. The mobile application currently receives 1,500 page views per month.

**Monitoring the Impact and Safety of the Early-Onset Sepsis Calculator**

We are actively monitoring the impact of the EOS calculator by following monthly rates of sepsis evaluations in the first 24 hours (defined by obtaining a blood culture), as well as antibiotics administered in the first 24 hours (ascertained from the

### Table 1. Classification of Clinical Presentation

<table>
<thead>
<tr>
<th>Clinical illness</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent need for NCPAP/HFNC/mechanical ventilation (outside of the delivery room)</td>
<td>(a) If EOS risk was &lt; 1 case/1,000 births, no need for antibiotics.</td>
</tr>
<tr>
<td>Hemodynamic instability requiring vasoactive drugs</td>
<td>(b) If EOS risk was 1-3 cases/1,000 births, strongly consider antibiotics.</td>
</tr>
<tr>
<td>Neonatal encephalopathy/Perinatal depression</td>
<td>(c) If EOS risk was ≥ 3 cases/1,000 births, antibiotics.</td>
</tr>
<tr>
<td>Seizure</td>
<td></td>
</tr>
<tr>
<td>Apgar Score @ 5 minutes &lt; 5</td>
<td></td>
</tr>
<tr>
<td>Need for supplemental O₂ &gt; 2 hours to maintain oxygen saturations &gt; 90% (outside of the delivery room)</td>
<td>(d) Add posterior probability for EOS.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Equivocal presentation</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent physiologic abnormality &gt; 4 hours</td>
<td>(a) If EOS risk was &lt; 1 case/1,000 births, no need for antibiotics.</td>
</tr>
<tr>
<td>Tachycardia (HR &gt; 160)</td>
<td>(b) If EOS risk was 1-3 cases/1,000 births, strongly consider antibiotics.</td>
</tr>
<tr>
<td>Tachypnea (RR &gt; 60)</td>
<td>(c) If EOS risk was ≥ 3 cases/1,000 births, antibiotics.</td>
</tr>
<tr>
<td>Temperature instability (&gt; 100.4°F or &lt; 97.5°F)</td>
<td></td>
</tr>
<tr>
<td>Respiratory distress (grunting, flaring, or retreating) not requiring supplemental O₂</td>
<td></td>
</tr>
<tr>
<td>Two or more physiologic abnormalities lasting for &gt; 2 hours</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical illness</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well appearing</td>
<td>No persistent physiologic abnormalities</td>
</tr>
</tbody>
</table>

NCPAP, nasal continuous positive airway pressure; HFNC, high-flow nasal cannula; HR, heart rate; RR, respiratory rate.
electronic medication administration record). Rates are determined for KPNC, as well as individual medical centers. To ensure that we are not missing infants with EOS with our lower rate of sepsis evaluations, we are tracking any readmissions in the first week of life with a positive blood or cerebrospinal fluid (CSF) culture. As an integrated system, we can track all subsequent laboratory evaluations and readmissions anywhere in the KPNC system. In addition, we review every EOS case to determine if antibiotics would have been started earlier under the CDC guidelines and if any adverse outcomes occurred, such as meningitis, need for mechanical ventilation, need for inotropic agents, and death. We plan to publish data on utilization and safety after 18 months of implementation of the EOS calculator.

**Results and Lessons Learned**

We have developed a Web-based EOS calculator that provides perinatal practitioners with an explicit risk estimate. The calculator’s Bayesian structure reflects the actual flow of clinical experience while simultaneously providing the capability of updating a risk estimate. By calculating explicit risk and using a guideline with specific intervention thresholds, it is possible to better target the use of antibiotics in high-risk situations, while forgoing their use when the risk is low. Use of the calculator fits well with standard hospital work flow, which has contributed to its broad adoption within KPNC. The potential benefits of reduced antibiotic exposure in low-risk situations is significant, as emerging evidence has shown associations between early antibiotic therapy and subsequent diseases such as asthma, inflammatory bowel disease, and childhood obesity.22,39–43

Reduction in sepsis evaluations and antibiotic usage will have to be weighed against other important clinical outcomes. Hospital readmission for an infant with sepsis despite an assessment that the infant was “low-risk” is the obvious concern. However, this scenario is unlikely, given that nearly all cases of EOS present with clinical illness before 24 hours, and most before 12 hours of age.44–46 We have an active surveillance system. EOS cases (if any) are reviewed on a monthly basis. In addition, because KPNC is an integrated system in which newborns are covered under their mother’s insurance for at least the first 30 days, we are tracking any readmissions with a positive blood or CSF culture in the first seven days of life.

An important element of the EOS calculator is that it provides individualized risk estimates in conjunction with management recommendations (as opposed to the CDC’s isolated management recommendations). First, it provides physicians (and potentially parents) with an actual numeric risk value. This is beneficial as one weights the benefit and risks of treatment with nontreatment. Treatment thresholds become more explicit and transparent, enabling the physician to use the actual risk value to explain to parents why treatment is or is not needed. The EOS calculator also allows for a further Bayesian approach in select cases with use of the LR for the complete blood count.46,47

To implement the calculator, modifications from the initial research studies were necessary to increase face validity, add additional safeguards, and promote clinical adoption. Our administrative structure supported the physician education and consensus building necessary to change clinical practice. Links to the calculator and documentation templates in the EHR further support and standardize the new quantitative tool as it is adopted in an entire hospital network. Anytime one strays from the specifications in a research study, there is the possibility of not obtaining the identical results produced by the study. However, a protocol that does not garner clinical acceptance will
Table 2. Key Issues in Incorporating Early-Onset Sepsis Calculator into Clinical Practice

<table>
<thead>
<tr>
<th>Issue</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical acceptance of calculator</td>
<td>Avoided “black box” calculator</td>
</tr>
<tr>
<td>Information loss due to recommendations based on EOS risk in large infant subsets</td>
<td>Use of actual likelihood ratios to generate individual risk estimates</td>
</tr>
<tr>
<td>Limitations of clinical exam categories in original report</td>
<td>Modification made to original clinical categories</td>
</tr>
<tr>
<td>Safety concerns around uncertainty of risk estimates</td>
<td>Use of likelihood ratios’ upper 95% confidence intervals for calculations to maximize risk estimates</td>
</tr>
<tr>
<td>Manual calculation of model coefficients impractical</td>
<td>Development of Web-based calculator</td>
</tr>
<tr>
<td>How to translate probabilities into discrete clinical actions</td>
<td>Recommendations embedded in calculator</td>
</tr>
<tr>
<td>Departing from CDC guideline</td>
<td>Educational component highlighting evidenced-based approach with analyses of more recent KPNC data</td>
</tr>
<tr>
<td>Prospective data collection strategy implemented that includes balancing measures (such as readmissions for EOS and complications due to delayed antibiotic treatment), tracking possible adverse outcomes</td>
<td></td>
</tr>
</tbody>
</table>

EOS, early-onset sepsis; CDC, Centers for Disease Control and Prevention; KPNC, Kaiser Permanente Northern California.

References

11. Muck W, Risnes KR, Bracken MB. Prenatal or early-life exposure to anti-