2010 Perinatal GBS Prevention Guideline and Resource Utilization

WHAT'S KNOWN ON THIS SUBJECT: An algorithm for neonatal early-onset sepsis risk based on Centers for Disease Control and Prevention 2002 guidelines for prevention of perinatal Group B *Streptococcus* disease results in the evaluation of ~12–15% of well-appearing term and late preterm infants.

WHAT THIS STUDY ADDS: A revised algorithm based on the Centers for Disease Control and Prevention 2010 guidelines eliminated 25% of all early-onset sepsis evaluations and resulted in significant cost savings, without short-term evidence of harm.

abstract

OBJECTIVES: To quantify differences in early-onset sepsis (EOS) evaluations, evaluation-associated resource utilization, and EOS cases detected, when comparing time periods before and after the implementation of an EOS algorithm based on the Centers for Disease Control and Prevention (CDC) 2010 guidelines for prevention of perinatal Group B *Streptococcus* (GBS) disease.

METHODS: Retrospective cohort study of infants born at ≥ 36 weeks' gestation from 2009 to 2012 in a single tertiary care center. One 12-month period during which EOS evaluations were based on the CDC 2002 guideline was compared with a second 12-month period during which EOS evaluations were based on the CDC 2010 guideline. A cost minimization analysis was performed to determine the EOS evaluation-associated costs and resources during each time period.

RESULTS: During the study periods, among well-appearing infants ≥ 36 weeks' gestation, EOS evaluations for inadequate GBS prophylaxis decreased from 32/1000 to $<1/1000$ live births; EOS evaluation-associated costs decreased by \$6994 per 1000 live births; and EOS evaluation-associated work hours decreased by 29 per 1000 live births. We found no increase in EOS evaluations for other indications, total NICU admissions, frequency of infants evaluated for symptoms before hospital discharge, or incidence of EOS during the 2 study periods.

CONCLUSIONS: Implementation of an EOS algorithm based on CDC 2010 GBS guidelines resulted in a 25% decrease in EOS evaluations performed among well-appearing infants ≥ 36 weeks' gestation, attributable to decreased evaluation of infants born in the setting of inadequate indicated GBS prophylaxis. This resulted in significant changes in EOS evaluation-associated resource expenditures. *Pediatrics* 2014;133:196–203

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KEY WORDS

group B *Streptococcus*, intrapartum antibiotic prophylaxis, neonatal infection, early-onset sepsis

ABBREVIATIONS

BWH—Brigham and Women's Hospital
CBC—complete blood cell
CDC—Centers for Disease Control and Prevention
CDC2002—first time period of the study
CDC2010—second time period of the study
CMA—cost minimization analysis
COFN—Committee on the Fetus and Newborn
EOS—early-onset sepsis
GA—gestational age
GBS—Group B *Streptococcus*
IAP—intrapartum antibiotic prophylaxis
IQR—interquartile range
IV—intravenous
LB ≥ 36 —live births at ≥ 36 weeks' gestation
ROM—rupture of membranes
WBC—white blood cell

Dr Mukhopadhyay designed the study, designed the data collection instruments, collected and analyzed the data, and drafted the initial manuscript; Dr Dukhovny designed the cost minimization study design, analyzed the data for the cost calculations, and reviewed and revised the manuscript; Ms Mao conducted bootstrapping and sensitivity analysis for the study; Dr Eichenwald conceptualized the study question, reviewed the analysis and conclusions, and reviewed and revised the manuscript; Dr Puopolo conceptualized and designed the study, reviewed the data collection instruments, reviewed the data analysis and conclusions, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-1866

doi:10.1542/peds.2013-1866

Accepted for publication Oct 31, 2013

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The Centers for Disease Control and Prevention (CDC) guidelines for the use of intrapartum antibiotic prophylaxis (IAP) to prevent perinatal Group B *Streptococcus* (GBS) infection were first issued in 1996, and subsequently revised in 2002 and 2010.^{1–3} These guidelines are based on studies that quantified the risk of GBS early-onset sepsis (EOS) among infants of GBS-colonized mothers, and the efficacy of IAP in preventing perinatal GBS disease.^{4,5} Multiple studies have identified other perinatal risk factors for EOS, including low gestational age (GA), prolonged rupture of membranes (ROM), intrapartum maternal fever, and other evidence of evolving chorioamnionitis.^{4,6–8} These predictors are incorporated in the CDC guidelines for secondary prevention of EOS. Implementation of these guidelines has led to a significant decrease in the national incidence of both overall and GBS-specific neonatal EOS.^{9–12} At the Brigham and Women's Hospital, use of a local EOS evaluation algorithm based on the CDC 2002 guidelines results in the evaluation of ~15% of well-appearing infants born at ≥ 35 weeks' GA, and ~50% of those evaluated are empirically treated with antibiotics.¹³

The CDC 2010 revised guidelines contain one significant change in recommendations for secondary prevention of GBS EOS. The evaluation of infants born to mothers with inadequately indicated GBS IAP is advised only if additional risk factors are present: GA < 37 weeks, ROM ≥ 18 hours, maternal fever, or chorioamnionitis.³ In our previous study, we estimated that implementation of the CDC 2010 guidelines would result in ~25% fewer EOS evaluations among well-appearing infants, but the real-life impact of changes in medical policy is rarely straightforward.¹³ In the current study, we compared use of local algorithms based on the CDC 2002 and 2010 guidelines and sought to

answer 3 questions: (1) was there a change in frequency of EOS evaluation, (2) what was the economic impact of the revised algorithm, and (3) would the revised algorithm result in detectable short-term harm?

METHODS

Study Design

This study was approved by the Partners Healthcare Human Research Committee. This is a retrospective cohort study of infants born at Brigham and Women's Hospital (BWH) over 2 time periods: May 1, 2009 to April 30, 2010, and May 1, 2011 to April 30, 2012. Infants born between May 1, 2009 and August 31, 2009 were included in our earlier report.¹³ The first time period (CDC2002) reflects use of a CDC 2002–based local EOS algorithm.¹³ A revised algorithm consistent with the CDC 2010 guidelines was implemented in March 2011 (Fig 1). The second time period (CDC2010) reflects use of this revised algorithm, allowing for a 2-month “washout period” after implementation. Inclusion criteria for study infants were (1) birth at BWH; (2) GA at birth ≥ 36 weeks; (3) evaluation for EOS ≤ 48 hours of life; (4) “well-appearing” status, defined by EOS evaluation performed only because of algorithm-defined intrapartum risk factors, with regular newborn nursery care after EOS evaluation. Exclusion criteria included: EOS evaluation performed for symptoms (eg, respiratory distress) and/or NICU care after EOS evaluation. Because BWH infants born at < 36 weeks' gestation are routinely admitted to the NICU by policy, these infants were excluded from our study. We examined the total number of infants evaluated for EOS per 1000 live births at ≥ 36 weeks GA (LB ≥ 36); total EOS-associated costs and time per 1000 LB ≥ 36 ; and EOS-associated costs and time for the sole indication of inadequately indicated GBS IAP, comparing the 2 time periods.

Data Sources

The NICU admission log was used to identify study infants and collect time spent in EOS evaluation. Clinical, laboratory, and demographic data were obtained from infant and maternal medical records and hospital summary statistics.

EOS Algorithms

The CDC 2002–based local EOS algorithm has been previously described.¹¹ The CDC 2010–based local algorithm (Fig 1) differs from the CDC 2002–based algorithm in 2 significant ways: (1) infants born to mothers treated with inadequate indicated IAP are evaluated only if additional risk factors of GA < 37 weeks or ROM ≥ 18 hours are present; (2) complete blood cell (CBC) count is included as part of EOS evaluation only when done at > 4 hours of neonatal life. Both CDC guidelines recommend empirical antibiotic treatment of the neonate if maternal chorioamnionitis is present. Both the obstetric and NICU teams use intrapartum maternal fever $\geq 100.4^\circ\text{F}$ as the primary indication for the diagnosis of “chorioamnionitis” among women delivering at ≥ 36 weeks' gestation.

EOS Evaluation Care Structure

Infants meeting criteria for EOS evaluation are transferred to the NICU Triage area. This unit is staffed by NICU nurses and physicians. EOS evaluation consists of vital sign measurements, blood samples, and a physical examination. Well-appearing, asymptomatic infants are transferred to the newborn nursery after EOS evaluation. Peripheral intravenous (IV) catheters and initial antibiotic doses are administered in NICU Triage; subsequent doses are administered in the newborn nursery. Symptomatic infants are observed in the NICU Triage unit for up to 6 hours for symptom resolution; persistently symptomatic infants are admitted to the NICU.

FIGURE 1

Guidelines for the management of asymptomatic infants born at ≥36 weeks' gestation at risk for EOS. Local algorithm used at BWH since March 2011, based on the CDC 2010 perinatal GBS prevention guidelines.⁵ ANC, absolute neutrophil count; I/T, immature neutrophil to total neutrophil.

Blood Culture Methods and Identification

Blood cultures were performed with an automated BACTEC system (BD Diagnostics) by using both aerobic and anaerobic bottles. Cases of culture-confirmed EOS were identified by query of the microbiology laboratory electronic database. Case criteria were growth of a known pathogenic species, and antibiotic treatment of ≥7 days. Cultures growing common skin flora (ie, *Bacillus* species, coagulase: negative staphylococci) were considered contaminants if the infant remained well in the absence of appropriate antibiotic treatment.

Economic Analysis

A cost minimization analysis (CMA) with third-party payer perspective was used with individual patient data, comparing costs and resource use between the study periods. As is required for the CMA approach,^{14,15} we made the assumption of equal effectiveness of both algorithms in detecting EOS cases. All costs were expressed in 2011 US dollars. The time horizon extended from birth until hospital discharge. EOS-associated costs included were the following: time spent in NICU Triage (represented by nursing wages), laboratory fees, physician fees, medication fees, and any additional costs from false-positive evaluations (Supplemental

Table 6). Costs associated with EOS cases (repeat evaluations, antibiotic therapy, and NICU admission) were excluded. Missing NICU Triage times (17 infants) were imputed by using mean costs from infants of comparable cohort and treatment.

Statistical Analysis

Data analysis was performed by using SAS 9.3 (SAS Institute, Inc, Cary, NC). Discrete data were compared by using Fisher's exact test or χ^2 ; continuous data using *t* test or Wilcoxon rank test. Nonparametric bootstrapping was used to test differences of total cost, and total EOS evaluation time for all study infants and for those infants evaluated for inadequate GBS IAP alone, between the 2 study periods. Sensitivity analyses were performed exploring the strength of the analysis when varying the costs from 50% and 200% of their base value.

RESULTS

Frequency of EOS Evaluation and Distribution of Risk Factors

The study population is shown in Fig 2. Demographic characteristics and distribution of reasons for EOS evaluation are shown in Table 1. EOS evaluation frequency decreased from 126 per 1000 LB≥36 in the CDC2002 period to 68 per 1000 LB≥36 in the CDC2010 period ($P < .001$). The most striking difference between the study periods was in EOS evaluations performed for inadequate GBS IAP alone (Table 2; 32/1000 LB≥36 to <1/1000 LB≥36, $P < .001$). After removing evaluations performed for this indication, we found no significant differences between the 2 periods (Supplemental Table 7).

Maternal fever was the most common indication for EOS evaluations in both cohorts.

Inadequately indicated GBS IAP (without additional risk factors) was the second

FIGURE 2
Study population.

TABLE 1 Clinical Characteristics of Study Population

	CDC2002, n = 920	CDC2010, n = 476	P Value
LB ≥ 36	7282	7004	
Total evaluations (1000 LB ≥ 36)	920 (126)	476 (68)	<.001
Birth weight, g, mean (SD)	3385 (450)	3437 (444)	.04
GA, wk, mean (SD)	39.6 (1.3)	39.7 (1.3)	.22
Male, n (% of total evaluated)	490 (53.3)	242 (50.9)	.42
Multiple gestation, n (% of total evaluated)	27 (2.9)	12 (2.5)	.73
Epidural analgesia, n (% of total evaluated)	746 (81.1)	448 (94.1)	<.001
Vaginal deliveries, n (% of total evaluated)	678 (73.7)	307 (64.5)	<.001

most common indication during CDC2002 but accounted for <1% of evaluations during CDC2010. Of the 234 infants evaluated for this indication in CDC2002, 95 (40.6%) of 234 mothers received no antibiotic prophylaxis; 139 (59.4%) of 234 received partial treatment with a median duration 1.93 hours (interquartile range [IQR] 1.2–3.0) before delivery. The median duration of ROM for this group was 1 hour (IQR 0.2–2.7), suggesting that rapid progression to delivery was associated with inadequate IAP.

Neonatal Outcomes

There was a significant decline in the incidence of antibiotic treatment per 1000 LB ≥ 36 in the CDC2010 cohort compared with CDC2002 (Table 3). Maternal fever and concern for chorioamnionitis were the primary reasons for empirical treatment in both periods. There was no difference in the incidence of initially well-appearing, EOS-evaluated infants subsequently developing signs of illness resulting in NICU admission (Table 3).

CBC Counts

As per the evaluation algorithm, there was a significant decrease in CBC counts obtained as part of EOS evaluation from the CDC2002 to the CDC2010 period (919/920 vs 100/476, $P < .0001$) (Table 4). There was no difference in the proportion of abnormal white blood cell (WBC) count and differential between the cohorts (Table 4). Combining the 2 periods, 51 (5%) of 1019 infants had abnormal WBC count values. None of the 51 infants had blood culture–confirmed infection. Overall, 123 (12.1%) of the 1019 infants had repeat CBC count testing, for reasons given in Table 4. In 10 of 11 instances of low platelet counts, repeat testing was within the normal range; in 1, a repeat value of 100 000 prompted referral for outpatient follow-up.

Blood Culture Results

There were 6 positive cultures in the CDC2002 epoch, 4 of which were considered to be contaminants, and none in the CDC2010 epoch. The overall incidence of culture-confirmed EOS, including cases identified among well-appearing infants, as well as those identified among symptomatic infants, did not differ between the epochs (0.25 vs 0.39/1000 LB ≥ 36, $P = .96$). One case of GBS EOS occurred in a term infant born to a GBS-positive mother who received no IAP during the CD2010 epoch; this infant presented with tachypnea at 9 hours of age.

Outcomes Including Unevaluated Infants

A potential unintended consequence of decreasing the number of well-appearing infants evaluated for EOS shortly after birth could be an increase in evaluation of infants who become symptomatic later in their hospital course. To assess this, we determined the frequency of NICU Triage visits

TABLE 2 Reasons for EOS Evaluation of Well-Appearing Infants

	CDC2002, <i>n</i> = 920	CDC2010, <i>n</i> = 476	<i>P</i> Value ^a
No maternal fever, <i>n</i> (% of total evaluated)	272 (29.6)	32 (6.7)	<.001
Inadequate IAP alone	234 (25.4)	2 (<1) ^b	<.001
Inadequate IAP plus other risk factors ^c	16 (1.7)	15 (3.2)	.12
Other indications	22 (2.4)	15 (3.2)	.48
Maternal fever, <i>n</i> (% of total evaluated)	648 (70.4)	444 (93.3)	<.001
>101°F	331 (35.9)	216 (45.4)	<.001
100.4–100.9°F	317 (34.5)	228 (47.9)	<.001
ROM >18 h	182 (19.8)	124 (26.1)	.01
GA <37 wk	34 (3.7)	15 (3.2)	.65

^a The *P* values refer to the difference in the proportion attributable to each reason for EOS evaluation among the total number of infants evaluated, comparing the 2 study periods.

^b In the CDC2010 cohort, 2 were infants evaluated for inadequate GBS alone, due to failure of compliance with the algorithm.

^c In the CDC2002 cohort, other risk factors were ROM >18 h (1) and GA <37 wk (15). In the CDC 2010 cohort, other risk factors were ROM >18 h (8), fetal tachycardia (4), maternal fever of 100.3°F (2), and previous sibling with GBS sepsis (1).

TABLE 3 Outcomes of Neonates Evaluated

	CDC2002, <i>n</i> = 920	CDC2010, <i>n</i> = 476	<i>P</i> Value
Empirical antibiotics administered, <i>n</i> (<i>n</i> per 1000 LB≥36)	527 (72)	365 (52)	<.001
NICU admission, ^a <i>n</i> (<i>n</i> per 1000 LB≥36)	15 (2)	8 (1)	.21
Length of stay, days, median (IQR) ^b			
Vaginal deliveries	2.25 (1.7–3.6)	2.28 (1.7–2.9)	.75
Cesarean deliveries	4.12 (3.4–5.5)	4.27 (3.4–5.4)	.05

^a In each case, an infant was evaluated for EOS, then admitted to newborn nursery for ongoing care; and later transferred to the NICU for admission for new onset of symptoms. The reasons for NICU admission were as follows: oxygen desaturation events (4), respiratory distress (4), hypoglycemia (3), hyperbilirubinemia (2), neonatal abstinence syndrome (2), positive blood culture (2), and 1 infant each for the following reasons: hypothermia, seizures, bradycardia, bilious emesis, bleeding, and need for isolation due to maternal illness.

^b Length of stay includes all infants evaluated, including days of care in the newborn nursery and days of care in the NICU, if admitted.

TABLE 4 Laboratory Results of EOS Evaluation

	CDC2002, <i>n</i> = 920	CDC2010, <i>n</i> = 476
CBC count obtained, <i>n</i> ^a (% of total evaluated)	919 (99.6)	100 (21)
Abnormal CBC count, <i>n</i> (% of total evaluated)	46 (5.0)	5 (5.0)
ANC <1000	2	0
I/T ratio >0.2	44	5
WBC count <5000	1	0
Repeat CBC count (% of total CBC count during both study periods)	123 (12.1)	
Reason for repeat CBC count		
Inadequate specimen		37
Abnormal hematocrit (>60 or <45)		26
Abnormal WBC count/differential		11
Abnormal platelet (<150 000)		11
False-positive blood culture		4
Non-EOS-associated indication ^b		34

ANC, absolute neutrophil count; I/T, immature neutrophil to total neutrophil.

^a *P* < .001.

^b Primary indication was hyperbilirubinemia.

among all infants born during the study periods, and found no increases during the CDC2010 period (data not shown). The rate of NICU admission did not differ between the periods (126 vs 125 per 1000 live births, *P* = .92)

Cost Evaluation

EOS evaluation–associated costs decreased from CDC2002 to CDC2010 (Table 5), due to the absolute reduction in number of infants evaluated, amounting to \$15 876/1000 LB≥36 (*P*

< .001). The decrease in evaluations for inadequate GBS IAP contributed to 44% of the total reduction (\$6994/1000 LB≥36). This difference remained significant in a sensitivity analysis varying the cost range from 50% to 200% for individual cost parameters (Supplemental Table 8). EOS evaluation–associated work hours decreased by 64 hours/1000 LB≥36 from CDC2002 to CDC2010 (*P* < .001) with the decrease in evaluation for inadequate GBS prophylaxis alone accounting for 46% of that reduction (29.5 hours/1000 LB≥36). The initial EOS evaluation resulted in repeat NICU Triage utilization in 9.5% of infants during the 2 study periods, primarily for IV replacement or repeat laboratory testing (Table 5).

DISCUSSION

We found that our local algorithm for neonatal sepsis evaluation based on the CDC 2010 revised GBS guidelines resulted in a decrease in the frequency of sepsis evaluation as well as in the costs associated with those evaluations, without detectable short-term harm.

In previous work, we predicted that implementation of the CDC 2010 criteria for evaluation would result in a significant decrease in EOS evaluations among term and late preterm infants.¹³ We found that the change in approach to inadequate GBS prophylaxis itself resulted in a 25% decrease in EOS evaluations, with no evidence that clinicians shifted to other criteria for EOS evaluation.

The observed declines in EOS evaluation and laboratory testing had no apparent negative effects within the horizon of our study. It was possible that eliminating 25% of EOS evaluations immediately after birth might lead to an increase in NICU evaluation and/or admission at later points in newborn hospital care, due to later recognition of symptoms. However, we found no

TABLE 5 Cost and Resources Utilization

	CDC2002, <i>n</i> = 920	CDC2010, <i>n</i> = 476	<i>P</i> Value
Total cost for all evaluations, \$ (1000 LB $\geq$ 36)	253 724 (34 843)	132 843 (18 967)	<.01
Cost from inadequate GBS, \$ (1000 LB $\geq$ 36)	51 329 (7049)	386 (55)	<.001
Median total cost per patient (IQR), \$	293 (188–371)	292 (164–365)	.71
Total triage hours for all evaluations (1000 LB $\geq$ 36)	1361 (187)	864 (123)	<.01
Total triage hours from inadequate GBS (1000 LB $\geq$ 36)	215 (29.5)	1.1 (0.2)	<.001
Median triage hours per patient (IQR)			
No antibiotics	1.4 (0.4–2.9)	1.8 (0.5–3.2)	<.01
Antibiotics	0.8 (0.3–2)	0.7 (0.3–1.9)	.06
Return visits (% of total evaluated) ^a			
No antibiotics	1.8 (1.1–3.1)	2 (1.3–3.3)	<.01
Antibiotics	75 (8.2)	58 (12.2)	.02
No antibiotics	15 (1.6)	2 (0.4)	.07
Antibiotics	59 (6.4)	56 (11.8)	<.001

IQR from 5% to 95%.

^a Reasons for repeat visits included IV restart (49 in CDC2002 and 54 in CDC2010), repeat CBC count (17 in CDC2002 and 2 in CDC2010), start of antibiotic therapy due to abnormal I/T ratio or chorioamnionitis diagnosed in mother later by obstetrics (5 in CDC2002 and 2 in CDC2010), and repeat cultures for a false-positive blood culture (4 in CDC2002 group).

increase in NICU Triage visits or in NICU admissions between our study periods. It can be anticipated that some initially well-appearing infants born in the setting of inadequately indicated GBS IAP will become ill later in their newborn hospitalization. In the absence of IAP, the incidence of GBS bacteremia among term infants born to GBS-colonized women without fever or prolonged ROM was 0.4% in the only randomized controlled trial of GBS IAP.⁴ We identified 1 such infant during our study. To place this case in perspective, we reviewed all cases of early-onset GBS disease at our institution from 1997 to 2012. Among 140 989 live births, 4 cases of GBS EOS occurred among infants born at ≥ 37 weeks' gestation to GBS-positive mothers who received inadequate IAP (0.03 cases/1000 live births) (refs 13 and 23, and data not shown). These infrequent cases highlight the importance both of proper administration of GBS IAP whenever possible, and of the recommendation to observe infants born to women with inadequate GBS IAP in the hospital for a minimum of 48 hours.³

An unexpected finding in our study was a decline in the incidence of EOS evaluations prompted by maternal fever. Among all deliveries in our first study period, 8.9% had intrapartum fever

$\geq 100.4^{\circ}\text{F}$, but only 6.3% in our second study period. There are no differences between our CDC2002-aligned and CDC2010-aligned guidelines that can explain this finding. The CDC reports an incidence of maternal intrapartum fever of 3% to 4%,³ but other studies have reported intrapartum fever incidence ranging from 1% to 19% among term singleton deliveries, influenced by the use of epidural analgesia during labor.^{16–18} There were no changes in the GA distribution, in the use of epidural analgesia, in the overall rate of cesarean delivery (32.9% vs 33.1%, $P = .83$), or between the percentage of delivering women known to be GBS colonized (19.5% vs 20.3%, $P = .26$) between the 2 study periods. We speculate that the observed decline in incidence of maternal intrapartum fever may be due to secular trends in obstetrical practice, including increased use of acetaminophen during labor.

Multiple studies have questioned the utility of the CBC count in predicting neonatal EOS.^{19–22} Recent studies suggest that the optimal use of this laboratory test should account for age of the infant in hours after birth.²¹ Accordingly, the CDC 2010 revised guidelines suggest that CBC counts used in EOS evaluation may be delayed until the infant is 6 to 12 hours old.³ In our

previous study of EOS evaluation at our center in 2008 to 2009, we found no correlation between abnormal CBC count values and blood culture-confirmed infection, and little impact on care decisions.¹³ Our CDC2010-aligned algorithm advocates CBC count measurement only when the EOS evaluation takes place beyond 4 hours of age, resulting in a significant decline in CBC count measurement between our study cohorts. In agreement with our previous findings,¹³ abnormal WBC count/differential values were found in only 5% of tested well-appearing infants, with no cases of EOS among those infants.

Previous economic studies of neonatal EOS have focused on the costs associated with maternal screening, intrapartum prophylaxis, or neonatal GBS disease^{24–28} with little attention to the costs of neonatal evaluation. The resources expended over the study periods among asymptomatic infants at risk for EOS were considerable; more than 2200 nursing hours were required to evaluate 1396 infants, including 890 uninfected infants treated with antibiotics, at an estimated cost of nearly \$400 000. These efforts detected 2 EOS cases. We chose to take the CMA perspective, as this allowed us to quantify the immediate cost changes directly attributable to the change in local algorithm. Costs are directly related to the local structure of care delivery; associated costs would be significantly higher in centers that admit all antibiotic-treated infants to a NICU or special care nursery. Quantifying the specific sources of EOS-associated cost and the magnitude of change associated with a CDC2010-aligned algorithm may inform decisions about resource utilization in different care delivery models.

Our study has several limitations. Our local EOS algorithms are based on CDC published guidelines for prevention of

neonatal GBS disease. Recently, the American Academy of Pediatrics Committee on the Fetus and Newborn (COFN) published guidelines for EOS evaluation and prevention that advocate clinical observation alone for well-appearing infants born in the setting of inadequately indicated GBS IAP, even if born in the 36th week, and even if duration of ROM is ≥ 18 hours.²⁹ The COFN recommends CBC count and/or C-reactive protein be obtained at 6 to 12 hours of age as part of all EOS evaluations. Differing approaches, such as those advocated by COFN, are likely to have a different impact on the frequency and costs of EOS evaluation. As a retrospective cohort study we cannot account for secular trends in obstetrical practice. Our study is limited to the period from birth to hospital discharge, and we have no information on neonatal outcomes after discharge. Given the incidence of EOS among infants born at ≥ 36 weeks' gestation, even a study of 14 286 live births is unlikely to detect rare catastrophic outcomes, the cost of which could overwhelm the savings

found in our analysis. Furthermore, our study did not account for social costs, such as lower early breastfeeding rates and greater use of formula supplementation among infants who undergo EOS evaluation.^{30,31}

Finally, it is important to note that the obstetrical and neonatal practice at our center is to use intrapartum maternal fever as a surrogate for chorioamnionitis among deliveries occurring at ≥ 36 weeks' gestation. This practice is recognized as a legitimate approach in the CDC 2010 guidelines.³ Centers that focus on combinations of signs and symptoms to diagnose chorioamnionitis may find different rates of overall EOS evaluation. However, our study findings with regard to the management of infants born to women with inadequate GBS IAP in the absence of chorioamnionitis should be applicable to most birth centers.

CONCLUSIONS

A local algorithm for neonatal EOS evaluation based on the CDC 2010

guidelines resulted in a significant decrease in evaluation of well-appearing infants and demonstrable cost savings, without apparent harmful consequences. Even with a more restrictive algorithm, a significant proportion of uninfected, asymptomatic term infants were treated with systemic broad-spectrum antibiotics, highlighting the need for more effective diagnostic tests and/or predictive models for neonatal EOS.

ACKNOWLEDGMENTS

The authors thank Vineeta Vaidya and the Centers for Clinical Excellence at BWH for hospital demographic information, and the Research Patient Data Repository for laboratory data. The authors also acknowledge Dr Stella Kourembanas, the Division of Newborn Medicine at Children's Hospital, and the Scholars in Clinical Science Program (supported in part by National Institutes of Health award 8UL1TR000170-05) for ongoing support of Dr Mukhopadhyay.

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This work was conducted with support from Harvard Catalyst/The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health award 8UL1TR000170–05 and financial contributions from Harvard University and its affiliated academic health care centers). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.