OBSTETRICS

Cost-effectiveness of risk-based screening for cervical length to prevent preterm birth

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BACKGROUND: Despite much debate, there is no consensus on whether women without a history of prior spontaneous preterm birth should receive universal cervical length screening. Risk-based screening has been proposed as an alternative to universal cervical length measurement and may represent a more cost-effective approach to preterm birth prevention.

OBJECTIVE: We sought to evaluate the cost-effectiveness of risk-based screening compared to universal cervical length screening or no screening for preterm birth prevention in low-risk women.

STUDY DESIGN: A decision analytic model compared the cost and effectiveness of 3 cervical length screening strategies in a population of women with no prior preterm birth. Risk-based screening, universal screening, and no screening were compared using cost, probability, and utility estimates derived from the existing literature and the incremental cost-effectiveness ratios for each strategy were calculated.

RESULTS: In the base-case analysis, risk-based screening and universal screening were more effective and less costly than no screening. In comparison to the risk-based strategy, universal screening of the United States population of women without a prior preterm birth (N = 3.5 million annually) would result in 2.19 million more transvaginal ultrasounds, 11,027 more women treated with vaginal progesterone, 913 fewer preterm births <35 weeks gestational age, and 63 fewer neonatal deaths at an additional cost of $51,936,699 annually. Despite costing more, the additional health benefits of universal screening resulted in that strategy being more cost-effective than risk-based screening, with an incremental cost-effectiveness ratio of $21,144 per quality-adjusted life-year.

CONCLUSION: In women without a prior spontaneous preterm birth, universal cervical length screening is cost-effective in comparison to both risk-based screening and no screening.

Key words: cervical length, cost-effectiveness, preterm birth, screening

The rate of preterm birth in the United States has remained relatively constant during the last several decades despite extensive resources devoted to finding its cause, prevention, and treatment. The use of progesterone among women with a previous spontaneous preterm birth has been shown to be efficacious[1]; however, because the majority of preterm births occur in women without a history of previous preterm birth, any reduction in the number of preterm births has been relatively small, and the rate remains greater than 11%.[2-4] Thus, attention has turned to other high-risk populations, including women with a short cervix, in an effort to further reduce the rate of preterm birth.[5-7]

Results from 2 randomized controlled trials support the use of vaginal progesterone to reduce the risk of preterm birth in women discovered to have a short cervix on transvaginal ultrasound in the midtrimester.[8,9] Another randomized trial has demonstrated benefit from cerclage placement among women with a previous spontaneous preterm birth less than 34 weeks and a short cervix.[10] Thus, both the American College of Obstetricians and Gynecologists[11] and the Society for Maternal-Fetal Medicine[12] endorse the use of cervical length screening for women with a history of spontaneous preterm delivery and both recommend treatment with progesterone for any women with a short cervix, but there is no consensus on whether low-risk women should be universally screened with transvaginal sonogram.

EDITORS' CHOICE

Two cost-effectiveness analyses published before 2012 concluded that universal cervical length screening is less costly and more effective than no screening[13,14]; however, subsequent studies of low-risk women (women without a previous spontaneous preterm birth) have shown a prevalence of short cervix that is lower than previously estimated.[15-18] Subsequently, a third cost-effectiveness analysis concluded that universal cervical length screening is cost-effective compared with no screening, even when accounting for a lower prevalence of short cervix in a low-risk population.[19] Alternatively, some authors advocate for selective cervical length screening only in subgroups of women without a previous preterm birth who have other risk factors for short cervical length and, correspondingly, preterm birth.[15,17] Recent data suggest that the use of risk factors could both identify the majority of women who have a short cervix and significantly reduce the number of transvaginal cervical length measurements.[18] Given these recent data, we sought to examine whether, among women without a previous preterm birth, a risk-based screening approach would be cost-effective in comparison with universal screening or no screening at all.

Methods

Study design

We performed a cost-effectiveness analysis of 3 cervical length screening strategies in women without a history of previous spontaneous preterm birth. The first strategy, no screening, was one in which no women underwent cervical

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length screening. The second strategy, universal screening, involved screening all women in the second trimester. The third strategy, risk-based screening, involved cervical length screening only for women who had one or more previously identified risk factors that could be used to identify the majority of women with a short cervix.[18] These risk factors included black or Hispanic race/ethnicity, tobacco use, previous indicated preterm birth, or a previous cervical excisional procedure.

The study population included women with a singleton pregnancy. Women with a history of spontaneous preterm birth were excluded because cervical length screening is recommended in this population to determine whether they are candidates for cerclage and because they are recommended to receive progesterone regardless of cervical length.[8] Cervical length screening was performed via transvaginal ultrasound between 18 weeks, 0 days and 23 weeks, 6 days at the time of the routine fetal anatomic survey. A short cervix was defined as cervical length $\leq$20 mm, given that this is the threshold at which progesterone has proven efficacy. In the universal screening arm and the risk-based screening arm, women who were found to have a short cervix were offered daily treatment with 200 mg of micronized progesterone vaginally from diagnosis until 36 weeks and 6 days' gestation. Women in the no-screening arm did not receive any cervical surveillance or vaginal progesterone.

The probability of preterm delivery was based on the population-level risk of preterm birth and modified by whether a short cervix existed and progesterone treatment was received. We used 35 weeks and 0 days' gestational age to define preterm delivery, because this cutoff has been used in previous studies about the risk of preterm birth with a short cervix and is a gestational age associated with a greater chance of neonatal morbidity than 37 weeks of gestation.[5,20-22] The effectiveness of each strategy was expressed as quality-adjusted life years (QALYs), and the cost incurred by each strategy was expressed in US dollars, inflated to the year 2014.

Probabilities

Probabilities of each event were derived from the literature after we conducted a PubMed search using the key terms *short cervix*, *progesterone*, *preterm birth*, and *preterm labor*. These probabilities are presented in Table 1.[8,9,13-16,18-40] Each base-case probability was calculated as a weighted average of identified study point estimates. Ranges of probability estimates were determined from the lowest and highest estimates reported in the literature search. When only 1 point estimate was available, we used the 95% confidence interval, calculated by the use of the binomial distribution, to determine the range.

Baseline sensitivity and specificity of a risk-based screening strategy for identification of a woman with a short cervix were derived from the literature.[18] Because these data were from a single study, baseline estimates for sensitivity and specificity ranged widely in sensitivity analysis.

We estimated the probability of neonatal mortality or long-term morbidity on the basis of the probability of delivering at each gestational age and the probability of morbidity and mortality at each gestational age. Severe neonatal morbidity was defined as the composite of bronchopulmonary dysplasia, culture-proven sepsis, grade 3 or 4 intraventricular hemorrhage, seizures, and necrotizing enterocolitis.

Costs

Cost estimates were derived from the literature and were inflated to 2014 US dollars by the use of the medical care component of the Consumer Price Index. Future costs were discounted at 3% yearly rate. Base-case cost estimates are presented in Table 1.

The costs of cervical length screening when using transvaginal ultrasound and of treatment with vaginal progesterone from 18 to 37 weeks of gestation were based on Medicaid reimbursement rates published in the literature.[13,14,23] Cost of care for neonates differed on the basis of the gestational age and health status of the neonate, including (1) healthy, (2) surviving with long-term morbidity, or (3) death within the first 28 days.[24-26] For neonates surviving with long-term morbidity, costs included long-term disability-related care. This cost was assumed to be similar to the cost of care for an individual living with cerebral palsy, and this cost assumption varied widely to account for heterogeneity in the cost of ongoing care. For neonates who died, we included the initial hospital costs associated with their care before the time of death.

Utilities

Utilities were derived from the published literature, and QALYs were calculated for surviving neonates on the basis of an average life span of 75 years for an healthy infant and 45 years (range, 25−75 years) for infants with long-term morbidity. Similar to costs, utilities were discounted at a 3% yearly rate and varied widely in the sensitivity analysis. Base-case utility estimates are presented in Table 1.

Analysis

We used risk-based screening as the reference to which universal screening and no screening were compared. Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the difference in costs by the difference in QALYs for each of the 2 strategies being compared. For a strategy to be considered cost-effective compared with risk-based screening, we used a cutoff of $100,000 per QALY but also considered $50,000 and $150,000 per QALY in sensitivity analyses.[27]

We performed univariable sensitivity analyses across all ranges for probabilities, costs, and utilities to test the robustness of the model's results. We also performed a bivariable sensitivity analysis, planned ante hoc, using combinations of sensitivity and specificity values from 0 to 0.99 to define the thresholds of these test characteristics required for a risk-based screening strategy to be cost-effective compared with universal screening.

This was an institutional review board exempt study because it used only data from the published literature. The decision-tree model was constructed