Cost-effectiveness of transvaginal ultrasound cervical length screening in singletons without a prior preterm birth: an update

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OBJECTIVE: We sought to reevaluate the cost-effectiveness of universal transvaginal ultrasound (TVU) cervical length (CL) screening in singleton pregnancies without prior spontaneous preterm birth.

STUDY DESIGN: We developed a decision model to assess costs and effects of universal TVU CL screening at 18-23 weeks' gestation compared to routine care for singleton pregnancies without prior preterm birth. Based on recent data, the model contains the following updates: (1) reduced incidence of CL ≤20 mm at initial screening ultrasound (0.83%), (2) vaginal progesterone supplementation for women with CL ≤20 mm, (3) additional ultrasound(s) for women with CL 21-24.9 mm, and (4) the assumption that vaginal progesterone reduces the rate of preterm birth <34 weeks' gestation by 39% if a short CL is diagnosed. The primary outcome was incremental cost-effectiveness ratio. We assumed a willingness to pay of $100,000 per quality-adjusted life year (QALY) gained. Additional outcomes included incidence of offspring with long-term neurological deficits and neonatal death. Sensitivity analyses were performed to assess the robustness of the results.

RESULTS: For every 100,000 women screened, universal TVU CL screening costs $9132 compared to routine care. Screening results in 215 QALYs gained and 10 fewer neonatal deaths or neonates with long-term neurologic deficits per 100,000 women screened. Based on the updated data, universal CL screening in low-risk women remains a cost-effective strategy (incremental cost-effectiveness ratio = $43/QALY), but is not cost saving as previously estimated. Sensitivity analyses reveal that when incidence of TVU CL ≤20 mm is <0.31%, universal TVU CL screening is no longer cost-effective. Additionally, when TVU CL costs >$314, progesterone reduces preterm delivery risk before 34 weeks <19%, or the incidence of a TVU CL 21-24.9 mm is >6.5%, CL screening is also no longer cost-effective.

CONCLUSION: Despite the reduced incidence and efficacy used in this model, universal TVU CL continues to be cost-effective when compared to routine care in singletons without prior preterm birth.

Over the past 5 years much has been written regarding the pros and cons of universal cervical length (CL) screening in women with singleton gestations and no history of spontaneous preterm birth. The benefits of universal screening emanate from the assumption that women identified as high risk for preterm birth based on a shortened CL will be started on vaginal progesterone, which will reduce their risk of preterm birth. Fonseca et al[1] performed the first randomized controlled trial demonstrating that vaginal progesterone significantly reduced the risk of preterm birth in women found to have a CL ≤15 mm between 20-25 weeks. In 2011, Hassan et al[2] published the results of their randomized controlled trial that demonstrate that vaginal progesterone significantly reduced the risk of preterm birth in women with CLs between 10-20 mm who had no history of preterm birth. Subsequent to these studies, an individualized patient metaanalysis examining the effect of progesterone on preterm birth in women with shortened cervix (≤25 mm at 16-25 weeks) found that among women with no history of preterm birth, vaginal progesterone led to a 39% reduction in birth <33 weeks (RR, 0.61; 95% confidence interval, 0.42−0.91) and a similar reduction in composite neonatal morbidity and mortality (RR, 0.62; 95% confidence interval, 0.43−0.91).[3] Q3

Following the initial randomized controlled trial by Fonseca et al,[1] a strategy of universal transvaginal CL screening was found to be cost-effective in at least 2 published studies.[4,5] Shortly thereafter, the Society of Maternal-Fetal Medicine and the American Congress of Obstetricians and

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Gynecologists (ACOG) published recommendations regarding screening to prevent preterm birth stating "although this document does not mandate universal cervical length screening in women without a prior preterm birth, this screening strategy may be considered."[6] With this guidance, some centers in the United States began universal CL screening programs for low-risk women. Orzechowski et al[7] recently published the outcomes of their universal CL screening program in Philadelphia. This study, in which 1569 low-risk women underwent transvaginal CL ultrasound between 18 weeks' and 23 weeks and 6 days' gestation, revealed a much lower incidence of CL ≤20 mm than was previously estimated. In fact, the incidence was outside of the range of that used in either of the aforementioned cost-effective studies.

Given the new population-based estimate of the incidence of short cervix and the recent metaanalysis data on the efficacy of progesterone, we sought to create an updated decision model to assess whether conclusions of past cost-effective studies remain valid.

Materials and Methods

We updated our prior decision tree model[5] comparing 2 clinical strategic approaches to preterm birth prevention in low-risk pregnancies. The first strategy assumed no ultrasound screening for preterm birth in asymptomatic low-risk pregnant women (ie, no history of spontaneous preterm birth) with a singleton gestation. The second strategy included performance of a single routine transvaginal ultrasound CL measurement on all asymptomatic, low-risk singleton pregnant individuals between 18-23 weeks' gestation. In this strategy the CL was considered short (≤20 mm), midlength (>20 mm but <25 mm), or normal (≥25 mm). Women with a short cervix were started on vaginal progesterone that was continued until delivery or 36 weeks' gestation, whichever came first.[6] Women who had a midlength cervix were scheduled to return for another CL ultrasound 1 week later, but <24 weeks' gestation. If their CL at that time was ≤20 mm, they were started on

vaginal progesterone. Based on 2 randomized controlled trials and a meta-analysis, in women with a shortened cervix, vaginal progesterone was assumed to confer a reduction in preterm birth <34 weeks.[1-3]

The primary outcome of interest was the incremental cost-effectiveness ratio (ICER). ICER is a measure of the amount of resources that society must spend to gain 1 quality-adjusted life year (QALY). For this study, we assumed a willingness to pay of $100,000 for each neonatal QALY gained. In other words, a strategy was considered cost-effective if it cost <$100,000 to gain 1 year of optimal health for the offspring of the pregnancy. Additional outcomes measured included total cost for each strategy, total QALYs for each strategy, incidence of offspring with long-term neurological deficits, neonatal death, and incidence of preterm birth.

The baseline probability and outcomes for each strategy were obtained based on a bibliographic survey of the English-language literature in PubMed. We used the following search terms: "vaginal progesterone," "Prometrium," "preterm birth," "preterm delivery," "preterm prevention," "cervical length," and combinations of these terms. Point estimates were determined from published randomized controlled trials and prospective cohorts when possible. Retrospective cohorts or review studies were used when no other sources of information were available. The decision tree was developed and the analysis performed with TreeAge Pro 2007 (TreeAge Software, Williamstown, MA). The probability estimates and the references used in support of our model are reported in Table 1.

The incidence of a CL ≤20 mm was significantly lower in the Philadelphia cohort reported on by Orzechowski et al[7] than suggested in prior studies. Orzechowski et al[7] found that 0.83% of women with singletons and no prior spontaneous preterm birth screened between 18-24 weeks had an initial ultrasound finding consistent with a short cervix. An additional 0.19% of the study population had an initial ultrasound demonstrating a mid CL but a

subsequent ultrasound <24 weeks' gestation showing a short cervix. We used the data from this cohort to inform our base-case estimates for the population incidence of a short cervix, a mid-length cervix, and a long cervix in this low-risk population. In sensitivity analysis we allowed these incidence estimates to vary based on prior studies and as such the incidence of a short cervix varied from 0.2-1.9% and a midlength cervix from 0-8.7%.[1,2,7-9]

The preterm birth rates used in the model were inversely related to CL. The overall incidence of preterm birth <34 weeks' gestation was estimated at 1.3%; this also was based on data provided by Orzechowski et al[7] for their unscreened population. As this rate was significantly lower than any previously found in the literature, it was used both as the minimum and the base case. In sensitivity analysis, the preterm birth rate ranged as high as 3.6% for preterm birth <34 weeks' gestation based on data from US National Vital Statistics.[10] In the base-case analysis, 43% of women with a CL ≤20 mm prior to 23 weeks were assumed to deliver between viability and 34 weeks' gestation.[7] Among women who had a CL >20 mm but <25 mm that did not shorten with a second ultrasound, 25% were assumed to deliver <34 weeks' gestation.[7] The preterm birth rates used in the base-case model are similar to those estimated using data from Hassan et al[11] in which 55% of women with a CL ≤20 mm delivered at <34 weeks and 22% of women with a CL >20 mm but <25 mm delivered at <34 weeks. These data points were included in the sensitivity analysis.

The risk of preterm birth associated with a short cervix was assumed to decrease by 39% with progesterone administration based on the meta-analysis by Romero et al.[3] In sensitivity analysis, we used the minimum and maximum reductions in preterm births found in the 2 randomized controlled trials assessing the efficacy of progesterone to reduce preterm birth in women with a shortened cervix (6-65%).[1,2] Furthermore, in base-case analysis, progesterone was assumed to provide no reduction in the preterm birth rate if the

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