

# Universal cervical length screening in singleton gestations without a previous preterm birth: ten reasons why it should be implemented

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In 1968, Wilson and Jungner<sup>1</sup> set a public health milestone by outlining the principles for using a screening test for early disease detection. These principles laid the foundation for the Papanicolaou smear test as an acceptable screening test for cervical cancer and are still used by the World Health Organization. Since 1968, the application of these screening test criteria has become a main pillar of preventive medicine by improving public health and contributing to society's well-being.

Spontaneous preterm birth (PTB) is a major public health challenge. A short cervical length (CL) detected by transvaginal ultrasound (TVU) in the second trimester is 1 of the best current predictors of subsequent PTB.<sup>2</sup> TVU CL screening of singleton gestations with previous PTB already has been recommended by American College of Obstetricians and Gynecologists (ACOG),<sup>3</sup> Society for Maternal Fetal Medicine (SMFM),<sup>4</sup> and Royal College of Obstetricians and Gynaecologists.<sup>5</sup> Universal TVU CL screening for singleton gestations has been proposed.<sup>3,4</sup> As previously concluded by Combs,<sup>6</sup> TVU CL is a good screening test for PTB prevention because it meets the screening test criteria by Wilson and Jungner,<sup>1</sup> which is further evidence that supports it being a health-promoting effective screening test that meets all the World Health Organization criteria (Table).

Here are 10 reasons:

## 1. PTB is an important global health issue.

PTB is a global health issue. In 2010, 14.9 million babies were born preterm, which caused >1 million neonatal deaths<sup>7</sup> or approximated 1 death every 30 seconds. In addition to its contribution to mortality rate, PTB has lifelong sequelae on neurodevelopmental functioning.<sup>8</sup> Rates of neonatal morbidity and mortality vary between the developing and the developed world, but that variation also exists among different high-income countries, as well. The United States accounts for 42% of all PTBs among high-income countries.<sup>9</sup>

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Of the approximately >450,000 annual PTBs in the United States, 93% occur in women without a previous PTB (Joyce Martin, National Center for Vital Statistics, Center for Disease Control; written personal communication; January 7, 2015). Moreover, almost all of singleton gestations without previous PTB (96%) do have at least 1 (if not more) of the >30 risk factors for PTB.<sup>10</sup>

## 2. There is accepted treatment for women diagnosed with a short cervix in pregnancy.

Vaginal progesterone in singleton gestations with a short cervix with or without a previous PTB reduces the risk of PTB and neonatal morbidity and death, as per 2 well-designed randomized controlled trials<sup>11,12</sup> and a metaanalysis.<sup>13</sup> Given these data, ACOG and SMFM recommend giving progesterone 200-mg suppositories or 90-mg gel daily to singleton gestations without a previous PTB but with TVU CL of  $\leq 20$  mm at <25 weeks of gestation.<sup>3,4</sup>

## 3. Facilities for diagnosis and treatment are available.

All pregnancies are recommended to have an ultrasound scan for fetal anatomy screening at 18-24 weeks of gestation.<sup>14</sup> Including a TVU CL measurement at the time of the visit does not impact visit length or patient attitudes significantly.<sup>15,16</sup> Once the risk of PTB is diagnosed, treatment with vaginal progesterone and follow-up evaluation easily could be integrated into routine prenatal care. Thus, every effort should be made to increase the number of certified sonographers for TVU CL measurement, which could be a limitation for widespread screening.

## 4. A short cervix is a recognizable indicator of preterm delivery in asymptomatic women.

Spontaneous PTB almost always involves early dilation of the cervix. TVU CL is a better predictor of PTB than digital physical examination.<sup>17</sup> A short cervix is associated closely with subsequent spontaneous PTB<sup>2</sup> and a reliable sign of its latency. The lack of success of a digital examination in the prediction of PTB because of its subjectivity, high interobserver variability,<sup>18</sup> inaccuracy for evaluation of the internal os,<sup>19</sup> and nonspecificity<sup>20</sup> makes TVU CL far superior to manual examination of the cervix in PTB prediction. It is the internal os, which is visible only on ultrasound scanning, that first starts to open, and not the external os, which is the only cervical portion that is palpable by digital examination.

## 5. There is a reliable and validated test for CL measurement.

TVU is a reproducible and reliable test with <10% intra- and interobserver variability.<sup>17</sup> Initial attempts to measure CL

TABLE

**Wilson and Jungner's classic screening criteria (1968)<sup>1</sup>**

Criteria	Universal transvaginal ultrasound cervical length screening
1. The condition sought should be an important health problem.	Preterm birth is associated with 1 million neonatal deaths worldwide.
2. There should be an accepted treatment for patients with recognized disease.	Vaginal progesterone is a proven treatment for preterm birth prevention in singleton gestations with a short cervix.
3. Facilities for diagnosis and treatment should be available.	All pregnant women are offered ultrasound at 18-24 weeks of gestation and can be offered transvaginal ultrasound cervical length.
4. There should be a recognizable latent or early symptomatic stage.	A short transvaginal ultrasound cervical length is an early predictor of preterm birth.
5. There should be a suitable test or examination.	Transvaginal ultrasound is a validated reliable test for cervical length measurement.
6. The test should be acceptable to the population.	Transvaginal ultrasound cervical length is acceptable by more than approximately 75% of women with singleton gestations and no previous spontaneous preterm birth.
7. The natural history of the condition, including development from latent to declared disease, should be understood adequately.	Transvaginal ultrasound cervical length shortening precedes, by weeks or months, digitally detected cervical changes, symptomatic uterine contractions, and eventual preterm birth.
8. There should be an agreed policy on whom to treat as patients	Transvaginal ultrasound cervical length $\leq 20$ mm at $<24$ weeks of gestation is the currently accepted indication for treatment in singleton gestations without previous preterm birth.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be balanced economically in relation to possible expenditure on medical care as a whole.	Several studies have confirmed the cost-effectiveness of universal transvaginal ultrasound cervical length screening.
10. Case-finding should be a continuing process and not a "once and for all" project.	Preterm birth prevention is a continuous process; preterm birth is not an infection for which a vaccine can be devised, and the disease eradicated.

*Khalifeh. Universal CL screening for the prediction and prevention of PTB. Am J Obstet Gynecol 2016.*

date back to the 1970s, starting with a transabdominal ultrasound scan (TAU), with TVU CL initially reported in the early 1990s.<sup>21</sup> TAU, however, has been proved to be significantly inferior to TVU CL screening for at least 6 reasons. First, several factors contribute to suboptimal CL assessment: obesity makes it difficult to visualize the cervix by TAU; many studies require a full bladder, which falsely can elongate the cervix or mask funneling/short cervix; the large distance between the cervix and the probe and fetal parts may obscure the image; and manual pressure can also elongate the cervix. Second, all randomized controlled trials with proven beneficial intervention in a short cervix have used a TVU approach.<sup>11,12</sup> Third, the sensitivity of transvaginal approach is significantly higher than that of a transabdominal approach).<sup>22-26</sup> Fourth, prospective studies that compare TAU and TVU show that a high CL cutoff (eg, 36 mm) is necessary to make TAU sensitive (96%) for the detection of TVU CL of  $<25$  mm, along with technical problems and image limitations,<sup>26</sup> which then requires that most women (about two thirds) who are screened with TAU get screened also with TVU anyway.<sup>27,28</sup> Fifth, universal TVU screening is more cost-effective than TAU screening.<sup>27</sup> Sixth, ACOG and SMFM recommend against TAU CL screening, stating that TVU is superior and the only recommended technique.<sup>3,4</sup>

Today, TVU is the gold standard for CL measurement that has been adopted by both ACOG and SMFM. This screening should be done according to strict quality criteria, which are now easily accessible by practitioners in the United States via CLEAR (Cervical Length Education and Review) and the Perinatal Quality Foundation (<https://clear.perinatalquality.org>),<sup>29</sup> and in Europe through the Fetal Medicine Foundation.<sup>30</sup>

#### **6. CL measurement with the use of a TVU is an acceptable test for pregnant women.**

TVU is acceptable by women, with  $<2\%$  experiencing severe discomfort.<sup>31</sup> Most women find TVU less difficult than cervical smears; approximately 75% of women with singleton gestations and without a previous spontaneous PTB agree to undergo TVU CL screening at 18-24 weeks of gestation.<sup>16</sup> In addition, the safety of TVU among pregnant women is well-documented. In a randomized controlled trial to assess maternal infection in the setting of preterm premature rupture of membranes, TVU did not increase the risk of infection.<sup>32</sup>

#### **7. The natural history of CL shortening leading to PTB is well understood.**

Once CL shortening occurs, the risk of PTB is increased several folds.<sup>2</sup> CL shortening progressively worsens with time

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