

Fetal fibronectin testing in threatened preterm labor: time for more study!



TO THE EDITORS: I am concerned that the recent systematic review and meta-analysis by Berghella and Saccone,¹ as well as the accompanying editorial by Macones,² may overstate the appropriate conclusions. While Berghella and Saccone do acknowledge that “further study must be undertaken to better understand whether and under what circumstances the predictive characteristics of the fetal fibronectin [FFN] test can be translated into better clinical management,” this is perhaps not made sufficiently clear in either the abstract or the editorial.

Of the studies reviewed, only 3 used FFN as part of a strict protocol. Of these, one is unpublished, a second is underpowered, and the third in fact did show reduced admission and length of stay.³ The remaining 4 studies left management to physician discretion.

Obtaining an FFN and leaving management entirely to physician discretion would be analogous to obtaining a midtrimester cervical length on all women and leaving management to physician discretion. Imagine the mix of bed rest, cerclage, and tocolysis that might ensue.

All that we can currently conclude is that obtaining a fetal fibronectin outside a strict clinical protocol is of no benefit. Thus, I submit that the more appropriate conclusion should be that further study of FFN within a strict clinical protocol, possibly in conjunction with cervical sonography, is warranted. Failure to continue such study might deprive us of a tool that, appropriately used, might save many women from needless interventions. ■

Kent D. Heyborne, MD
 Department of Obstetrics and Gynecology
 Denver Health and Hospital Authority
 777 Bannock St, mc 0660
 Denver, CO 80204
 Department of Obstetrics and Gynecology
 University of Colorado Denver
 Aurora, CO
kent.heyborne@dhha.org

The author reports no conflict of interest.

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REPLY



We thank Dr Heyborne for his interest in our work. As he says, we did state in our meta-analysis on women with threatened preterm labor (PTL),¹ that “further study must be undertaken to better understand whether and under what circumstances the predictive characteristics of the fetal fibronectin [FFN] test can be translated into better clinical management.”

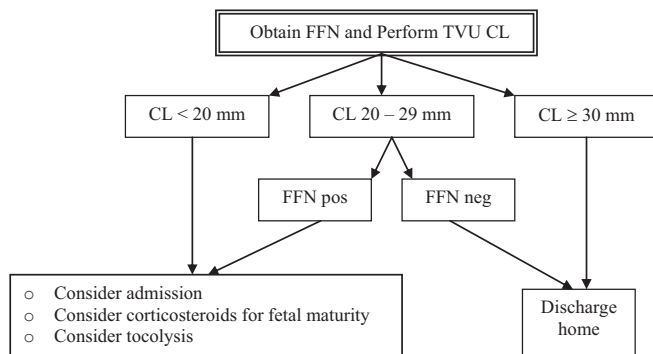
This is for several reasons, of which we want to highlight at least two. First, as Dr Heyborne states, protocols were not used in all randomized controlled studies (RCTs) included. FFN is predictive of preterm birth (PTB) in women with PTL, but we might not have studied the right interventions for those with positive results.

Second, our meta-analysis might have been underpowered to detect an effect. The incidence of spontaneous PTB <37 weeks was 20.7% in the FFN knowledge group and 29.2% in the no FFN knowledge group, with a relative risk of 0.72 (so a 28% decrease in spontaneous PTB), but the 95% confidence intervals just crossed 1 (0.52–1.01).¹ A bigger sample size, which can be achieved by further and larger RCTs, might certainly make FFN eventually associated with significant benefits.

Unfortunately, until further studies are done, in 2017 so far one cannot recommend FFN to be routinely done for women with PTL. That is why neither the Society for Maternal-Fetal Medicine² nor the American College of Obstetricians and Gynecologists³ recommend FFN use alone for women with PTL. The use of transvaginal ultrasound (TVU) cervical length (CL) in women with PTL has instead been better supported by evidence from RCTs.⁴

The best evidence for use of FFN in women with PTL is for those with TVU CL 20–29 mm when a positive FFN can lead to more aggressive management with admission, steroids, and possibly tocolysis, while a negative FFN can lead to a discharge home.^{4,5} This is part of a PTL management algorithm based mostly on TVU CL screening, as shown in the [Figure](#) and suggested in the Society for Maternal-Fetal Medicine PTB Toolkit, both on the website⁵ and on the app.⁶

In conclusions, we do agree with Dr Heyborne that “the more appropriate conclusion should be that further study of

FIGURE**Suggested algorithm for the management of PTL in women with cervix < 3cm dilated on initial exam**

PTL, preterm labor; CTX, contractions; FFN, fetal fibronectin; TVU CL, transvaginal ultrasound cervical length. Modified from².

Berghella and Saccone. *Am J Obstet Gynecol* 2017.

FFN within a strict clinical protocol, possibly in conjunction with cervical sonography, is warranted.” ■

Vincenzo Berghella, MD
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
Sidney Kimmel Medical College
Thomas Jefferson University
833 Chestnut
Philadelphia, PA 19107
vincenzo.berghella@jefferson.edu

Gabriele Saccone, MD
Department of Neuroscience, Reproductive Sciences and Dentistry
School of Medicine
University of Naples Federico II
Naples, Italy
The authors report no conflict of interest.

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REPLY

I thank Dr Heyborne for his comments about my recent editorial.¹ I certainly agree with Dr Heyborne that additional research is useful and needed in almost all areas of clinical obstetrics. However, we need to use the available data to make decisions today about how best to care for our patients. This is where the recent meta-analyses of Berghella and Saccone² is so useful because it clearly demonstrates that, based on data available today, the promise of fetal fibronectin in the assessment of women with threatened preterm labor has not been realized, and therefore, this test should not be used routinely in clinical care (outside a research study).

I do disagree with Dr Heyborne's assessment that future research on fetal fibronectin should be driven primarily by a strict protocol that prescribes a specific course of action based on the results of the test. That is certainly a reasonable place to start. But in the end, what we really care about is how real doctors use test results in real practice. It is this type of research that is most generalizable and reflective of how a screening/diagnostic test has an impact on clinical care and patient outcomes. ■

George A. Macones, MD
Department of Obstetrics and Gynecology
Washington University in St Louis
School of Medicine
Campus Box 8064
St Louis, MO 63110-1094
maconesg@wudosis.wustl.edu

The author reports no conflict of interest.

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