

specific group of women would result in a 10% reduction in transfers, maternal admission, and treatment.¹⁴ This information did not need an RCT, and limitation of the meta-analysis of Berghella and Saccone¹ to RCTs only does not justify the conclusion that fetal fibronectin testing in women with threatened preterm labor cannot be justified.

Based on the aforementioned issues, we are not convinced that the meta-analysis of Berghella and Saccone¹ of RCTs justifies the abandonment of the fibronectin test in symptomatic women, as proposed in the editorial comment. Although RCTs are considered the gold standard in evidence synthesis and provide the best answer in many research questions, they do not necessarily do so in the evaluation of diagnostic tests. ■

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The authors received fibronectin test from Hologic to perform the European Fibronectin Study (Bruijn MM, Kamphuis EI, Hoesli IM, et al. The predictive value of quantitative fibronectin testing in combination with cervical length measurement in symptomatic women. *Am J Obstet Gynecol* 2016;215:793.e1-8).

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REPLY

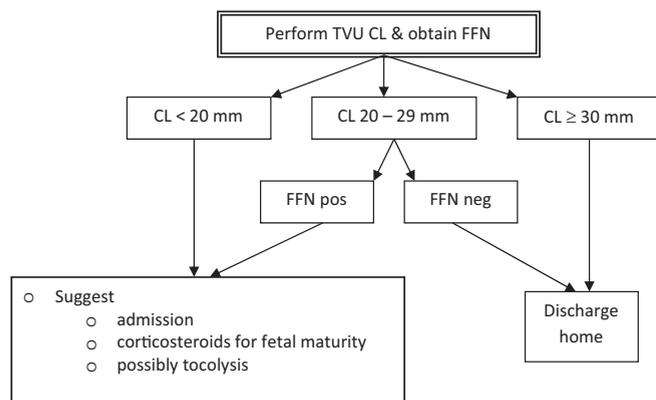


We thank van Baaren et al for their letter and their interest in our study on fetal fibronectin (FFN) for management of women with preterm labor (PTL) at around 23-34 weeks.¹ We congratulate their group for having done important work in this area, and confirmed themselves the good prediction of transvaginal ultrasound (TVU) cervical length (CL) in combination with FFN for prediction of preterm birth (PTB) in women with threatened PTL.²⁻⁵

We agree that a test, eg, FFN, by itself would not prevent the outcome, eg, PTB. Nonetheless, if a test is done, one must be ready with a therapy for that test in case it is positive. It's like ordering a cholesterol level for a patient, and hoping it comes back negative. The test may come back positive, and it would not be helpful to just say to the patient, "Given your high cholesterol level, you are at high risk for a heart attack. Good-bye." Same is true of FFN. If the FFN comes back high (ie, positive), the obstetric provider cannot just say, "Given your high FFN level, you are at high risk for delivering preterm. Good-bye." This would be not only unhelpful, but detrimental, as it would just increase the stress level of a woman already having discomfort from threatened PTL. Unfortunately, while several interventions are available for a patient with high cholesterol (eg, change in diet, exercise, medications), no intervention (little research has been done in this area) has been shown to be beneficial for a positive FFN.⁶

van Baaren et al make the case nonetheless that FFN use in women with PTL would perhaps save utilization of resources. As they state in their letter, maternal hospitalization,

FIGURE
Suggested management algorithm for women presenting with threatened preterm labor



Suggested algorithm for management of threatened preterm labor (PTL) in women with cervix <3 cm dilated on initial manual exam.⁷

CL, cervical length; CTX, contractions; FFN, fetal fibronectin; TVU, transvaginal ultrasound.

Berghella. RCTs for FFN. *Am J Obstet Gynecol* 2018.

administration of tocolysis, administration of steroids for fetal maturity, time in triage, and hospitalization costs were not lower in the FFN group compared to controls in whom FFN was not used in our meta-analysis.¹ In fact, hospitalization charges were \$153 significantly higher in the FFN group.¹ Neither the Society for Maternal-Fetal Medicine (SMFM),⁷ nor the American Congress of Obstetricians and Gynecologists,⁸ recommend FFN use alone for women with threatened PTL.

We agree with van Baaren et al that the way forward involves TVU CL in the management of women with threatened PTL. Their group has shown that, in women with threatened PTL, a TVU CL <15 mm is consistent with a high risk for PTB and warrants interventions (eg, hospitalization, steroids, and possibly tocolysis); a TVU CL ≥30 mm is associated with a very low risk of PTB within 7 days (<2%) and therefore these women can be discharged, while FFN can be best used for women with a “borderline” TVU CL of 15-30 mm.⁴ Their group has indeed shown this management strategy is cost-effective.⁵

Randomized studies and meta-analyses of these trials have been done using this strategy of mainly TVU CL screening for evaluating women with threatened PTL, with FFN only for borderline TVU CL measurements.^{9,10} The most informative studies are, as van Baaren et al point out, those using a management protocol (Figure).⁹ The management protocol in the Figure has indeed been associated in a randomized trial and a meta-analysis of randomized trials with a significant decrease in PTB <37 weeks.^{9,10} We encourage the reader to download the free “SMFM PTB toolkit” (type these words in the App store) App^{7,11} on their

iPhone (Apple, Cupertino, CA) or any Android device for easy use of this protocol during their clinical management of women with threatened PTL. ■

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