

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Study Protocol: Quantitative Fibronectin to help Decision-making in women with Symptoms of Preterm Labour (QUIDS) Part One- Individual Patient Data Meta-analysis and Health Economic Analysis
<b>AUTHORS</b>	Stock, Sarah; Wotherspoon, Lisa; Boyd, Kathleen; Morris, R. K.; Dorling, Jon; Jackson, Lesley; Chandiramani, Manju; David, Anna; Khalil, Asma; Shennan, Andrew; Hodgetts Morton, Victoria; Lavender, Tina; Khan, Khalid; Harper-Clarke, Susan; Mol, Ben; Riley, Richard; Norrie, John; Norman, Jane

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Giuseppe Rizzo Università Roma Tor Vergata Division of Maternal and Fetal Medicine Ospedale Cristo Re Rome Italy
<b>REVIEW RETURNED</b>	17-Jan-2018

<b>GENERAL COMMENTS</b>	This is an interesting paper joinining a meta-analysis with a prospective study so I would like to ongratulate Authors for theire effort My concern is that Authors did non consider the role of ultrasonographic assssment of verical length that may have a pivotal role in predicting preterm delivery. My suggestion are either to add in the prospective protocol (preferred) or to add as a limitaion of the study
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<b>REVIEWER</b>	Nigel Simpson University of Leeds
<b>REVIEW RETURNED</b>	19-Jan-2018

<b>GENERAL COMMENTS</b>	A clear and commendably pragmatic rationale and approach towards developing a decision-assist tool in women presenting in suspected preterm labour is described. I have no concerns about the study protocol nor the admirably framed prose in which it is presented.
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### VERSION 1 – AUTHOR RESPONSE

Response to Reviewers Comments

Reviewer: 1

Reviewer Name: Giuseppe Rizzo

This is an interesting paper joinining a meta-analysis with a prospective study so I would like to ongratulate Authors for theie effort

My concern is that Authors did non consider the role of ultrasonographic assssment of verical length that may have a pivotal role in predicting preterm delivery. My suggestion are either to add in the prospective protocol (preferred) or to add as a limitaion of the study

-Many thanks to the reviewer for their comments. We agree that cervical length is potentially important, and have considered it's inclusion carefully.

i) We have always planned to include cervical length as a variable in the individual patient data level meta-analysis and prognostic model (as documented e.g. on Page 13 line 22; Page 15 line 12).

ii) Cervical length is also included as a variable (where available) in the prospective cohort study -see table 1 page 16 in the supplementary material prospective cohort study protocol "Quantitative Fibronectin to help Decision-making in women with Symptoms of Preterm Labour (QUIDS) Part Two-Prospective Cohort Study".

iii) The inclusion of cervical length is also discussed in detail in the supplementary prospective cohort study protocol on page 19; lines 6-24 (" It is possible that the IPD meta-analysis will find there is potential added value of combining quantitative fFN testing with cervical length measurement.[12,13] As cervical length measurement has significant resource requirement (estimated NHS cost £68.16 per test) and lack of out of hours provision further limits availability in many NHS hospitals, we think it is very unlikely that cervical length scanning will improve performance of the prognostic model to such a degree as to make it cost effective. We will assess the incremental costs and effects of cervical length measurement in the proposed health economic model performed in parallel with the IPD meta-analysis, and will feed into design considerations during the first iteration of the prognostic model. If inclusion of cervical length ultrasound is found to be potentially cost-effective, we will assess the feasibility of including it in the prospective cohort study. We anticipate that including cervical length measurement in the prospective cohort study would be extremely difficult in the current NHS setting as the majority of units do not have 24 hour availability of transvaginal ultrasound and/or trained personnel to perform scans. Inclusion of cervical length would also likely decrease recruitment rate (due to need for additional transvaginal ultrasound examination) and require significant additional resources.")

-As we are in agreement with the reviewer, and will consider inclusion of cervical length in our model, we have made no changes to the text.

Reviewer: 2

Reviewer Name: Nigel Simpson

A clear and commendably pragmatic rationale and approach towards developing a decision-assist tool in women presenting in suspected preterm labour is described. I have no concerns about the study protocol nor the admirably framed prose in which it is presented.