BMJ Open

Assessment of cervical softening and the prediction of preterm birth (STIPP): protocol for a prospective cohort study

Sofie Breuking ,[1,2] Martijn A Oudijk ,[2,3] Rik van Eekelen,[2] Marjon A de Boer,[2,3] Eva Pajkrt,[1,2] Frederik Hermans[1,2]

To cite: Breuking S, Oudijk MA, van Eekelen R, *et al*. Assessment of cervical softening and the prediction of preterm birth (STIPP): protocol for a prospective cohort study. *BMJ Open* 2023;**13**:e071597. doi:10.1136/bmjopen-2023-071597

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-071597).

Received 03 January 2023
Accepted 17 October 2023

[1]Obstetrics and Gynaecology, Amsterdam UMC Location AMC, Amsterdam, North-Holland, Netherlands
[2]Amsterdam Reproduction and Development Research Institute, Amsterdam, Netherlands
[3]Obstetrics and Gynaecology, Amsterdam UMC Location VUmc, Amsterdam, North-Holland, Netherlands

Correspondence to
Sofie Breuking;
s.h.breuking@amsterdamumc.nl

ABSTRACT

Introduction Preterm birth (PTB) is among the leading causes of perinatal and childhood morbidity and mortality. Therefore, accurate identification of pregnant women at high risk of PTB is key to enable obstetric healthcare professionals to apply interventions that improve perinatal and childhood outcomes. Serial transvaginal cervical length measurement is used to screen asymptomatic pregnant women with a history of PTB and identify those at high risk for a recurrent PTB. Cervical length measurement, fetal fibronectin test or a combination of both can be used to identify women at high risk of PTB presenting with symptoms of threatened PTB. The predictive capacity of these methods can be improved. Cervical softening is a precursor of cervical shortening, effacement and dilatation and could be a new marker to identify women a high risk of PTB. However, the predictive value of cervical softening to predict spontaneous PTB still needs to be determined.

Methods and analysis This is a single-centre, prospective cohort study, conducted at the Amsterdam University Medical Centers in the Netherlands. Cervical softening will be investigated with a non-invasive CE-marked device called the Pregnolia System. This device has been developed to evaluate consistency of the cervix based on tissue elasticity. Two different cohorts will be investigated. The first cohort includes women with a history of spontaneous PTB <34 weeks. These women undergo biweekly measurements between 14 and 24 weeks of gestation. The second cohort includes women with symptoms of threatened PTB. These women will receive the measurement once at presentation between 24 and 34 weeks of gestation. The primary outcome is spontaneous PTB before 34 weeks for women with a history of PTB and delivery within 7 days for women with threatened PTB. The minimum sample size required to analyse the primary outcome is 227 women in the cohort of women with a history of PTB and 163 women in the cohort of women with symptoms of threatened PTB. Once this number is achieved, the study will be continued to investigate secondary objectives.

Ethics and dissemination The study is approved by the Medical Ethics Committee of Amsterdam UMC (METC2022.0226). All patients will give oral and written informed consent prior to study entry. Results will be disseminated via a peer-reviewed journal.

Trial registration number NCT05477381.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The strength of this study is that it is organised with minimal interference in daily practice and therefore a high participation rate is expected.
⇒ Another notable strength of the study is its prospective cohort design, which includes women across a range of all cervical lengths, thereby establishing an internal control group of women with longer cervix lengths within the cohorts.
⇒ This study investigates the Cervical Stiffness Index in a population women with a high risk for preterm birth (PTB) and combines the results with other important predictors for PTB.
⇒ As a prospectively cohort study, we expect less bias than in a retrospective cohort.
⇒ The limitation of the study is the single-centre setting, potentially limiting external validity and generalisability.

INTRODUCTION

Spontaneous preterm birth (PTB), defined as delivery before 37 weeks of gestation, is the leading cause of perinatal and neonatal morbidity and mortality.[1] Rates of spontaneous PTB appear to be increasing. Annually, 15 million children are born preterm which directly contributes to the death of one million neonates.[2 3] Neonates who survive PTB are at increased risk for long-term neurological sequelae and developmental disabilities.[4 5] Identifying pregnant women at risk is important to be able to take precautionary measures; however, this is a challenge for obstetric healthcare professionals.

Important obstetric and gynaecological risk factors for PTB are mid-trimester short cervical length, prior cervical surgery and previous spontaneous PTB.[6–9] Women with a history of spontaneous PTB before 34 weeks of gestation are at a fivefold increased risk of a spontaneous PTB in a subsequent pregnancy compared to women with a previous term birth.[10] In addition to vaginal progesterone

administration, biweekly cervical length screening is recommended for these women. This can identify women at high risk of recurrent PTB based on short cervical length who benefit from a vaginal cerclage. However, in women with a previous PTB, the positive predictive value (PPV) of a short cervical length is 34%.[11] Therefore, this approach only identifies a proportion of women who will have a recurrent PTB. This calls for additional measurements to identify the group more adequately at risk for recurrent PTB.

Another group of pregnant women at risk of PTB are women presenting with symptoms of threatened PTB in their current pregnancy. These women can be triaged with transvaginal cervical length measurement and fetal fibronectin (fFN) to identify women with an increased risk of delivery within 7 days. Women with a high risk of PTB, at less than 32 weeks of gestation, are admitted to a centre with NICU facilities and treated with antenatal corticosteroids and tocolysis for 48 hours to improve perinatal outcome.[12] This combination fFN and cervical length measurements are characterised by a high negative predictive value but a poor PPV. This results in overtreatment and unnecessary healthcare costs. A large proportion of women with symptoms of threatened PTB will not deliver within 7 days due to the low PPV; however, these women remain at risk for PTB later in pregnancy.[13–15]

More adequate techniques to assess women at high risk of recurrent PTB or at high risk of delivering in a short time frame when presenting with symptoms of threatened PTB are urgently needed. Therefore, objective measurement of the cervical consistency is a promising technique.

To maintain pregnancy and deliver at term, an appropriate function of the cervix is required. Delivery is preceded by softening and shortening of the cervix.[16] Changes in cervical consistency can be detected from fertilisation until delivery. Throughout pregnancy the consistency of the cervix changes and will start softening when approaching delivery.[17 18] Softening of the cervix precedes shortening and therefore could be a promising marker to identify an upcoming delivery at an earlier stage.

Parra-Saavedra *et al*[19] investigated this phenomenon with transvaginal ultrasound. The cervical consistency was measured by measuring the difference of the anteroposterior cervical diameter before (AP) and after (AP^1) application of pressure on the cervix with the transvaginal probe. The cervical consistency was then calculated with the following formula: ((AP^1/AP) * 100) = Cervical consistency index. Cervical consistency had an inverse linear relationship with gestational age. This means that cervical consistency declines, thus becoming softer, during progression of pregnancy and this phenomenon can be detected during pregnancy. Second, it demonstrated that pregnant women with a more progressive decline in cervical consistency are more likely to have a spontaneous PTB compared with women with physiological decline in cervical consistency.

Other techniques that show positive results in evaluating cervical softness are by using elastography methods, including strain elastography (SE) and shear wave elastography (SWE).[20] Nonetheless, there are technical considerations that first need to be resolved before elastography can be applied extensively. For example, the results of SE are affected by operator-applied pressure on the cervix, resulting in an interobserver variability making the technique less objective and standardised.[21 22] Moreover, for SWE safety concerns such as the unknown risk on fetal tissues, first must be addressed before elastography methods can be applied extensively.[23]

Recently, a non-invasive technique has been developed to evaluate consistency of the cervix based on tissue elasticity. The Pregnolia System is a market-available, CE-marked device designed to measure cervical stiffness. This system provides quantitative measurements of the cervical consistency based on aspiration technique.

A prototype has been tested and measurements were carried out in 50 non-pregnant and 50 pregnant women.[18] The results were in line with the study by Parra-Saavedra *et al*[19] and showed that as pregnancy progresses, the cervix softens and this process starts before shortening. Therefore, by measuring the Cervical Stiffness Index (CSI), delivery could be detected earlier compared with conventional shortening of the cervix measured with transvaginal ultrasound.

Also, a recent study by Stone *et al*[22] investigated cervical softness before cerclage placement with the Pregnolia System. This study demonstrated that women with an ultrasound-indicated cerclage had significantly softer cervices compared to a control group of healty pregnant women without a history of cervical insufficiency. They also stated this aspiration technique is a promising technique for objective and quantitative measurement of cervical softness.

Since cervical softening is a precursor of cervical shortening; this could be a novel marker to predict spontaneous PTB and contribute to better identification of women with an increased risk of PTB. Also, the predictive value of cervical softening in combination with cervical length could be promising to improve prediction of PTB. However, these hypotheses still must be examined.

Therefore, the aim of this cohort study is to evaluate the predictive value of the CSI to predict the risk of spontaneous PTB in pregnant women with an increased risk of PTB.

METHODS AND ANALYSIS

Study design

This study is an investigator-initiated, single-centre prospective cohort study being conducted at the Amsterdam University Medical Centers in the Netherlands. Recruitment started on 18 August 2022. We expect a study duration of 3 years to investigate the primary objectives.

Two cohorts will be investigated:

1. Pregnant women with a history of spontaneous PTB before 34 weeks of gestation (A-STIPP Cohort).
2. Pregnant women presenting with symptoms of threatened PTB between 24 and 34 weeks of gestation (S-STIPP Cohort).

The measurements of cervical stiffness will be performed in addition to standard care (online supplemental appendix 1), using the aspiration technique-based device named the Pregnolia System.

Participants

In order to be eligible to participate in this study, pregnant women must meet all of the following criteria:

1. Age 18 years or above.
2. Ability to understand Dutch or English (both spoken and written).
3. Ultrasound-based gestational age determined by measurement of crown rump length (CRL), determined between 9 and 11 weeks of gestation.
4. Singleton and twin pregnancies.

A-STIPP cohort

Pregnant women with an increased risk of PTB based on a medical history of spontaneous PTB before 34 weeks of gestation will be included.

S-STIPP cohort

Pregnant women, with a gestational age between 24 and 34 weeks presenting with symptoms of threatened PTB, such as abdominal pain, vaginal blood loss, contractions or other complaints suggestive for threatened PTB, will be included.

A potential subject who meets any of the following criteria will be excluded from participation:

1. Signs of intrauterine infection.
2. Obstetric indication for immediate delivery (eg, advanced labour, cord prolapse, abruption, signs of fetal distress).
3. Confirmed fetal abnormality.
4. Confirmed preterm rupture of membranes.
5. Confirmed vasa/placenta praevia.
6. Severe vaginal bleeding and light bleeding that cannot be stopped.
7. Signs of imminent labour such as advanced dilatation, making it impossible to measure the cervix.

Measurements

Cervical stiffness measurement

The CSI will be measured subsequent to measurement of the cervical length. The Pregnolia System is composed of two components: an active, reusable device and a disposable single-use sterile probe.

1. The control unit is an active device with a power supply, foot switch, connector cable and an integrated pump that generates vacuum.
2. The single-use sterile probe is connected to the control unit console through a connector cable. Air filters on the probe prevent microbiological contamination of the control unit. This probe is designed to minimise the contact interaction between the user and the patients during the measurement. The probe tip diameter is 12 mm. Each single-use, disposable probe is packed in a sterile pouch.

To perform the measurement, the cervix is visualised with a speculum. The disposable probe is placed on the anterior lip of the cervix (12 o'clock position). The control will create a weak vacuum inside the probe that pulls the cervical tissue, very gently and slowly, into the probe tip by a fixed distance of 4 mm. The negative aspiration pressure needed to deform the tissue is the outcome of the measurement. A high-pressure value corresponds with stiff tissue and a low pressure corresponds with soft tissue. The CSI assessment is performed in three consecutive measurements at the same location, without any time lag and without removing the probe from the cervix. For an overview of the measurement procedure, please refer to the figure available at the Pregnolia website (https://en.pregnolia.com/fachpersonen2-1).

Sonographic measurement

Cervical length measurement with transvaginal ultrasound is routine care in both cohorts.

The cervical length will be determined as the linear distance between internal and external cervical os, excluding the endocervical funnel as described by Kagan and Sonek.[24]

In the A-STIPP cohort, transvaginal ultrasound will be done biweekly from 14 until 24 weeks of gestation. In case a short cervix of less than 25mm is detected, a cerclage is placed. Afterwards, the measurement of CSI will not be continued.

In the S-STIPP cohort, the transvaginal ultrasound will be performed when a woman presents with any symptom of threatened PTB, between 24 and 34 weeks of gestation.

Questionnaire

Participants will be asked to fill out a structured questionnaire to screen for additional risk factors of PTB. The questionnaire contains questions about the current pregnancy and details about previous pregnancies, if applicable. Moreover, details on cervical surgery in the past and family history of PTB are requested. Baseline characteristics such as height, weight, smoking and medical history, including gynaecological history and uterus malformations, will be collected. The questionnaire will be checked with the patient's electronic file.

For the S-STIPP cohort, participants will be asked about the specific symptoms associated with threatened PTB.

Blinding

For the A-STIPP cohort, clinicians and participants are blinded for the results of the CSI measurement.

In the S-STIPP cohort, the clinician working at the emergency department performs the measurement,

Table 1 Sample size: A-STIPP cohort

Predictors (n)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Minimum required sample size (n)	227	240	360	480	600	720	840	960	1080	1200	1320	1440	1560	1680	1799

therefore making it impossible to blind the treating clinician. The participant however is blinded for the results.

Follow-up

Participants will be followed up from inclusion until delivery. Detailed information regarding the pregnancy outcomes, including maternal and neonatal outcomes, will be gathered.

Also, if applicable, detailed information about hospital admittance during pregnancy will be noted. Moreover, if a participant is admitted due to threatened PTB, received treatments such as antenatal corticosteroids, tocolytic medicines or magnesium sulfate for neonatal neuroprotection will be documented.

Primary outcomes

1. The primary outcome for the A-STIPP cohort is spontaneous PTB before 34 weeks of gestation.
2. The primary outcome for the S-STIPP cohort is delivery within 7 days.

Secondary outcomes

1. Spontaneous PTB before 37 weeks of gestation.
2. Spontaneous PTB before 34 weeks of gestation (for the S-STIPP only).
3. Spontaneous PTB before 32 weeks of gestation.
4. Spontaneous PTB before 28 weeks of gestation.
5. Latency time (time between inclusion and delivery)
6. Delivery within 48 hours (for the S-STIPP only).
7. Preterm premature rupture of membranes.

Other outcomes

Safety of the use of the Pregnolia System (as defined in online supplemental appendix 2) will be investigated.

Also, patient discomfort of the measurement will be evaluated by a general questionnaire.

Power analysis

We used contemporary sample size calculations described by Riley *et al*[25] for developing prediction models, based on three criteria that each provide a sample size to satisfy that criterion, then picking the highest sample size out of the three. The following input parameters are used to calculate the required number of inclusions: (1) expected prevalence of the primary outcome, (2) expected amount of explained variance by the prediction model and (3) number of predictors (input variables).

For the A-STIPP cohort, the prevalence (0.18) was derived from the QUIPP study.[26–28] The standard level of variance (0.15) was used to calculate the sample size.

For the S-STIPP cohort, the prevalence (0.12) and variance (0.45) were derived from the Apostel I study.[12 29] Both studies have comparable patients as the A-STIPP and S-STIPP cohorts.

To investigate additional input predictors with sufficient power, an increase in sample size is needed. When inclusion of participants continues and the second threshold is reached, another input parameter is added until the next threshold and so on. The baseline predictors used in the first step will be the CSI measurement combined with cervical length measurement in the A-STIPP cohort and cervical length with fFN in S-STIPP cohort.

See tables 1 and 2 for the steps and the threshold sample sizes. In both calculations, the number of predictors was gradually increased. Continuous variables count as a single-input variable, as well as dichotomous input variables. Categorical variables are counted as C-1; thus, the number of input variables is the number of categories minus one. The additional predictor variables are summarised in table 3.

Sample size calculations were performed using R (a language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/) with the use of the *pmsampsize* package .[25]

For the A-STIPP, the minimum sample size of 227 patients is required to achieve the primary objective of this study. Once this number is achieved, the study will be continued to investigate secondary objectives. For the S-STIPP, the minimum sample size of 163 patients is required to achieve the primary objective of this study. Once this number is achieved, the study will be continued to investigate secondary objectives, by using the dynamical sample size as explained.

Statistical analysis

Baseline characteristics will be calculated using descriptive statistics. Continuous variables will be reported as mean with SD or median with IQR. Categorical variables will be reported as proportions.

Out of the three repetitive CSI measurements conducted, depending on which proves to be the best

Table 2 Sample size S-STIPP cohort

Predictors (n)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Minimum required sample size (n)	163	163	163	163	188	225	263	300	338	375	413	450	488	525	563

Table 3 Predictor variables

	Predictor variable
1	Cervical length
2	Fetal fibronectin*
3	Twin gestation
4	History of spontaneous preterm birth
5	Cervical surgery
6	Interpregnancy interval
7	Presence of infection
8	Family history
9	Social economic status
10	Smoking
11	BMI

*S-STIPP only.

predictor, the first, the average or the lowest measurement values will be utilised.

To incorporate repeated measures of CSI from the A-STIPP cohort, a logistic generalised mixed model will be used. As CSI is a continuous outcome, linear and non-linear functions will be compared using restricted cubic splines. A lower Akaike's Information Criterion (AIC) or overall p value will determine which functional form is chosen.[25] If there is censoring (ie, loss to follow-up), a Cox proportional hazards model for time to delivery including a time-varying covariate for CSI will be used. As a sensitivity analysis, a comparison of either of these models with a joint survival model will be done (combining a Cox model for time to delivery with a linear mixed model for CSI measurements).

For the S-STIPP cohort, a logistic regression will be used to determine the relationship between input variables and a dichotomous outcome.

Subgroup analysis

The following subgroup analyses are planned for participants and treatments that may potentially affect cervical stiffness, in order to assess their impact on the CSI:

1. Nulliparous versus multiparous women.
2. Singleton versus multiple pregnancies.
3. Women with previous cervical surgery versus women without.
4. Women with a (abdominal or cervical) cerclage in current pregnancy versus no cerclage.
5. Women treated with progesterone versus no treatment.

A-STIPP cohort subgroup analysis

The subgroups of interest in asymptomatic participants are as follows:

1. Women with a short cervix (≤25 mm) during screening versus women with a long cervix (>25 mm).
2. Women who received additional treatment (pessary or cerclage) versus no treatment.

S-STIPP cohort subgroup analysis

The following subgroups of interest in symptomatic participants are performed based on clinical risk stratification:

1. Cervical length ≥30 mm.
2. Cervical length ≥15 and <30 mm with negative fFN.
3. Cervical length ≥15 and <30 mm with positive fFN.
4. Cervical length <15 mm.

Monitoring and safety

An independent Data and Safety Monitoring Board (DSMB) is assigned to safeguard the safety of the study participants and provide recommendations.

Since the measurement with the Pregnolia System is minimally invasive, the risk of adverse events (AEs) related to the measurement is small. However, any AEs and serious adverse events (SAEs) will be reported. If evaluation by the DSMB demonstrates increased safety risks within the study, the DSMB can always advice to stop the study.

Data management

Data will be collected using an accredited electronic data capture system (Castor). To protect the privacy of the participant, personal data is encrypted. Data cannot be traced back to participants in reports and publications about the study. All personal data is protected according to the General Data Protection Regulation (GDPR and Dutch privacy regulation (AVG)).

All agreements regarding data sharing are defined in a signed Clinical Trial Agreement (CTA) and GDPR is applicable to this agreement.

Clinical impact

This STIPP study will provide evidence on the value of the cervical stiffness as a single clinical marker and in combination with other clinical markers such as cervical length to predict the risk of spontaneous PTB in groups of pregnant women with an increased risk of PTB.

Patient and public involvement

The patient organisation Care4Neo was informed about the study and was favourable about the purpose of the study.

Contributors FH initiated the research. FH and SB designed the study. SB wrote the proposal and the manuscript. FH, MAO, RvE, MAdB and EP critically revised the proposal and manuscript. All authors read and approved the final manuscript.

Funding This work was supported and funded by the Pregnolia Institute. They also provided the system and the probes. The funders had no role in the study design, conduction of the study, collection, management, analysis and interpretation of the data. Also, the funder had no role in preparation, reviewing or approval of the manuscript. Funding was not provided by the study sponsor.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not actively involved in the design, or conduct, or reporting of this research. However, the patient organistaion Care4Neo was informed about the study and was favourable about the purpose.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Sofie Breuking http://orcid.org/0000-0003-4812-2042
Martijn A Oudijk http://orcid.org/0000-0001-8672-4365

REFERENCES

1 Blencowe H, Cousens S, Oestergaard MZ, *et al*. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet* 2012;379:2162–72.
2 Liu L, Johnson HL, Cousens S, *et al*. Child health epidemiology reference group of WHO, Unicef. global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012;379:2151–61.
3 Liu L, Oza S, Hogan D, *et al*. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. *The Lancet* 2015;385:430–40.
4 Marlow N, Wolke D, Bracewell MA, *et al*. Neurologic and developmental disability at six years of age after extremely preterm birth. *N Engl J Med* 2005;352:9–19.
5 Mwaniki MK, Atieno M, Lawn JE, *et al*. Long-term neurodevelopmental outcomes after Intrauterine and neonatal insults: a systematic review. *Lancet* 2012;379:445–52.
6 van Zijl MD, Koullali B, Mol BW, *et al*. Prevention of preterm delivery: current challenges and future prospects. *Int J Womens Health* 2016;8:633–45.
7 van der Ven J, van Os MA, Kazemier BM, *et al*. The capacity of mid-pregnancy cervical length to predict preterm birth in low-risk women: a national cohort study. *Acta Obstet Gynecol Scand* 2015;94:1223–34.
8 Iams JD, Berghella V. Care for women with prior preterm birth. *Am J Obstet Gynecol* 2010;203:89–100.
9 Conner SN, Frey HA, Cahill AG, *et al*. Loop electrosurgical excision procedure and risk of preterm birth: a systematic review and meta-analysis. *Obstet Gynecol* 2014;123:752–61.
10 Kazemier BM, Buijs PE, Mignini L, *et al*. Impact of obstetric history on the risk of spontaneous preterm birth in singleton and multiple pregnancies: a systematic review. *BJOG* 2014;121:1197–208;
11 Hughes K, Kane SC, Araujo Júnior E, *et al*. Cervical length as a predictor for spontaneous preterm birth in high-risk singleton pregnancy: current knowledge. *Ultrasound Obstet Gynecol* 2016;48:7–15.
12 Vis JY, van Baaren G-J, Wilms FF, *et al*. Randomized comparison of nifedipine and placebo in fibronectin-negative women with symptoms of preterm labor and a short cervix (APOSTEL-I trial). *Am J Perinatol* 2015;32:451–60.
13 Wilms FF, Vis JY, de Wit-Zuurendonk L, *et al*. What is the risk of preterm delivery after arrested preterm labor *Am J Perinatol* 2015;32:63–70.
14 Cornelissen LGH, van Oostrum NHM, van der Woude DAA, *et al*. The diagnostic value of fetal fibronectin testing in clinical practice. *J Obstet Gynaecol Res* 2020;46:405–12.
15 Berghella V, Saccone G. Fetal fibronectin testing for reducing the risk of preterm birth. *Cochrane Database Syst Rev* 2019;7:CD006843.
16 Mazza E, Parra-Saavedra M, Bajka M, *et al*. In vivo assessment of the biomechanical properties of the uterine cervix in pregnancy. *Prenat Diagn* 2014;34:33–41.
17 Badir S, Bajka M, Mazza E. A novel procedure for the mechanical characterization of the uterine cervix during pregnancy. *J Mech Behav Biomed Mater* 2013;27:143–53.
18 Badir S, Mazza E, Zimmermann R, *et al*. Cervical softening occurs early in pregnancy: characterization of cervical stiffness in 100 healthy women using the aspiration technique. *Prenat Diagn* 2013;33:737–41.
19 Parra-Saavedra M, Gómez L, Barrero A, *et al*. Prediction of preterm birth using the cervical consistency index. *Ultrasound Obstet Gynecol* 2011;38:44–51.
20 Shiina T, Nightingale KR, Palmeri ML, *et al*. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: part 1: basic principles and terminology. *Ultrasound Med Biol* 2015;41:1126–47.
21 Ge W, Brooker G, Mogra R, *et al*. Measured hyperelastic properties of cervical tissue with shear-wave elastography. *Sensors (Basel)* 2021;22:302.
22 Stone J, House M. Measurement of cervical softness before cerclage placement with an aspiration-based device. *Am J Obstet Gynecol MFM* 2023;5:100881.
23 Issaoui M, Debost-Legrand A, Skerl K, *et al*. Shear wave elastography safety in fetus: a quantitative health risk assessment. *Diagn Interv Imaging* 2018;99:519–24.
24 Kagan KO, Sonek J. How to measure cervical length. *Ultrasound in Obstet &Amp; Gyne* 2015;45:358–62. 10.1002/uog.14742 Available: https://obgyn.onlinelibrary.wiley.com/toc/14690705/45/3
25 Riley RD, Ensor J, Snell KIE, *et al*. Calculating the sample size required for developing a clinical prediction model. *BMJ* 2020;368:m441.
26 Watson HA, Carter J, Seed PT, *et al*. The quipp app: a safe alternative to a treat-all strategy for threatened preterm labor. *Ultrasound Obstet Gynecol* 2017;50:342–6.
27 Carter J, Seed PT, Watson HA, *et al*. Development and validation of predictive models for quipp app V.2: tool for predicting preterm birth in asymptomatic high-risk women. *Ultrasound Obstet Gynecol* 2020;55:357–67.
28 Goodfellow L, Alfirevic Z. Effect of quipp prediction algorithm on treatment decisions in women with a previous preterm birth: a prospective cohort study. *BJOG* 2019;126:1643.
29 van Baaren G-J, Vis JY, Wilms FF, *et al*. Cost-effectiveness of diagnostic testing strategies including cervical-length measurement and fibronectin testing in women with symptoms of preterm labor. *Ultrasound Obstet Gynecol* 2018;51:596–603.