Editor's key points

- Obstetric evacuation of Indigenous women from their communities for childbirth has reduced morbidity and mortality in high-risk pregnancies but has negative social and cultural effects on the women and their families. Emerging clinical techniques show promise for predicting time to delivery. The fetal fibronectin assay is effective in predicting preterm labour.
- A negative fetal fibronectin test result at the 50-ng/mL cutoff was not predictive of a delay of labour at term, suggesting that the test does not have adequate specificity or sensitivity to be useful in predicting a delay in the onset of labour in isolated northern communities.
- The efficacy of similar methods, such as quantitative fetal fibronectin testing concurrent with other established biological assessments, should be explored in a larger sample before ruling out this approach.

Exploring fetal fibronectin testing as a predictor of labour onset

In parturient women from isolated communities

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Abstract

Objective To investigate whether the fetal fibronectin assay would be useful for determining if a woman was close to a term delivery. If effective, this test would allow parturient women to stay in their communities longer.

Design This feasibility study used a prospective cohort design to examine the negative predictive value of the fetal fibronectin test at term.

Setting Iqaluit, NU.

Participants A total of 30 parturient women from rural and isolated communities in Nunavut.

Intervention Starting at 36 weeks' gestation, women were tested every 2 days, and after 39 weeks this increased to every day until labour.

Main outcome measures The negative predictive value of the fetal fibronectin test was assessed.

Results Women were no more likely to give birth at 7 or more days after their last negative fetal fibronectin test result relative to their likelihood of giving birth at 6 or fewer days after their last negative test result. Hence, the presence of fetal fibronectin in cervical secretion did not predict term delivery.

Conclusion This project indicated that the fetal fibronectin test did not have adequate sensitivity or specificity as a diagnostic measure to predict a delay of labour at term.

Étudier le dosage de la fibronectine fœtale comme prédicteur du déclenchement du travail

Chez des parturientes de communautés éloignées

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Résumé

Objectif Vérifier si le dosage de la fibronectine fœtale pourrait servir à déterminer si une femme se rapproche d'un accouchement à terme. Si c'était le cas, ce test permettrait à une femme enceinte de demeurer plus longtemps dans sa communauté.

Type d'étude Cette étude de faisabilité a utilisé une méthode de cohorte prospective pour établir la valeur prédictive négative du test de la fibronectine fœtale à terme.

Contexte Iqaluit, au Nunavut.

Participantes Un total de 30 parturientes de communautés rurales et isolées du Nunavut.

Intervention À partir de 36 semaines de grossesse, les tests ont été effectués à tous les 2 jours, et après 39 semaines, à chaque jour.

Principaux paramètres à l'étude On a évalué la valeur prédictive négative du test de la fibronectine fœtale.

Résultats Les femmes n'étaient pas plus susceptibles d'accoucher 7 jours ou plus après leur dernier résultat négatif au test de la fibronectine fœtale que d'accoucher 6 jours ou moins après un tel résultat. Par conséquent, la présence de fibronectine f'tale dans les sécrétions cervicales ne prédisait pas le moment de l'accouchement.

Conclusion Cette étude indique qu'en tant que méthode diagnostique, le test de la fibronectine fœtale n'a pas la sensibilité ou la spécificité suffisante pour prédire un retard du déclenchement du travail.

Points de repère du rédacteur

- Le fait que les femmes autochtones doivent quitter leur communauté lorsqu'elles accouchent pour accompagner le nouveau-né a contribué à réduire la morbidité et la mortalité des grossesses à risque élevé mais a eu des répercussions sociales et culturelles négatives pour ces femmes et leurs familles. Il existe maintenant de nouvelles méthodes cliniques qui pourraient éventuellement prédire le moment de l'accouchement. Le dosage de la fibronectine fœtale est une méthode efficace pour prédire un déclenchement prématuré du travail.
- Un résultat négatif au dosage de la fibronectine fœtale avec une valeur seuil de 50 ng/ml n'était pas prédicteur d'un retard du déclenchement du travail à terme, ce qui donne à croire que ce test n'a pas la spécificité ou la sensibilité nécessaire pour prédire un retard du déclenchement du travail dans des communautés nordiques éloignées.
- Certaines méthodes analogues, telles que le dosage quantitatif de la fibronectine fœtale associé à d'autres mesures biologiques éprouvées, devront être évaluées avec un plus grand échantillon avant d'abandonner cette méthode.

The evacuation of Indigenous women from their communities for childbirth owing to a lack of maternity services in rural areas is an emerging social issue across Canada.[1] This practice, termed *obstetric evacuation*, creates negative health and social outcomes for many rural women and their families.[2-6] It is especially an issue in Nunavut owing to its isolation and extreme physical environment.

Today, there are about 25 communities and approximately 900 births in Nunavut each year.[7] There are about 400 births per year at the Qikiqtani General Hospital, located in Iqaluit, NU (Qikiqtaluk region), and 55 at the 2 regional birthing centres in Rankin Inlet, NU (Kivalliq region), and Cambridge Bay, NU (Kitikmeot region). The remainder of births take place outside of Nunavut, in Yellowknife, NWT; Edmonton, Alta; Winnipeg, Man; or Ottawa, Ont. **Figure 1** shows a map of Nunavut.[8]

Although obstetric evacuation has reduced morbidity and mortality associated with high-risk pregnancies,[9] considerable social morbidities still arise, mainly owing to cultural isolation and familial stress.[2-6,10,11] The expectant mother is often evacuated alone, without family or friends, to a foreign environment[12,13] for a month or more where prenatal teaching, support, and recreation are inconsistent between locations. In southern communities, cultural isolation is an issue, as care is often not provided in the Inuit languages. Furthermore, at some boarding homes, women must adjust to a new diet in their final weeks of pregnancy[14] owing to a lack of availability of traditional foods such as caribou, seal, and whale.[9,15] The Executive Vice President of the Society of Obstetricians and Gynaecologists of Canada in 2010 reportedly referred to obstetric evacuations as the "residential schools of medicine."[14] Clearly, social and clinical solutions to keeping parturient women at home are a research priority.

Emerging clinical techniques, such as the fetal fibronectin assay, show promise for predicting time to delivery. Fetal fibronectin is a glycoprotein that leaks into cervical and vaginal secretions owing to mechanical factors such as uterine contractions or inflammatory products ascending in the cervical canal. A negative fetal fibronectin test result from anywhere between 22 and 35 weeks is highly predictive of labour not occurring and has been used to determine this in Nunavut since 2004.[16-18]

Few publications have examined the applicability of fetal fibronectin testing at term,[19-24] with most emphasizing the positive predictive value of the test to plan the timing of induction and to avoid postdates. Three studies noted the average number of days to delivery at term from the last negative fetal fibronectin test result: the study by Ahner et al found a mean interval of 3.8 days (interquartile range 2.4 to 7.0 days),[21] while the study by Luton et al found a mean interval of 5.7 days (range 2 to 16 days).[20] Results from the study by Lockwood et al showed that most women (63.3%) did not deliver within 1 week after a negative assay result.[24] Assay frequency and, thus, the number of days to delivery, is inconsistent across studies. More research is needed to determine the precise predictive value of fetal fibronectin testing at term.

Manufacturer-established protocols for using the test in suspected cases of preterm labour were modified based on protocols developed at the Ottawa General Hospital. The negative predictive value of the test was found to be 98.3%, leading one investigator (W.A.M.) to wonder if the test result would be useful for predicting delivery at term. Such results could influence obstetric evacuation policy in Nunavut, as women could potentially stay in their communities longer before being evacuated. This investigator partnered with the University of Ottawa Department of Family Medicine and the Centre for Rural Health Research at the University of British Columbia in Vancouver to undertake a research project to determine the efficacy of the test at term.

Methods

This feasibility study used a prospective cohort design to examine the negative predictive value of the fetal fibronectin test at term. Thirty parturient women from rural and isolated communities in Nunavut participated in the study and consented to begin testing at 36 weeks' gestation.

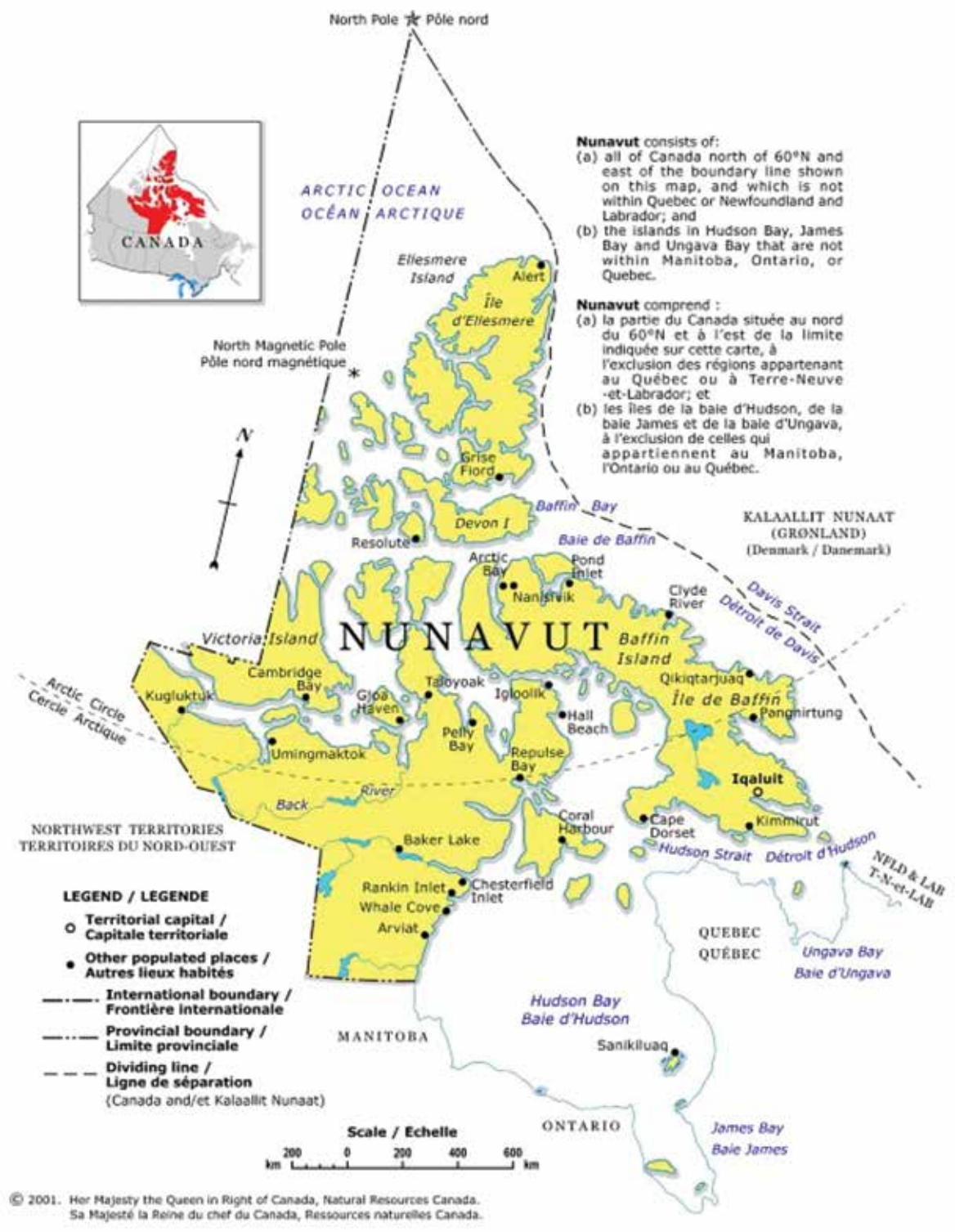
Site selection

The site was determined based on the following criteria: rural or remote location, appropriate volume of births to ensure recruitment targets were met, availability of obstetric specialist care, presence of a cohort of women who were evacuated from their communities at or around 36 weeks, and access to and familiarity with fetal fibronectin testing. Based on these criteria, the research site chosen for this pilot project was Iqaluit. Ethics approval was received from the Nunavut Research Institute in Iqaluit.

Participant selection

The study was open to all women with uncomplicated pregnancies that were at 36 weeks' gestation or more as established by last menstrual period or ultrasound dating between 16 and 20 weeks. Exclusion criteria consisted of pre-existing medical conditions, premature ruptured membranes, and any high-risk indication (eg, multiple gestation, breech presentation). Given that recent sexual intercourse could have affected the results of the tests, patients were asked about this at the time of testing. No participants were excluded based on this, although some participants might have been reluctant to share such intimate information. Participants were recruited through the hospital outpatient maternity clinics during routine prenatal visits at or after 36 weeks' gestation. Two local community recruiters who spoke the local language, Inuktitut, and were culturally fluent, provided participants with information about the study and undertook an informed consent process.

Figure 1. Map of Nunavut



Reproduced from the Atlas of Canada.[8]

Data collection

An obstetric study nurse in Iqaluit administrated the test and coordinated data collection. Thirty women underwent a series of fetal fibronectin tests. Participants were tested using the fast-reacting standard fetal fibronectin test starting at 36 weeks' gestation and were tested every 2 days until 39 weeks' gestation, after which they were tested every day until labour. Given the potential for a higher false-positive rate when the test is administered within 48 hours of a digital vaginal examination, swabs were taken before the digital examination. In total, 135 assay samples were collected. Fetal fibronectin testing ceased after 2 positive test results or after giving birth. The research team used a standard qualitative yes or no analysis of the test results at Qikiqtani General Hospital, using the standard cutoff level of 50 ng/mL to indicate a positive fetal fibronectin test result.

Data analysis

The research team was interested in determining if a negative fetal fibronectin test result meant that the woman would not go into labour within a minimum of 7 days. As it was a feasibility study, sample-size calculations were not conducted. As the number of participants in the final sample was small, we generated descriptive statistics demonstrating the average number of days elapsed from receiving the last negative test result to the onset of labour. Next, we summed the number of participants who went into labour in 6 or fewer days compared with those who went into labour in 7 days or more.

Results

Thirteen participants were not included in the analyses owing to 1 of the following factors: medical indication (eg, preeclampsia), delivery before sample collection, participation ceased for unknown reasons, the participant received labour induction or a cesarean section, or the participant received a positive fetal fibronectin test result on her first visit (**Table 1**).

The average number of days between the last negative fetal fibronectin test result and participant delivery was 4.94 days. A total of 5 women delivered in 7 or more days after their last negative test result (**Table 2**). A total of 12 women delivered in 6 days or fewer after their last negative fetal fibronectin test result (**Table 3**), defined as *cases of concern*. In all, 8 of 17 women gave birth spontaneously within 3 days after their last negative test result (**Table 4**).

Discussion

In the present study, a negative fetal fibronectin test result at the 50-ng/mL cutoff was not predictive of a delay in labour at term in the same way as it predicts the absence of preterm delivery. The results suggest that

Table 1. Women excluded from analyses: *N 13.*

REASON FOR EXCLUSION	N
Received a positive fetal fibronectin test result on first test*	5
Emergency cesarean section	1
Labour induced	1
Stopped participating	2
Delivered before sample collected	2
Medical indication (preeclampsia)	2

*Cases were confirmed not to be false positive.

Table 2. Women who delivered 7 or more days after last negative fetal fibronectin test

NO. OF DAYS BETWEEN LAST NEGATIVE FETAL FIBRONECTIN TEST RESULT AND DELIVERY	N
7	0
8	0
9	2
10	1
11	0
12	1
13	0
14	1

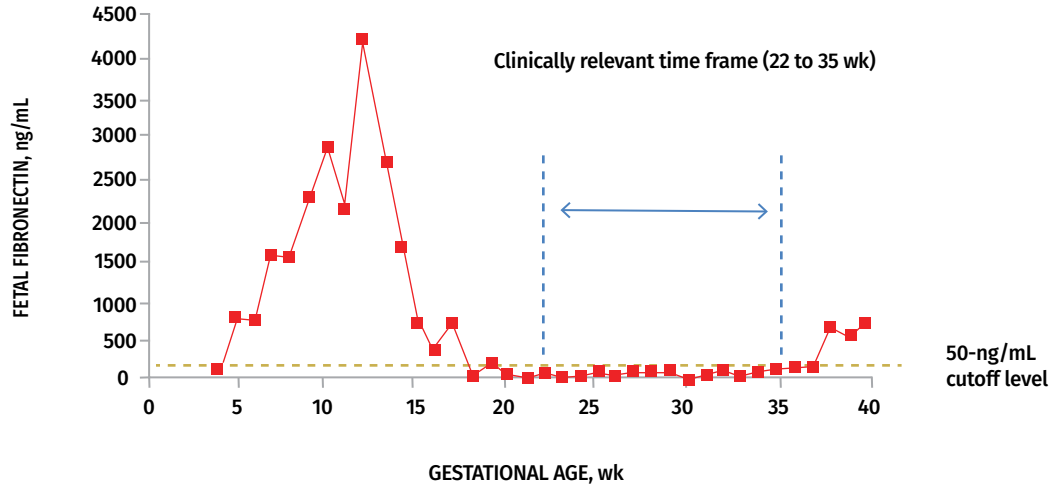
Table 3. Women who delivered 6 or fewer days after last negative fetal fibronectin test: *Cases of concern.*

NO. OF DAYS BETWEEN LAST NEGATIVE FETAL FIBRONECTIN TEST RESULT AND DELIVERY	N
1	2
2	4
3	2
4	2
5	0
6	2

Table 4. Gestational age of infants born to women who delivered 3 days or fewer after last negative fetal fibronectin test result

PARTICIPANT	NO. OF DAYS BETWEEN LAST NEGATIVE TEST RESULT AND DELIVERY	GESTATIONAL AGE OF INFANT
1	1	37 weeks, 5 days
2	1	41 weeks
3	2	38 weeks, 2 days
4	2	38 weeks, 4 days
5	2	38 weeks, 6 days
6	2	38 weeks, 4 days
7	3	37 weeks, 5 days
8	3	40 weeks, 5 days

Figure 2. Differences in fetal fibronectin level released by gestational week



Adapted from Garite and Lockwood.[26]

the test does not have adequate specificity or sensitivity to be useful in predicting a delay in the onset of labour in isolated northern communities.

Future work on how to best predict the delay in labour at term could use a quantitative test to explore whether it is more appropriate to use an adjusted cutoff level, as opposed to the 50-ng/mL threshold used in the standard fast-reacting qualitative test.[25] Garite and Lockwood show the amount of fetal fibronectin released at each gestational week (**Figure 2**), illustrating the difference in fetal fibronectin release patterns after 35 weeks and the potential for a different cutoff level at term.[26] Currently, we know of no studies that have examined the efficacy of the fetal fibronectin test at an adjusted cutoff level, most likely because the intended purpose of the test is to predict preterm birth; the 50-ng/mL cutoff is the standard tested and is set by the manufacturer when used for this purpose. The potential also exists for developing a diagnostic protocol that includes established clinical assessments of the cervix and uterine activity, such as the Bishop score or cervical score,[27] in conjunction with a recalibrated fetal fibronectin test. Future research should investigate other potential biological markers.[28,29]

Limitations

This project was conceived as an initial feasibility study and therefore the sample size was small. Given that 8 of 17 women with a negative test result delivered within 3 days, it is unlikely that a larger sample size would have changed the result. It should be noted that shortly after this study was conducted, a study of 75 pregnant women living in remote areas in Australia found that negative fetal fibronectin test results at term were associated with more than half of the participants giving birth in fewer than 7 days.[30]

In our study, 13 women (nearly half) were not included in the analyses for a number of expected reasons, as indicated in **Table 1**. While voluntary loss to follow-up was not overly problematic, it should also be considered that the invasiveness of frequent cervical fluid sampling might encourage participant dropout.

Conclusion

The fetal fibronectin test used in this sample was not shown to be predictive enough to inform the decisions of clinicians and pregnant mothers to delay evacuation to a regional birthing centre. However, we suggest that the efficacy of similar methods, such as quantitative fetal fibronectin testing concurrent with other established biological assessments, be explored in a larger sample before ruling out this approach. The harsh consequences of obstetric evacuation encountered by many young women and their families in Nunavut still need to be addressed.

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Contributors
All authors contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

Competing interests
None declared

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