QIAGEN

Strength in your decision with PartoSure®

Your aid in assessing the risk of preterm birth

Sample to Insight

Preterm birth: A major diagnostic challenge

Clinical evaluation alone, including the measurement of cervical length (CL) and dilatation, is not sufficiently predictive of imminent delivery in women with signs of threatened preterm labor (PTL). Accurately assessing this risk can be difficult and not diagnosing PTL can have significant implications for the well-being of the patient and her unborn child.

Traditional biomarker tests, such as those based on the detection of fetal fibronectin (fFN), have been reported to have poor positive predictive values (PPV) for imminent delivery (1). The increased chance of false positives, indicated by a lower PPV, with these tests can lead to unnecessary admissions and interventions.

- 28% who present with signs and symptoms of threatened PTL may be hospitalized (2)
- 7 to 20% will deliver within 7 days (3,4,5)

A more accurate assessment of patients with signs and symptoms of PTL is urgently needed to identify women truly at risk

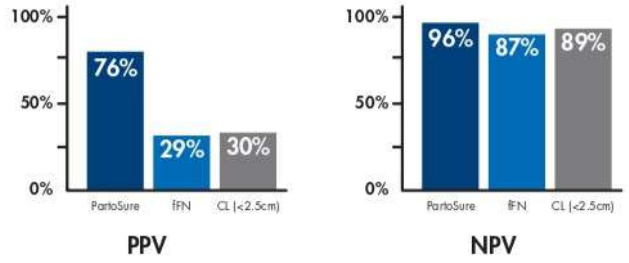
Review of published literature

Improved confidence for your assessment of spontaneous preterm birth

Cervical length (CL) is a less accurate predictor of imminent spontaneous delivery in PTL than the PartoSure test, which can be used to identify women at greatest risk of PTL (6). While CL and fetal fibronectin testing (fFN) can be used to predict this risk, published data indicate PartoSure has a better PPV and NPV.

A European study reported a 67% decrease in false positive test results after switching to PartoSure (8)

Comparison of positive predictive value (PPV) and negative predictive value (NPV) for delivery within 7 days based on results of the PartoSure test, fFN assay (QuikCheck™ fFN Test), or cervical length <2.5 cm (7).



A European maternity hospital retrospectively reviewed the medical records of women presenting to the emergency obstetrical unit with threatened PTL. In this study, data were compared between when the hospital used QuikCheck fFN as its standard biomarker test and a separate year when PartoSure was used to predict PTL (8).

Retrospective European study comparing PartoSure and QuikCheck fFN testing on predicting preterm labor

	PartoSure Test Period	QuikCheck fFN Test* Period
Calendar year evaluated	2016	2012
Evaluable subjects	367	378
GA at testing-weeks (mean ± SD)	30.52 ± 2.98	30.41 ± 2.88
Prevalence of sPTD ≤ 7 days	3.3 (12/367)	2.6 (10/378)
Positive test % (n)	4.6 (17/367)	10.1 (38/378)
False positive test % (n)	3.1 (11/355)	9.5 (35/368)
PPV	35.3	7.9
NPV	98.3	97.9

Data show PartoSure can be used to more accurately predict PTL than fFN even when different concentrations of fFN are used as the cut-off for a positive test (9). Use of PartoSure rather than fFN could therefore lead to a reduction in the number of false positive results and hence unnecessary admissions, transfers or treatments like tocolysis or induction of lung maturation as shown in the United Arab Emirates (9).

Accuracy of PartoSure versus fFN testing at different cut-off values in women presenting with signs and symptoms of preterm labor in the United Arab Emirates (N=72)

	PartoSure	fFN test*			
		10 ng/ml	50 ng/ml	200 ng/ml	500 ng/ml
Sensitivity, % (95% CI)	66.67 (9.43-99.16)	66.67 (9.43-99.16)	66.67 (9.43-99.16)	33.33 (0.84-90.57)	0.00 (0.00-0.76)
Specificity, % (95% CI)	95.65 (87.82-99.09)	57.97 (45.48-69.76)	76.81 (65.09-86.13)	92.75 (83.80-97.61)	97.10 (89.92-99.65)
PPV, % (95% CI)	40.00 (5.27-85.34)	6.45 (0.79-21.42)	11.11 (1.38-34.71)	16.67 (0.42-64.12)	0.00 (0.00-84.19)
NPV, % (95% CI)	98.51 (91.96-99.96)	97.56 (87.14-99.94)	98.15 (90.11-99.95)	96.97 (89.48-99.63)	95.71 (87.98-99.11)
Positive likelihood ratio	15.33 (3.91-60.08)	1.59 (0.68-3.70)	2.87 (1.16-7.13)	4.60 (0.75-28.09)	Not available
Negative likelihood ratio	0.35 (0.07-1.73)	0.58 (0.11-2.88)	0.43 (0.09-2.16)	0.72 (0.32-1.60)	1.03 (0.99-1.07)

Values highlighted in blue indicate a statistically significant difference ($p<0.05$) in predicting spontaneous birth within 7 days of testing for PartoSure compared with fFN testing.

* fFN test not specified

PartoSure has also been compared with the Actim® Partus test, which is based on phosphorylated insulin-like growth factor-binding protein-1 (phIGFBP-1), either alone or in combination with transvaginal CL measurement (10). The PPV for PartoSure is over twice that of Actim Partus while maintaining a similar NPV in women with a CL of 1.5–3.0 cm.

Accuracy of PartoSure versus Actim Partus phIGFBP-1 testing in women presenting with signs and symptoms of preterm labor and a cervical length of 1.5–3.0 cm in Finland, Republic of Macedonia and Russia (N=383)

	PartoSure	Actim Partus phIGFBP-1 test
Sensitivity, % (95% CI)	73.7 (48.8–90.9)	84.2 (60.4–96.6)
Specificity, % (95% CI)	94.9 (90.6–97.7)	76.8 (69.9–82.8)
PPV, % (95% CI)	60.9 (43.8–75.6)	28.1 (21.9–35.2)
NPV, % (95% CI)	97.1 (94.1–98.6)	97.8 (94.1–99.2)
Positive likelihood ratio	14.5 (7.3–28.9)	3.6 (2.6–5.1)
Negative likelihood ratio	0.3 (0.1–0.6)	0.2 (0.1–0.6)

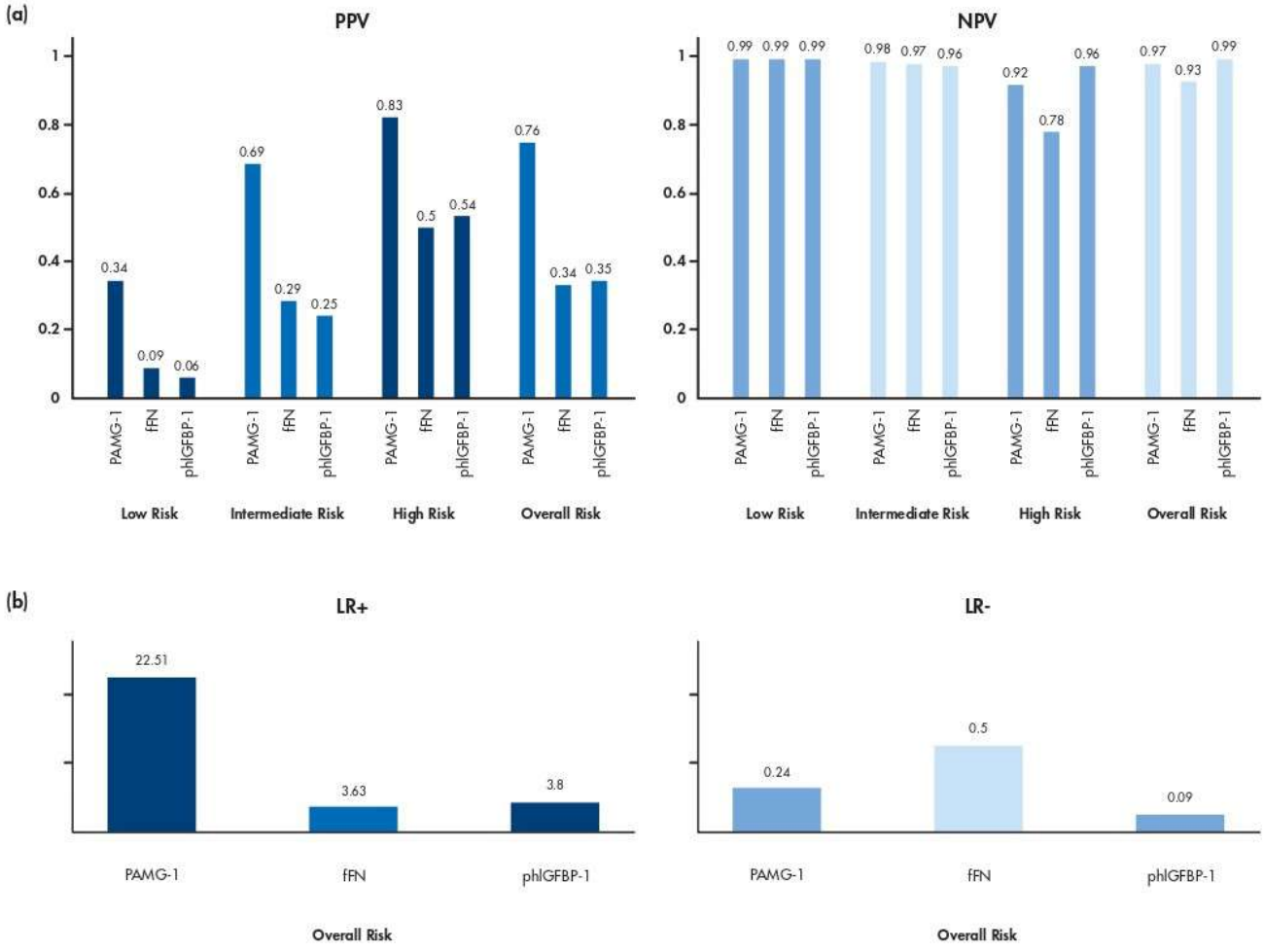
Values highlighted in blue indicate a statistically significant difference ($p<0.05$) in predicting spontaneous birth within 7 days of testing for PartoSure compared with fFN testing.

* fFN test not specified

A database search of published records until October 2017 indicated the positive predictive value (PPV) for PartoSure was significantly higher than that of fFN or phIGFBP-1 testing. This was also true for other diagnostic accuracy measures such as negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR–) (11). The sensitivity to specificity ratio was also higher with PartoSure compared with fFN or phIGFBP-1 tests (11).

Use of a highly specific assay like PartoSure in threatened PTL may optimize management (10)

Summary estimates for prediction of preterm birth within 7 days of testing using PartoSure, fetal fibronectin (fFN) and phosphorylated insulin-like growth factor-binding protein-1 (phIGFBP-1) biomarker tests, in all studies and according to risk group. (a) Positive and negative predictive values; (b) Likelihood ratio for positive and negative test.



Predictive accuracy for spontaneous preterm birth in symptomatic women within 7 days of testing (AUC from receiver-operating characteristics curves) and positivity rate for PartoSure, fFN testing and phIGFBP-1 tests

	PartoSure	fFN test	phIGFBP-1 test
Area under the curve (AUC)	0.961	0.874	0.801
Positivity rate, %	7.9	23.0	29.7

Published data indicate PartoSure can also be used in combination with CL in women with a CL of 1.5 to 3.0 cm to identify those at highest risk of PTL (6). In addition, as shown by Werlen et al., PartoSure provides reliable results even when used 30 minutes after digital examination or transvaginal ultrasound, providing confidence that this test can be administered without loss of accuracy (12).

Reducing unnecessary interventions may lead to decreased costs

85% of patients admitted to the hospital for threatened PTL do not deliver within the next 7 days (4)

Published studies suggest a lower rate of false positive test results and associated higher PPVs, such as those seen in the PartoSure test, may contribute to:

- Reducing the length of stay for high risk patients
- Decreasing unnecessary admissions and use of acute interventions
- Minimizing unnecessary patient transfers

The average admission during which the patient is treated can cost up to €8000, so reducing this can result in cost savings (13).

In the UK, the risk of PTL can be assessed using PartoSure or by measuring the level of fFN or phIGFBP-1. Cost savings are possible with PartoSure, as determined by a cost comparison analysis by the York Health Economics Consortium (YHEC), in both tertiary and non-tertiary UK hospitals (14).

Economic impact and cost-comparison analysis of PartoSure compared with other assessments for preterm labor in the UK

Tertiary UK hospital with 500 patients presenting with symptoms of preterm labor per year

Cost breakdown, £	PartoSure	phIGFBP-1*	Cost difference: phIGFBP-1* minus PartoSure	fFN* 50 ng/ml	Cost difference: fFN* 50 ng/ml minus PartoSure
Cost of test†	37,665	26,249	11,417	45,000	-7,335
Cost of treating patients eligible for test	89,232	202,804	-113,571	165,156	-75,924
Cost of treating patients not eligible for test	0	66,250	-66,250	66,250	-66,250
Total	126,897	295,302	-168,405	276,406	-149,509

Non-tertiary UK hospital with 300 patients presenting with symptoms of preterm labor per year

Cost breakdown, £	PartoSure	phIGFBP-1*	Cost difference: phIGFBP-1* minus PartoSure	fFN* 50 ng/ml	Cost difference: fFN* 50 ng/ml minus PartoSure
Cost of test†	22,599	15,749	6,850	27,000	-4,401
Cost of treating patients eligible for test	60,419	137,324	-76,905	111,831	-51,412
Cost of treating patients not eligible for test	0	44,874	-44,874	44,874	-44,874
Total	83,018	197,948	-114,929	183,706	-100,687

Cost savings are shown in the blue cells. These scenarios are based on the assumption that all patients are eligible for PartoSure and 90% are eligible for the comparator tests and there is an intermediate risk of preterm labor (PTL) based on the findings of Bruijn et al (15). In addition, in tertiary centers it is assumed 500 patients will present with symptoms of PTL out of 5,000 births. In non-tertiary centers, it is assumed 300 patients will present with symptoms of PTL. It is also assumed that any non-tertiary hospital would transfer a patient via in-utero transfer to a tertiary hospital if the patient presents with suspected PTL before 28 weeks' gestation.

* Findings based on data that assumed fFN testing was with Rapid fFN Q10 and phIGFBP-1 testing was with ActimPartus.

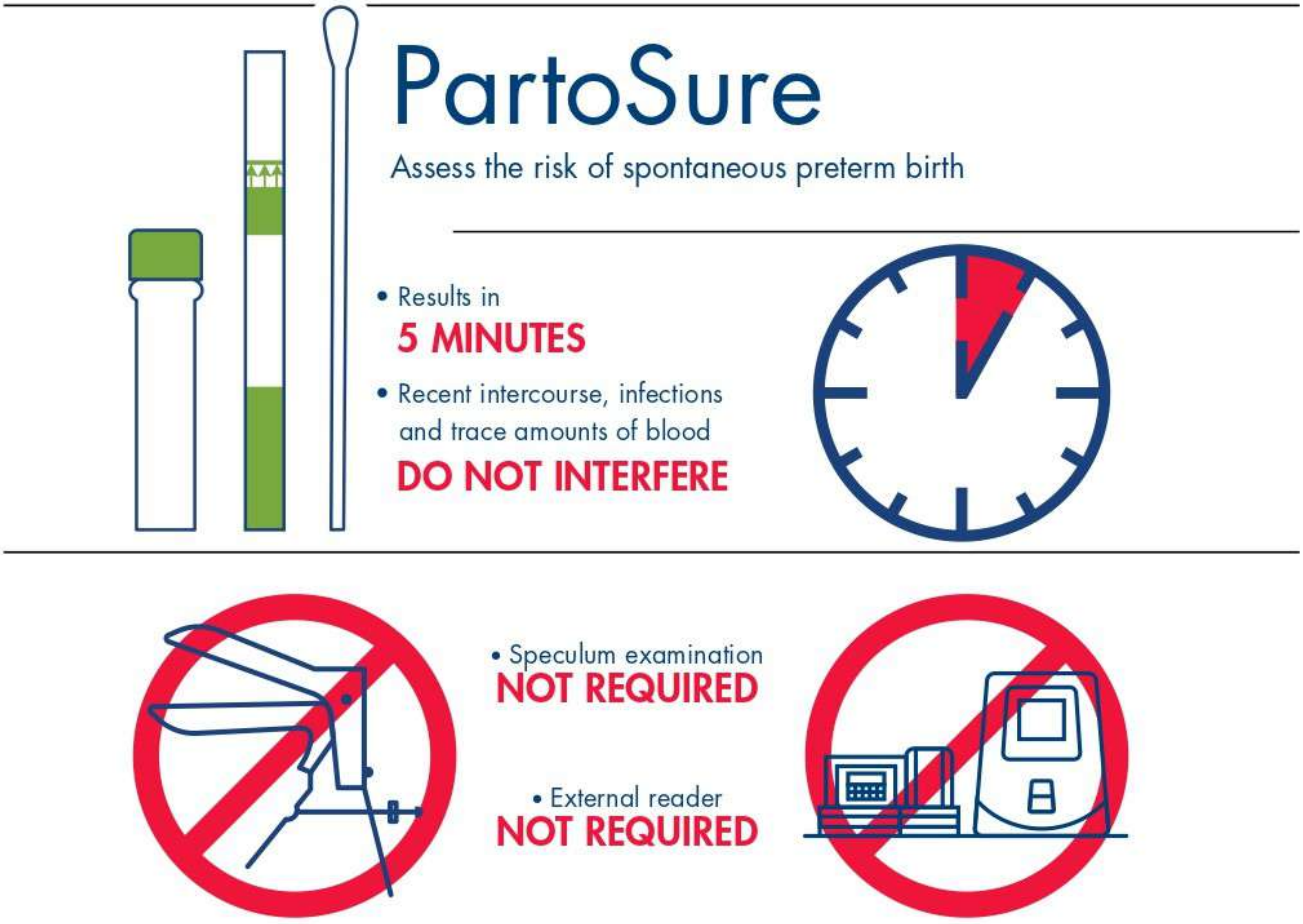
† Including staff time.

PartoSure is associated with lower total costs than other tests due to the avoidance of the need to treat PTL (11)

Simple steps, rapid results

PartoSure is a rapid, qualitative test for detecting the presence of placental alpha microglobulin-1 (PAMG-1) in cervicovaginal secretions in women with signs and symptoms of early PTL (16).

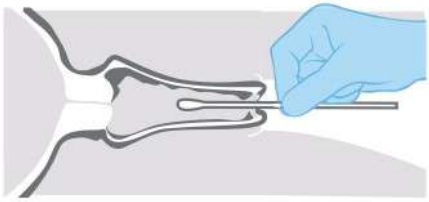
PAMG-1 is a placental protein found in high concentrations in the amniotic cavity. Due to the low concentration of PAMG-1 in normal vaginal discharge, studies have demonstrated a strong correlation between a positive PAMG-1 test and imminent delivery in women presenting with threatened PTL and intact membranes (17).



The PartoSure Test is a rapid, non-instrumented, qualitative immunochromatographic test for the in vitro detection of placental alpha microglobulin-1 (PAMG-1) in vaginal secretions of pregnant women. The device is designed as an aid to rapidly assess the risk of preterm delivery in ≤7 or ≤14 days from the time of cervicovaginal sample collection in pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes and minimal cervical (≤3 cm), sampled between 20 weeks, 0 days and 36 weeks, 6 days gestation.

PartoSure 4-Step Testing Procedure

1



Collect sample

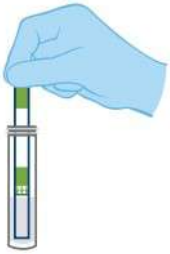
Collect sample of vaginal discharge with sterile collection swab for 30 secs (no active rotation or speculum required).

2

Transfer to solvent

Rinse specimen swab in solvent vial for 30 seconds. Discard swab.

3

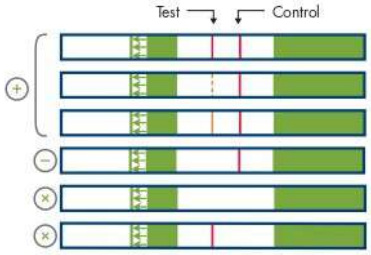


Insert test strip

Insert test strip into vial. Positive as soon as two lines are visible on strip. 5 minutes to call negative result.

Note: Please refer to package insert for complete instructions for use.

4



Read result

A positive result is indicated by two lines in the test region, while a negative result is indicated by a single control line in the test region. Do not read or interpret the result after 10 minutes have passed since inserting the test strip into the vial.

Note: A faint or broken test line should always be read as positive.

The unique features of the PartoSure Test include

- High PPV and NPV
- Applicable shortly after vaginal examination
- No speculum examination required
- Results in 5 minutes
- No special equipment or training needed
- Wide gestational age range from 20 weeks + 0 days to 36 weeks + 6 days

Notes

Ordering information

Product	Contents	Cat. no.
PartoSure Test (20)	Box of 20 test kits	TTDT-1-20-ML

The PartoSure Test is intended for *in vitro* diagnostic use.

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12. Werlen, S. et al. (2015) [Preterm labor: Reproducibility of detection test of PAMG-1 before and after digital examination, and transvaginal ultrasound cervical length]. Gynécologie Obstétrique & Fertilité. **43**, 640–5.
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15. Bruijn, M., et al. (2016). Quantitative fetal fibronectin testing in combination with cervical length measurement in the prediction of spontaneous preterm delivery in symptomatic preterm delivery in symptomatic women. BJOG. **123**, 1965-71.
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17. Lee, S.M., et al. (2012) The clinical significance of a positive Amnisure® test in women with preterm labor and intact membranes. J Matern Fetal Neonatal Med. **25**, 1690-8.