

## Erratum to Biomarker tests to help diagnose preterm labour in women with intact membranes

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### Corrections to the executable excel model:

i. There was an error in the executable excel model file in the formulae of column M of Sheet 'Decision Analysis'. This affects the level of costs but has no effect on the incremental and ICER figures. The terms highlighted in bold should be deleted from the formulae in all rows of the column; for example in cell M3:

```
=(1-Death_given_IVH)*IF(Type_of_analysis="Deterministic",
IF(Time_horizon="Lifetime", c_long_term_healthcare_IVH*baseline_IVH_risk*(1-
Death_given_IVH)
+C3*c_long_term_healthcare_IVH*baseline_IVH_risk*(RR_IVH_ANS_≤7_days-1)
+G3*c_long_term_healthcare_IVH*
baseline_IVH_risk_FP≤7d___TPIt37w*(RR_IVH_ANS_7_days-1),
IF(Time_horizon="Discharge", c_long_term_healthcare_IVH*baseline_IVH_risk*(1-
Death_given_IVH)
+C3*c_neonatal_hospital_RDS*baseline_IVH_risk*(RR_IVH_ANS_≤7_days-1)
+G3*c_neonatal_hospital_RDS*baseline_IVH_risk_FP≤7d___TPIt37w*(RR_IVH_A
NS_7_days-1), 0)),
IF(Time_horizon="Lifetime", 'Unit costs'!$E$10*baseline_IVH_risk*(1-
Death_given_IVH)
+C3*'Unit costs'!$E$10*baseline_IVH_risk*(RR_IVH_ANS_≤7_days-1)
+G3*'Unit costs'!$E$10*
baseline_IVH_risk_FP≤7d___TPIt37w*(RR_IVH_ANS_7_days-1),
IF(Time_horizon="Discharge", 'Unit costs'!$E$10*baseline_IVH_risk*(1-
```

## Death\_given\_IVH)

+C3\*c\_neonatal\_hospital\_RDS\*baseline\_IVH\_risk\*(RR\_IVH\_ANS\_≤7\_days-1)  
+G3\*c\_neonatal\_hospital\_RDS\*baseline\_IVH\_risk\_\_FP≤7d\_\_TPIt37w\*(RR\_IVH\_A  
NS\_\_7\_days-1), 0)))

ii. There was an error in the executable excel model file in the formulae of column I of Sheet 'Decision Analysis'. Correcting it changes the base case (women presenting at 30 weeks) ICER figures by 4 units or less and other lifetime scenarios by less than £300. The terms highlighted in bold should be deleted from the formulae in all rows of the column; for example in cell I3:

=(C3+E3+F3)\*(c\_maternal\_steroid\_injection+IF(AND(Setting<3,Gestational\_age\_at\_presentation<28),c\_atosiban\_\_atosiban\_infusion\_equipment,0))

## Corrections to the Assessment Report

1. Page 4, Abstract, second paragraph: the incremental cost per QALY gained or lost figures are incorrect.

The corrected page 4 is presented below.

2. Page 4, Abstract, second paragraph, in referring to cost saving per QALY lost relative to qfFN 50ng/ml, qfFN at 500ng/ml is incorrectly referred to as qfFN at 200ng/ml.

The corrected page 4 is presented below.

3. Page 25, Scientific Abstract, second paragraph: The cost difference of Actim Partus and the ICERs of Actim Partus and PartoSure are incorrect.

Page 25 is reproduced below.

4. Page 117, Figure 8: Title misses the study reference; it should read 'Decision tree of fFN testing strategy in Chuck and Nguyen (2015)'.

The corrected Page 117 is presented below.

5. Pages 158-165, Sections 6.2-6.4: The ICER figures in the text and in Tables 32-40, the total cost in Tables 32-37, and the costs of intraventricular haemorrhage in Tables 34 and 37, are incorrect.

The corrected pages 158-165 are presented below.

6. Pages 159 and 162, Tables 34 and 37: The label of costs of Intraventricular haemorrhage and of costs of respiratory distress syndrome are incorrectly placed in each other's rows.

The corrected pages 159 and 162 are presented below.

7. Page 160, Figure 17: The label of the cost effectiveness threshold is incorrect.

The corrected page 160 is presented below.

8. Page 161, first paragraph: the text has been revised to correct meaning.

The corrected page 161 is presented below.

9. Pages 166-169, Figures 18-23: The Tornado diagrams show the most sensitive parameters without ranking them by importance.

The corrected pages 166-169 are presented below.

10. Pages 172-177, Section 6.2.6, scenario analyses: The ICERs figures in the text and Tables 41-48 are incorrect.

The corrected pages 172-177 are presented below

11. Page 175, second paragraph: There is an error in referencing the results of Table 45.

The corrected p. 175 is presented below.

Page 4:

One partial economic evaluation was identified for predicting preterm birth. It assessed the number needed to treat to prevent a respiratory distress syndrome case of a 'treat-all' strategy, relative to testing with qualitative qfFN.

In our de-novo base case analysis (for woman at 30 weeks' gestation) Actim Partus had lower healthcare costs and fewer quality-adjusted life-years than qfFN 50 ng/ml, reducing costs at a rate of £56,033 per QALY lost vs. qfFN 50ng ml. PartoSure is less costly than Actim Partus whilst being equally effective, but this is based on diagnostic accuracy data from a small study. No study provided data that allowed us to compare all three tests simultaneously. Testing with qfFN at 10ng/ml cost £140,270 per QALY gained relative to fFN 50ng/ml, whilst testing with qfFN at 200ng/ml and 500ng/ml resulted in lower cost savings per QALY lost relative to fFN 50ng/ml than those with Actim Partus. Similar qualitative results obtained for women presenting at different gestational ages.

## **Discussion and Conclusion**

There is a high degree of uncertainty surrounding the test accuracy and cost-effectiveness results. We are also aware of four ongoing UK trials, two of which plan to enrol over 1,000 participants. The results of these trials may alter the findings presented here.

### **Registration**

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### **Word Count**

492 words.

Page 25:

A review of cost studies informed the selection of relevant costs for inclusion in the model. Unlike the economic analysis that informed the NICE guidelines, our model accounts for the additional costs of saving a preterm neonatal life.

The results from our base case analysis (for a woman presenting at 30 weeks' gestation) are as follows. Using test accuracy data from Buijn et al., we find that Actim Partus is £346 cheaper and 0.006 QALYs less effective than fFN at 50 ng/ml. This results in an ICER for Actim Partus of £56,033 cost saving per QALY lost vs fFN 50 ng/ml. Using test accuracy data from Hadzi-Lega (2017), we find that PartoSure is less costly than Actim Partus whilst being equally effective. No study provided data that allowed us to compare all three tests simultaneously. Indirectly comparing PartoSure to fFN 50 ng/ml (using APOSTEL-1 and Hadzi-Lega (2017)) yields an ICER of £81,925. Again, this represents both a cost saving and a QALY reduction and is highly uncertain given the indirect comparison source and the small size of the study by Hadzi-Lega (2017).

## **Discussion and Conclusion**

There is a high degree of uncertainty surrounding the test accuracy results, primarily as a result of the substantial methodological, clinical and statistical heterogeneity between included studies. Nevertheless, our results suggest that the NICE Guideline recommendation that symptomatic women presenting at 30 weeks' gestation be admitted to hospital (i.e. the no test, treat all policy) may not be cost-effective. We are also aware of four ongoing UK trials, two of which are planning to enrol over 1000 participants (QUIDS and PETRA), whose results are likely to affect these conclusions.

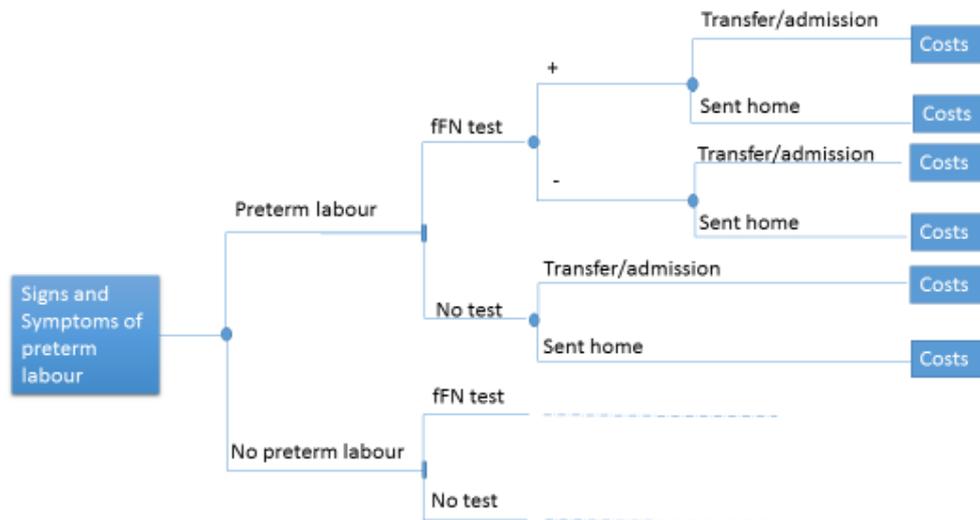
### **Registration**

PROSPERO: CRD42017072696

### **Word Count**

2399 words.

**Figure 1 Decision tree of fFN testing strategy in Chuck and Nguyen (2015)**



**Key:** fFN, fetal fibronectin

Chuck and Nguyen estimated that the introduction of fFN led to an extra 27 ambulance transfers, one fewer hospital admission, and 143 more hospital days for women who were not in labour, relative to what would have happened had testing not been done, during the 2008-2013 period of observation.<sup>79</sup> There were 69 more ambulance transfers and an additional 1,379 days in hospital among women in premature labour. The costs of these health care resources and the additional testing led to an overall increase in costs of US\$4 million.

One limitation of Chuck and Nguyen’s study is that it was a retrospective study that relied on administrative coding data to identify cases of preterm labour and preterm birth, which is likely to render estimates of ‘real world’ test accuracy performance unreliable. Another limitation, also acknowledged by the authors, is in their omission of the costs and benefits associated with fFN testing from additional false negatives and true positives mediated through the increases in the proportion of patients born in tertiary care units. Furthermore, the major limitation of this study from our perspective is the lack of assessment of health outcomes. The strengths of the study are found in its documenting of patient management consequent upon test results, particularly in relation to transfers from lower level to tertiary units, and hospital admissions.

Page 158-169:

## 6 Independent economic assessment

### 6.1 Methods

### 6.2 Results

Since our results vary by gestational age, we present details for the base case of a symptomatic woman presenting at 30 weeks of gestation (the average age on diagnostic accuracy studies), and general results for older, 33 weeks, and younger, 26 gestational ages.

#### 6.2.1 Base case results

The base case deterministic results are presented in Table 1. These are based on the preferred comparative studies APOSTEL-1 and Hadzi-Lega.<sup>45-47</sup> The base case considers women presenting at 30 weeks' gestation to a level 2 hospital. Whilst all ICERs are positive, they should be interpreted with caution since, other than 'treat all' and fFN 10 ng/ml vs. fFN 50 ng/ml, they represent both a reduction in costs and QALYs. Actim Partus results in £56,033 of cost savings per QALY lost relative to fFN 50 ng/ml, which are higher than those of fFN 200 ng/ml (£25,213) and fFN 500 ng/ml (£17,013). Incremental costs and QALYs for PartoSure vs fFN 50 ng/ml are the result of an indirect comparison between Bruijn et al. and Hadzi-Lega et al., since no included study directly compares these two tests. Subject to this caveat, PartoSure would produce the same QALY loss but more cost savings than Actim Partus, relative to fFN 50 ng/ml.

**Table 1 Summary of ICERs for women presenting at 30 weeks' gestation (at a level 2 hospital)\***

Test	Versus treat all					Versus fFN 50 ng/ml		
	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (per QALY)	Incremental costs	Incremental QALYs	ICER (per QALY)
<i>Actim Partus</i> <sup>a</sup>	£5,055	22.010	-£1,116	-0.010	<b>£108,323*</b>	-£346	-0.006	<b>£56,033*</b>
<i>PartoSure</i> <sup>b</sup>	£4,895†	22.010†	-£1,276	-0.008	<b>£123,858*</b>	-£506	-0.006	<b>£81,925*</b>
<i>Treat all</i>	£6,171	22.020	£0	0	-	£770	0.004	£186,757
<i>fFN 10 ng/ml</i> <sup>a</sup>	£5,690	22.018	-£481	-0.002	<b>£233,245*</b>	£289	0.002	£140,270
<i>fFN 50 ng/ml</i> <sup>a</sup>	£5,401	22.016	-£770	-0.004	<b>£186,757*</b>	£0	0	-
<i>fFN 200 ng/ml</i> <sup>a</sup>	£5,159	22.006	-£1,012	-0.014	<b>£73,676*</b>	-£242	-0.010	<b>£25,213*</b>
<i>fFN 500 ng/ml</i> <sup>a</sup>	£5,004	21.992	-£1,167	-0.027	<b>£42,474*</b>	-£398	-0.023	<b>£17,013*</b>

**Notes:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>; <sup>b</sup> Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs); † Inferred total cost and

QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years

Table 2 show the base case results as a full incremental analysis. The rows of the table are ordered from most to least effective testing option in terms of total QALYs. Incremental costs, QALYs, and cost-effectiveness for each test are shown in comparison to the following option in the table. For example, we see that fFN 50 ng/ml has an ICER of £56,033 relative to Actim Partus. Actim Partus, however, is itself dominated by PartoSure due to PartoSure having equal effectiveness but at a lower cost. (The ICER of fFN 50 ng/ml relative to PartoSure is £81,925, see Table 1). A graphical depiction of these results is presented in Figure 17.

**Table 2 Fully incremental analysis of ICERs for women presenting at 30 weeks' gestation at a level 2 hospital**

	Versus next option in the QALY ranking				
<i>Test</i>	Total costs	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER
<i>Treat-all (test none)</i>	£6,171	22.020	£481	0.002	£233,245
<i>fFN 10 ng/ml<sup>a</sup></i>	£5,690	22.018	£289	0.002	£140,270
<i>fFN 50 ng/ml<sup>a</sup></i>	£5,401	22.016	£346	0.006	£56,033
<i>Actim Partus<sup>a</sup></i>	£5,055	22.010	£160	0.000	Dominated by PartoSure
<i>PartoSure<sup>b</sup></i>	£4,895†	22.010†	-£264	0.003	-£76,870 (Dominates fFN 200 ng/ml)
<i>fFN 200 ng/ml<sup>a</sup></i>	£5,159	22.006	£155	0.014	£11,272
<i>fFN 500 ng/ml<sup>a</sup></i>	£5,004	21.992	-	-	-

**Notes:** Options have been ranked from most to least effective (in terms of QALYs). ICERs are relative to the next most effective option (i.e. the test in the row immediately below).

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>, <sup>b</sup> Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

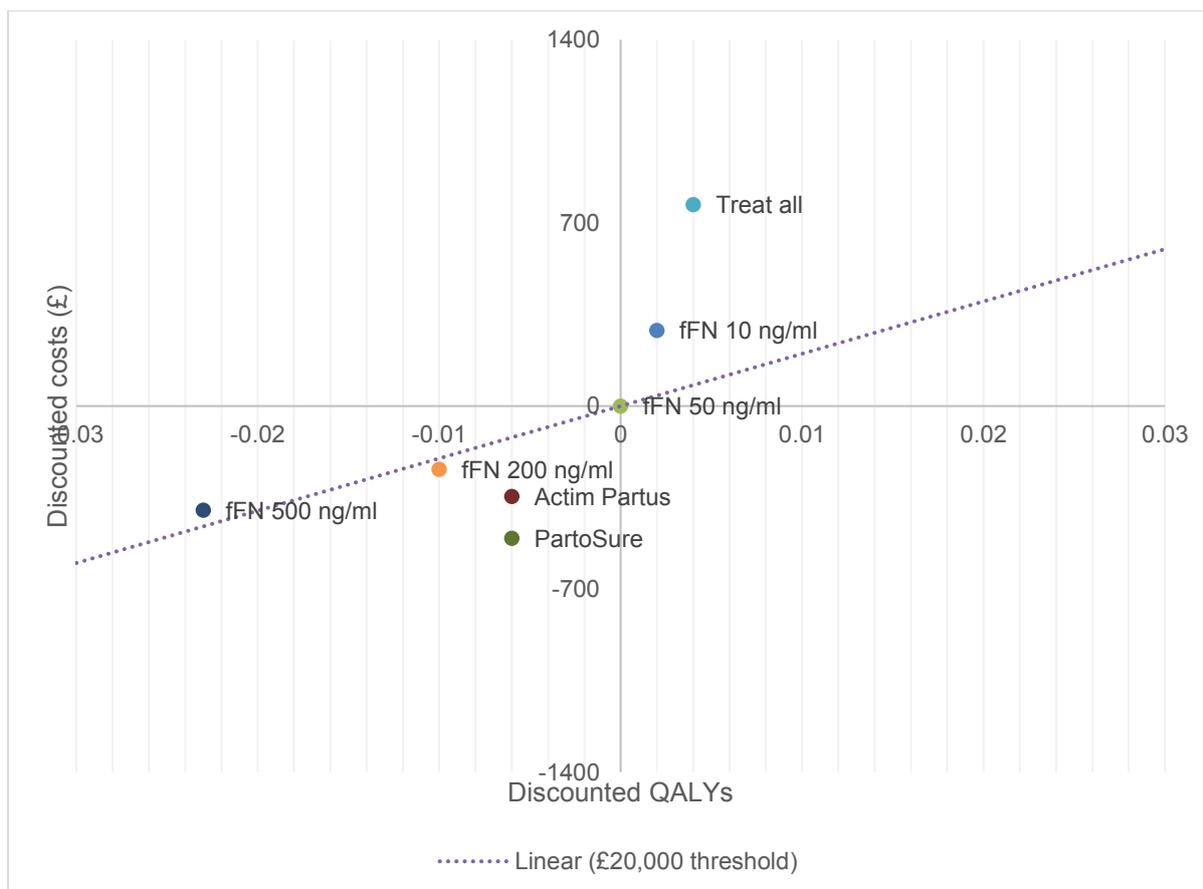
Table 3 breaks down the base case results shown in Table 1 in terms of their component discounted costs and QALYs. It should be noted, as in Table 1, that the ICER for PartoSure vs fFN 50 ng/ml is the result of an indirect comparison via Actim Partus. More specifically, the relative differences between PartoSure and Actim Partus obtained using Hadzi-Lega et al. were applied to the results for Actim Partus using Bruijn et al, and then compared to fFN 50 ng/ml.

**Table 3 Breakdown of base case results (discounted costs and QALYs)**

		Bruijn, 2016: APOSTEL-1					Indirect comparison†	
		Treat all	fFN	fFN	fFN	fFN	Actim Partus	PartoSure
			10	50	200	500		
	Threshold (ng/ml)							
<b>Discounted Costs</b>	Diagnosis	£0	£66	£66	£66	£66	£35	£52
	Treatment	£5	£3	£2	£1	£0	£1	£0
	Hospital admission	£1,325	£781	£493	£250	£95	£177	£1
	In-utero transfer	£0	£0	£0	£0	£0	£0	£0
	Neonatal RDS	£4,006	£4,008	£4,010	£4,018	£4,030	£4,015	£4,015
	Neonatal IVH	£788	£788	£789	£791	£793	£790	£789
	Neonatal death <sup>1</sup>	£47	£45	£43	£33	£20	£36	£36
	<b>Total</b>	£6,171	£5,690	£5,401	£5,159	£5,004	£5,055	£4,895
	Incremental Costs (vs. fFN 50ng/ml)	£770	£289	reference	£-242	£-397	£-346	£-506
	<b>Discounted QALYs</b>	Surviving neonate without morbidity	22.00	22.00	22.00	22.00	22.00	22.00
Loss new-born morbidity –IVH		-0.02	-0.02	-0.02	-0.02	-0.02	-0.02	-0.02
Loss new-born morbidity –RDS		0.00	0.00	0.00	0.00	0.00	0.00	0.00
Loss new-born mortality		0.04	0.04	0.04	0.03	0.02	0.03	0.03
<b>Total</b>		22.020	22.018	22.016	22.006	21.992	22.010	22.010
Incremental QALYs (vs. fFN 50ng/ml)		0.004	0.002	reference	-0.010	-0.023	-0.006	-0.006
<b>ICER vs. fFN 50ng/ml</b>		£186,757	£140,270	reference	£25,213*	£17,013*	£56,033*	£81,925*

**Notes** <sup>1</sup> These are the neonatal hospital costs associated with those infants saved by steroid treatment;  
**Key:** AE, adverse events; fFN, fetal fibronectin; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life years; \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs). † Costs and QALYs are inferred values computed via an indirect comparison between the Hadzi-Lega and Bruijn studies <sup>45-47</sup>

**Figure 2 Incremental costs and benefits of index tests against comparator (fFN @50 ng/ml)**



### 6.2.2 Women presenting at 26 weeks' gestation (at a Level 2 hospital)

As before, ICERs should be interpreted with caution since, other than 'treat all' and fFN 10 ng/ml vs. fFN 50 ng/ml, they represent both a reduction in costs and QALYs. Incremental costs and QALYs for PartoSure vs fFN 50 ng/ml are the result of an indirect comparison between Bruijn et al. and Hadzi-Lega et al., since no included study directly compares these two tests. Actim Partus results in £35,441 of cost savings per QALY lost relative to fFN 50 ng/ml, which are higher than those of fFN 200 ng/ml (£16,618) or fFN 500 ng/ml (£11,180), which is consistent with the results for women presenting at 30 weeks described above. Based on indirect comparison, PartoSure appears to offer the same QALY loss but higher cost savings than Actim Partus, relative to fFN 50 ng/ml.

**Table 4 Summary of ICERs for women presenting at 26 weeks' gestation (level 2 hospital)**

Test	Total costs	Total QALYs	Versus treat-all			Versus fFN 50 ng/ml		
			Incremental costs	Incremental QALYs	ICER (per QALY)	Incremental costs	Incremental QALYs	ICER (per QALY)
Actim Partus <sup>a</sup>	£17,745	21.619	-£2,261	-0.031	£72,871*	-£660	-0.019	£35,441*

<i>PartoSure</i> <sup>b</sup>	£17,409 †	21.619 †	-£2,2598	-0.031	£83,721*	-£997	-0.019	£53,524*
<i>Treat all</i>	£20,007	21.650	£0	0	-	£1,601	0.012	£129,017
<i>fFN 10 ng/ml</i> <sup>a</sup>	£18,982	21.643	-£1,025	-0.006	£165,111*	£577	0.006	£92,923
<i>fFN 50 ng/ml</i> <sup>a</sup>	£18,405	21.637	-£1,601	-0.012	£129,017*	£0	0	-
<i>fFN 200 ng/ml</i> <sup>a</sup>	£17,924	21.608	-£2,083	-0.041	£50,338*	-£481	-0.029	£16,618*
<i>fFN 500 ng/ml</i> <sup>a</sup>	£17,619	21.567	-£2,388	-0.083	£28,856*	-£786	-0.070	£11,180*

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup>Bruijn et al.<sup>45, 46</sup>, <sup>b</sup>Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

Full incremental analyses are presented in Table 5, and detailed costs and QALYs are presented in Table 6. Note that diagnostic options involving wider use of treatment have become more attractive for this group of women than women presenting at older gestation ages, e.g. ICER for Treat all in Table 4, £129,017, is lower than that in Table 1, £186,757.

**Table 5 Fully incremental analysis of ICERs for women presenting at 26 weeks' gestation (level 2 hospital)**

Versus next option in the QALY ranking					
<i>Test</i>	Total costs	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER
<i>Treat-all (test none)</i>	£20,007	21.650	£1,025	0.006	£165,111
<i>fFN 10 ng/ml<sup>a</sup></i>	£18,982	21.643	£577	0.006	£92,923
<i>fFN 50 ng/ml<sup>a</sup></i>	£18,405	21.637	£660	0.019	£35,441
<i>Actim Partus<sup>a</sup></i>	£17,745	21.619	£337	0.000	Dominated by PartoSure
<i>PartoSure<sup>b</sup></i>	£17,409 †	21.619 †	-£515	0.010	-£49,811 (Dominates fFN 200 ng/ml)
<i>fFN 200 ng/ml<sup>a</sup></i>	£17,924	21.608	£305	0.041	£7,373
<i>fFN 500 ng/ml<sup>a</sup></i>	£17,619	21.567	-	-	-

**Notes:** Options have been ranked from most to least effective (in terms of QALYs). ICERs are relative to the next most effective option (i.e. the test in the row immediately below).

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>, <sup>b</sup> Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

**Table 6 Breakdown of discounted costs and QALYs for women presenting at 26 weeks' gestation**

		Bruijn, 2016: APOSTEL-1					Indirect comparison†	
		Treat all	fFN	fFN	fFN	fFN	Actim Partus	PartoSure
Threshold (ng/ml)			10	50	200	500		
<b>Discounted Costs</b>	Diagnosis	£0	£66	£66	£66	£66	£35	£52
	Treatment	£367	£216	£136	£69	£0	£49	£0
	Hospital admission	£1,325	£781	£493	£250	£95	£177	£1
	In-utero transfer	£965	£569	£359	£182	£69	£129	£1
	Neonatal RDS	£5,232	£5,235	£5,237	£5,248	£5,264	£5,244	£5,244
	Neonatal IVH	£11,952	£11,958	£11,994	£12,036	£11,984	£11,965	£11,965
	Neonatal death <sup>1</sup>	£166	£158	£151	£118	£70	£130	£130
	<b>Total</b>	£20,007	£18,982	£18,405	£17,924	£17,619	£17,745	£17,409
	Incremental Costs (vs. fFN 50ng/ml)	£1,601	£577	reference	-£481	-£786	-£660	-£997
<b>Discounted QALYs</b>	Surviving neonate without morbidity	21.55	21.55	21.55	21.55	21.55	21.55	21.55
	Loss new-born morbidity –IVH	-0.03	-0.03	-0.03	-0.03	-0.03	-0.03	-0.03
	Loss new-born morbidity –RDS	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01

Loss new-born mortality	0.13	0.13	0.12	0.10	0.06	0.10	0.10
<b>Total</b>	21.650	21.643	21.637	21.608	21.567	21.619	21.619
Incremental QALYs (vs. fFN 50ng/ml)	0.012	0.006	reference	-0.029	-0.070	-0.019	-0.019
<b>ICER vs. fFN 50ng/ml</b>	£129,017	£92,923	<b>reference</b>	£16,618*	£11,180*	£35,441*	£53,524*

**Notes** <sup>1</sup> These are the neonatal hospital costs associated with those infants saved by steroid treatment; \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs). † Costs and QALYs are inferred values computed via an indirect comparison between the Hadzi-Lega and Bruijn studies <sup>45-47</sup>

**Key:** AE, adverse events; fFN, fetal fibronectin; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life years

### 6.2.3 Women presenting at 33 weeks' gestation (at a Level 2 hospital)

Qualitatively similar results to those described before for women presenting at 26 and 30 weeks were found for women presenting at 33 weeks' gestation. At £97,075, Actim Partus saves more costs per QALY lost relative to fFN 50 ng/ml than fFN 200 ng/ml (£43,787) and fFN 500 ng/ml (£29,609), while Treat all and fFN 10 ng/ml both have incremental costs per QALY gained that are above £200,000. Based on indirect comparison, PartoSure appears to dominate Actim Partus as it results in the same amount of QALYs and lower costs. Table 39 presents the summary results for each test relative to the comparators, Table 40 presents the fully incremental analyses and Table 41 the detailed costs and QALY elements.

**Table 7 Summary of ICERs for women presenting at 33 weeks' gestation (level 2 hospital)**

Test	Versus treat-all				Versus fFN 50 ng/ml			
	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (per QALY)	Incremental costs	Incremental QALYs	ICER (per QALY)
Actim Partus <sup>a</sup>	£2,716	22.096	-£1,117	-0.006	£187,479*	-£347	-0.004	£97,075*
PartoSure <sup>b</sup>	£2,556 †	22.096 †	-£1,111	-0.005	£243,269*	-£507	-0.004	£141,844*
Treat all	£3,833	22.102	£0	0	-	£770	0.002	£323,098
fFN 10 ng/ml <sup>a</sup>	£3,352	22.101	-£481	-0.001	£403,469*	£289	0.001	£242,722
fFN 50 ng/ml <sup>a</sup>	£3,063	22.100	-£770	-0.002	£323,093*	£0	0	-
fFN 200 ng/ml <sup>a</sup>	£2,820	22.094	-£1,013	-0.008	£127,575*	-£244	-0.006	£43,787*
fFN 500 ng/ml <sup>a</sup>	£2,663	22.086	-£1,170	-0.016	£73,650*	-£400	-0.014	£29,609*

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al. <sup>45,46</sup>, <sup>b</sup> Hadzi-Lega et al. <sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

Full incremental analyses are presented in Table 8, and detailed costs and QALYs are presented in Table 9. Diagnostic options involving wider use of treatment have become less attractive for this group of women than women presenting at younger gestation ages, e.g. ICER for Treat all in Table 38, £323,098 is higher than those in Table 4, £129,017, and Table 1, £186,757.

**Table 8 Fully incremental analysis of ICERs for women presenting at 33 weeks' gestation (level 2 hospital)**

<i>Test</i>	Versus next option in the QALY ranking				
	Total costs	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER
<i>Treat-all (test none)</i>	£3,833	22.102	£481	0.001	£403,475
<i>fFN 10 ng/ml<sup>a</sup></i>	£3,352	22.101	£289	0.001	£242,722
<i>fFN 50 ng/ml<sup>a</sup></i>	£3,063	22.100	£347	0.004	£97,075
<i>Actim Partus<sup>a</sup></i>	£2,716	22.096	£160	0.000	Dominated by PartoSure
<i>PartoSure<sup>b</sup></i>	£2,556 †	22.096 †	-£264	0.002	-£132,715 (Dominates fFN 200 ng/ml)
<i>fFN 200 ng/ml<sup>a</sup></i>	£2,820	22.094	£156	0.008	£19,684
<i>fFN 500 ng/ml<sup>a</sup></i>	£2,663	22.086	-	-	-

**Notes:** Options have been ranked from most to least effective (in terms of QALYs). ICERs are relative to the next most effective option (i.e. the test in the row immediately below).

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>; <sup>b</sup> Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

**Table 9 Breakdown of discounted costs and QALYs for women presenting at 33 weeks' gestation**

		Bruijn, 2016: APOSTEL-1					Indirect comparison†	
		Treat all	fFN	fFN	fFN	fFN	Actim Partus	PartoSure
	Threshold (ng/ml)		10	50	200	500		
<b>Discounted Costs</b>	Diagnosis	£0	£66	£66	£66	£66	£35	£52
	Treatment	£5	£3	£2	£1	£0	£1	£0
	Hospital admission	£1,325	£781	£493	£250	£95	£177	£1
	In-utero transfer	£0	£0	£0	£0	£0	£0	£0
	Neonatal RDS <sup>2</sup>	£2,477	£2,478	£2,479	£2,484	£2,492	£2,482	£2,482
	Neonatal IVH <sup>2</sup>	£0	£0	£0	£0	£0	£0	£0
	Neonatal death <sup>1</sup>	£26	£25	£24	£19	£11	£21	£21
	<b>Total</b>	£3,833	£3,352	£3,063	£2,820	£2,663	£2,716	£2,556
	Incremental Costs (vs. fFN 50ng/ml)	£770	£289	reference	-£244	-£400	-£347	-£507
	<b>Discounted QALYs</b>	Surviving neonate without morbidity	22.09	22.09	22.09	22.09	22.09	22.09
Loss new-born morbidity –IVH		-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01
Loss new-born morbidity –RDS		0.00	0.00	0.00	0.00	0.00	0.00	0.00
Loss new-born mortality		0.03	0.02	0.02	0.02	0.01	0.02	0.02
<b>Total</b>		22.102	22.101	22.100	22.094	22.086	22.096	22.096
Incremental QALYs (vs. fFN 50ng/ml)		0.002	0.001	reference	-0.006	-0.014	-0.004	-0.004
<b>ICER vs. fFN 50ng/ml</b>	£323,098	£242,722	-	£43,787*	£29,609*	£97,075*	£141,844*	

**Notes** <sup>1</sup> These are the neonatal hospital costs associated with those infants saved by steroid treatment;  
**Key:** AE, adverse events; fFN, fetal fibronectin; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life years; \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs). † Costs and QALYs are inferred values computed via an indirect comparison between the Hadzi-Lega and Bruijn studies <sup>45-47</sup>

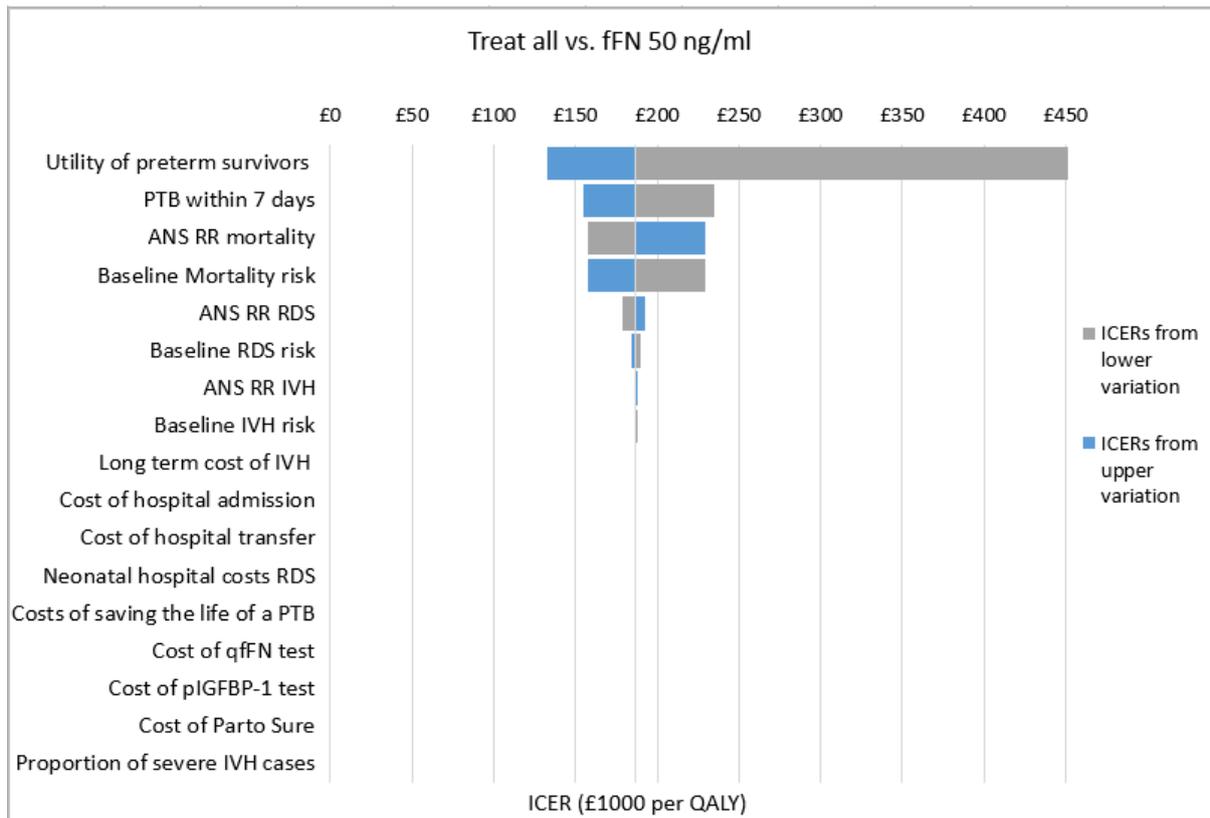
### 6.2.4 Tornado Analysis

For the tornado analysis, the parameter base-case values were increased and decreased by 20% (the upper and the lower variations, respectively) and the ICERs vs the comparator of fFN 50 ng/ml were plotted, with the intersection of the vertical and the horizontal axes at the ICER base-case. The tornado plots for each of the interventions in the Bruijn 2016: APOSTEL-1 study,<sup>46</sup> the Hadzi-Lega 2017 study<sup>47</sup> are presented below.

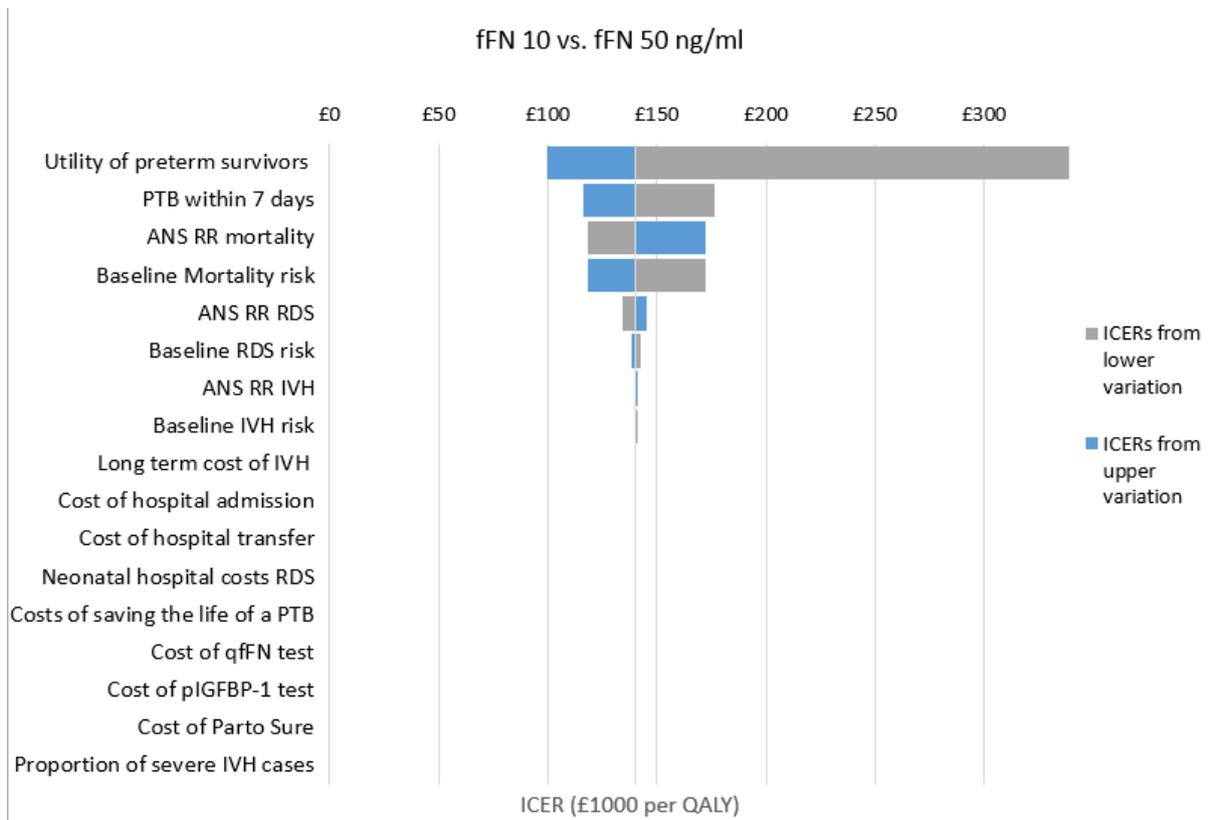
There is a consistent pattern across all comparisons, as depicted in Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, and Figure 8. The results are sensitive to the health related quality of life (state utility) of preterm survivors. Much less influential are the cost of hospital admission, the prevalence of preterm birth within 7 days, the effectiveness of steroid

treatment and the baseline mortality risks. Other parameter values appear to have no discernible influence on the results.

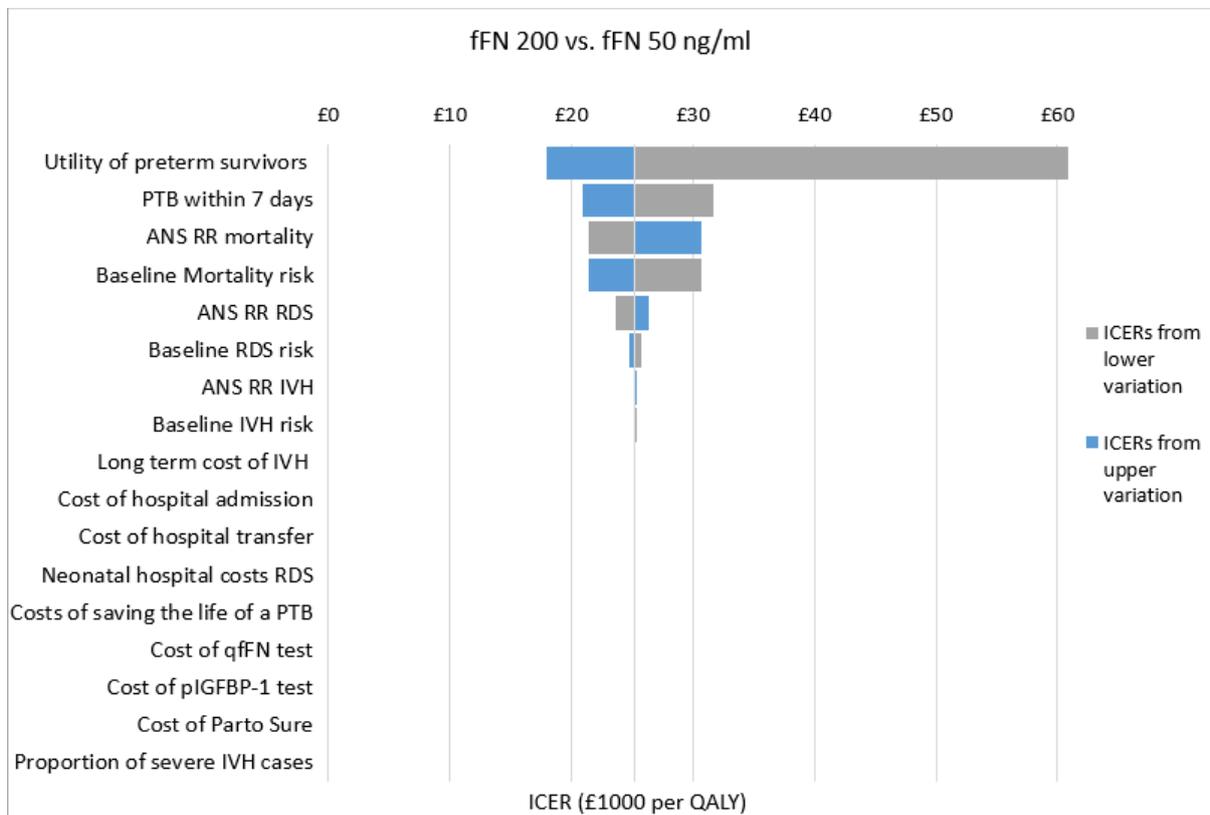
**Figure 3 Tornado diagram of most influential model parameter values –Treat all**



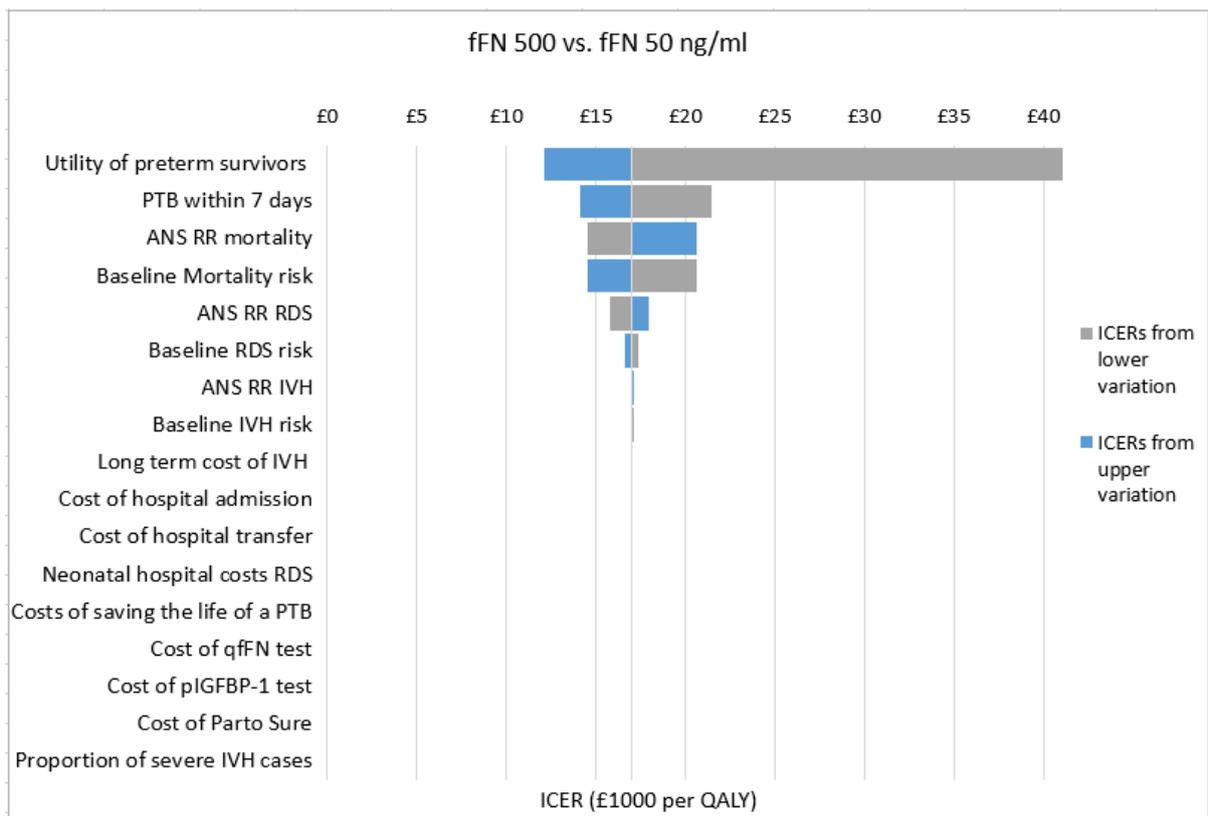
**Figure 4 Tornado diagram of most influential model parameter values –fFN 10ng/ml**



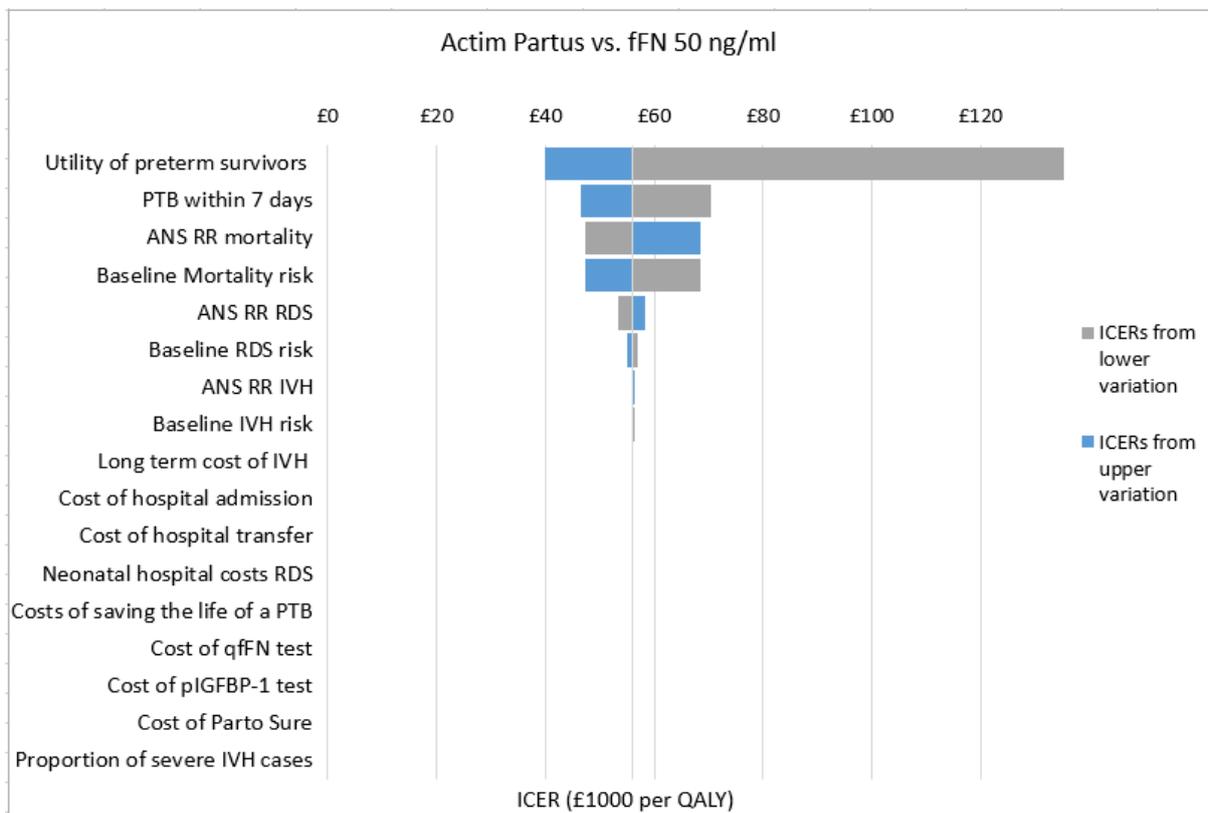
**Figure 5 Tornado diagram of most influential model parameter values –fFN 200ng/ml**



**Figure 6 Tornado diagram of most influential model parameter values –fFN 500ng/ml**

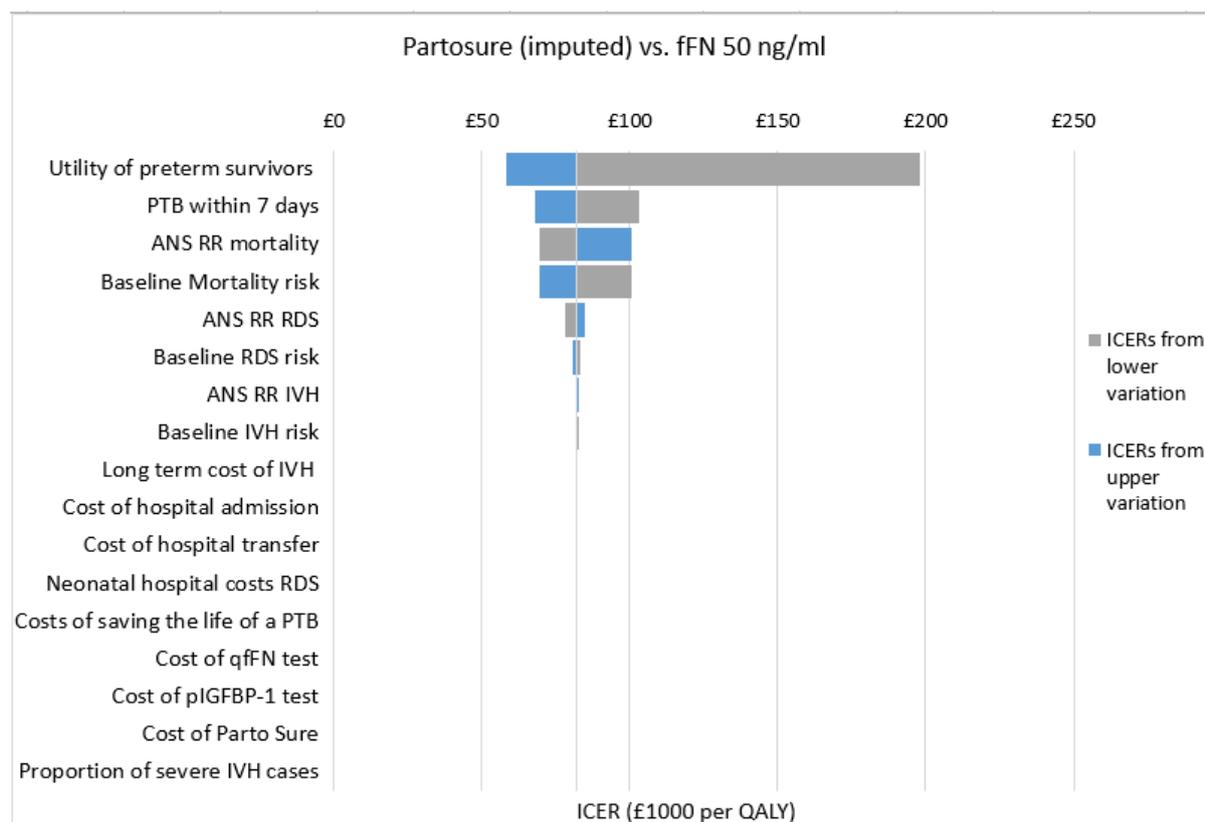


**Figure 7 Tornado diagram of most influential model parameter values –Actim Partus**



Hadzi-Lega, 2017

**Figure 8 Tornado diagram of most influential model parameter values –PartoSure**



### 6.2.5 Probabilistic sensitivity analyses

At £20,000 willingness to pay per QALY threshold, Actim Partus has a probability of being cost-effective of 14%, 21% and 21% for women presenting at gestational ages 33, 30 and 26 weeks, respectively (See **Error! Reference source not found.**, **Error! Reference source not found.**, and **Error! Reference source not found.**). PartoSure has probabilities of being cost-effective of 83%, 76%, and 75%, respectively, but these values are based on indirect comparison and have a lower strength of evidence than for other diagnostic options.

Treat all has a probability of being cost-effective of 0% at a £20,000 willingness to pay per QALY threshold for all women, and only becomes the option with the highest likelihood of being cost-effective for women presenting at 26 weeks' gestation at a willingness to pay per QALY threshold above £180,000 (**Error! Reference source not found.**).

## 6.2.6 Scenario Analyses

### 6.2.6.1 Alternative diagnostic accuracy data

Using the diagnostic test accuracy results of the study by Cooper and colleagues,<sup>1</sup> which did not include PartoSure, suggests that the fFN 50 ng/ml test provides lower costs with equal health benefit when compared to Actim Partus. The option of treating all women compared with fFN 50 ng/ml yields an ICER of £34,511 per QALY (Table 10).

**Table 10 Results for Actim Partus and no-testing vs fFN 50 ng/ml using data from Cooper 2012;<sup>1</sup> presenting at 30 weeks gestation (level 2 hospital)**

		Cooper 2012 <sup>1</sup>		
		Treat all	Actim Partus	fFN 50 ng/ml
<i>Discounted Costs</i>	Diagnosis	£0	£35	£66
	Medication	£5	£1	£1
	Admission	£1,325	£373	£171
	Transfer	£0	£0	£0
	RDS	£4,006	£4,034	£4,034
	IVH	£788	£794	£794
	Neonatal death	£47	£16	£16
	<b>Total</b>	<b>£6,171</b>	<b>£5,254</b>	<b>£5,080</b>
	Incremental costs vs. fFN 50	£1,090	£173	
<i>Discounted QALYs</i>	Baseline w/o morbidity	22.00	22.00	22.00
	RDS	-0.02	-0.02	-0.02
	IVH	0.00	0.00	0.00
	Newborn mortality	0.04	0.01	0.01
	<b>Total</b>	<b>22.02</b>	<b>21.99</b>	<b>21.99</b>
		Incremental QALYs vs. fFN 50	0.03	0.00
<b>ICER vs fFN 50 ng/ml</b>	<b>£34,511</b>	<b>Dominated</b>	<b>-</b>	

**Key:** fFN, fetal fibronectin; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life year



**Table 11 Results for fFN (various thresholds) vs fFN 50 ng/ml using data from Abbott 2013; presenting at 30 weeks gestation (level 2 hospital)**

		Abbott 2013 <sup>102</sup>				
		Treat all	fFN 10	fFN 200	fFN 500	fFN 50
<i>Discounted Costs</i>	Diagnosis	■	■	■	■	■
	Medication	■	■	■	■	■
	Admission	■	■	■	■	■
	Transfer	■	■	■	■	■
	RDS	■	■	■	■	■
	IVH	■	■	■	■	■
	Neonatal death	■	■	■	■	■
	<b>Total</b>	■	■	■	■	■
	Incremental costs vs. fFN 50	■	■	■	■	
<i>Discounted QALYs</i>	Baseline w/o morbidity	■	■	■	■	■
	RDS	■	■	■	■	■
	IVH	■	■	■	■	■
	Newborn mortality	■	■	■	■	■
	<b>Total</b>	■	■	■	■	■
	Incremental QALYs vs. fFN 50	■	■	■	■	
<b>ICER vs fFN 50 ng/ml</b>	■	■	■	■	■	

**Key:** fFN, fetal fibronectin; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life year  
 \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs).

When the diagnostic accuracy data from the meta-analysis of the four studies that compared Actim Partus with fFN 50ng/ml were used,<sup>45, 46, 53, 58, 59</sup> Actim Partus was dominant over fFN 50ng/ml as it resulted in cost savings of £41 per woman and health benefits of 0.01 more QALYs per woman. Treat all increased costs and QALYs, and resulted in an ICER of £70,471.

**Table 12 Results for no-testing and Actim Partus vs fFN 50 ng/ml using data from meta-analysis; presenting at 30 weeks gestation (level 2 hospital)**

		Meta-analysis <sup>45, 46, 53, 58, 59</sup>		
		Treat all	Actim Partus	fFN 50 ng/ml
<i>Discounted Costs</i>	Diagnosis	£0	£35	£66
	Medication	£5	£1	£1
	Admission	£1,325	£195	£204
	Transfer	£0	£0	£0
	RDS	£4,006	£4,013	£4,019
	IVH	£788	£789	£791
	Neonatal death	£47	£39	£32
	<b>Total</b>	<b>£6,171</b>	<b>£5,072</b>	<b>£5,113</b>
	Incremental costs vs fFN 50 ng/ml	£1,058	−£41	
<i>Discounted QALYs</i>	Baseline w/o morbidity	22.00	22.00	22.00
	RDS	−0.02	−0.02	−0.02
	IVH	0.00	0.00	0.00
	Newborn mortality	0.04	0.04	0.03
	Mother	0.00	0.00	0.00
	<b>Total</b>	<b>22.02</b>	<b>22.01</b>	<b>22.00</b>
	Incremental costs vs fFN 50 ng/ml	0.02	0.01	
<i>ICER (relative to fFN 50 ng/ml)</i>		<b>£70,471</b>	<b>Dominant</b>	-

**Key:** fFN, fetal fibronectin; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life year

### 6.2.6.2 Other scenarios

Including the negative impact on QALY outcomes the effect of an infant's death on mothers that is assumed to last for 10 years, favours options that involve more use of ANS treatment. That is, in Table 13, Table 14, and Table 15 the ICER for Treat all and fFN 10ng/ml under the column 'with maternal QALYs for 10 years' is lower than in the Base case column. When we limit the analytical horizon to the time of deliver, the assessment becomes in effect a cost-minimisation analysis since our model does not account for health related quality of life outcomes of mother during the antenatal period. In this scenario among women presenting at age 30 weeks, PartoSure is the least costly option with a £507 reduction in costs per woman, followed by fFN 500 ng/ml, £399, and Actim Partus, £347. As discussed before the values for PartoSure need to be considered with caution.

When we allow for partial benefits of ANS given earlier than 7 days before birth, the ICER for fFN 10 ng/ml and Treat all are £24,420 and £41,625, respectively, among women presenting at 30 weeks; as for the rest, only PartoSure results in savings per QALY lost >£20,000 relative to fFN 50 ng/ml (Table 13). Similar results apply to women presenting at gestational

ages of 26 and 33 weeks, except for the result that Actim Partus saves £24,534 in healthcare costs per QALY lost among women aged 33 weeks.

Of note, among women aged 26 weeks, presenting at a level 3 hospital (rather than a level 1 or 2 hospital) has the effect of halving the ICERs relative to fFN 50ng/ml. Therefore, this favours treatment-intensive options Treat All and fFN 10ng/ml, which now have an ICER of £61,792 and £46,359, respectively; other options, are favoured by the change, but all now save less than £20,000 per QALY lost relative to fFN 50 ng/ml, except for PartoSure, which saves £26,989 per lost QALY (Table 14).

**Table 13 Incremental cost –effectiveness ratios (ICERs) vs fFN 50 ng/ml for women presenting at 30 weeks (level 2 hospital)**

Option	Base case	With maternal QALYs for 10 years	Limiting the analysis to delivery (additional cost only)	Limiting the analysis to first year after birth	ANS earlier than 7 days before preterm delivery has partial benefits	Excluding additional neonatal hospital costs of death	Women presenting at level 3 hospital	Applying costs and disutilities of AEs to all AEs
<i>Treat all</i>	£186,757	£111,815	£770	£4,930,444	£41,625	£185,774	£186,757	£174,718
<i>fFN 10 ng/ml<sup>a</sup></i>	£140,270	£74,566	£289	£3,704,229	£24,420	£139,287	£140,270	£131,117
<i>fFN 200 ng/ml<sup>a</sup></i>	£25,213*	£18,971*	-£243	£669,308*	£9,729*	£24,230*	£25,213*	£23,204*
<i>fFN 500 ng/ml<sup>a</sup></i>	£17,013*	£13,337*	-£399	£453,004*	£7,422*	£16,029*	£17,013*	£15,513*
<i>Actim Partus<sup>a</sup></i>	£56,033*	£38,203*	-£347	£1,482,263*	£16,663*	£55,050*	£56,033*	£52,110*
<i>PartoSure<sup>b</sup></i>	£81,925*	£81,896*	-£507	£2,165,244*	£128,511*	£80,942*	£81,925*	£76,395*

**Key:** ANS, antenatal corticosteroids; AE, adverse event; ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>; <sup>b</sup> Indirect comparison between Bruijn et al. and Hadzi-Lega et al.<sup>47</sup> (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs).

**Table 14 Incremental cost –effectiveness ratios (ICERs) vs fFN 50 ng/ml for women presenting at 26 weeks (level 2 hospital)**

Option	Base case	With maternal QALYs for 10 years	Limiting the analysis to delivery (additional cost only)	Limiting the analysis to first year after birth	ANS earlier than 7 days before preterm delivery has partial benefits	Excluding additional neonatal hospital costs of death	Women presenting at level 3 hospital	Applying costs and disutilities of AEs to all AEs
<i>Treat all</i>	£129,017	£72,050	£1,604	£3,424,575	£41,178	£127,857	£61,792	£115,081
<i>fFN 10 ng/ml<sup>a</sup></i>	£92,923	£45,561	£578	£2,472,505	£23,977	£91,763	£46,359	£82,280
<i>fFN 200 ng/ml<sup>a</sup></i>	£16,618*	£11,971*	-£488	£459,792*	£8,597*	£15,459*	£8,162*	£12,938*
<i>fFN 500 ng/ml<sup>a</sup></i>	£11,180*	£8,437*	-£803	£316,343*	£6,407*	£10,020*	£5,439*	£7,996*
<i>Actim Partus<sup>a</sup></i>	£35,441*	£22,857*	-£664	£956,295*	£14,661*	£34,282*	£18,393*	£30,044*
<i>PartoSure<sup>b</sup></i>	£53,524*	£53,501*	-£1001	£1,431,265*	£68,956*	£52,364*	£26,989*	£46,476*

**Key:** ANS, antenatal corticosteroids; AE, adverse event; ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>; <sup>b</sup> Indirect comparison between Bruijn et al. and Hadzi-Lega et al.<sup>47</sup> (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs).

**Table 15 Incremental cost –effectiveness ratios (ICERs) vs fFN 50 ng/ml for women presenting at 33 weeks (level 2 hospital)**

Option	Base case	With maternal QALYs for 10 years	Limiting the analysis to delivery (additional cost only)	Limiting the analysis to first year after birth	ANS earlier than 7 days before preterm delivery has partial benefits	Excluding additional neonatal hospital costs of death	Women presenting at level 3 hospital	Applying costs and disutilities of AEs to all AEs
<i>Treat all</i>	£323,098	£194,774	£770	£8,522,520	£59,093	£322,132	£323,098	£306,512
<i>fFN 10 ng/ml<sup>a</sup></i>	£242,722	£130,063	£289	£6,402,387	£34,622	£241,755	£242,722	£230,262
<i>fFN 200 ng/ml<sup>a</sup></i>	£43,787*	£33,085*	-£243	£1,154,990*	£14,904*	£42,821*	£43,787*	£41,539*
<i>fFN 500 ng/ml<sup>a</sup></i>	£29,609*	£23,297*	-£399	£780,999*	£11,646*	£28,642*	£29,609*	£28,089*
<i>Actim Partus<sup>a</sup></i>	£97,075*	£66,545*	-£347	£2,560,596*	£24,534*	£96,109*	£97,075*	£92,092*
<i>PartoSure<sup>b</sup></i>	£141,844*	£141,794*	-£507	£3,741,474*	£267,492*	£140,877*	£141,844*	£134,562*

**Key:** ANS, antenatal corticosteroids; AE, adverse event; ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>; <sup>b</sup> Indirect comparison between Bruijn et al. and Hadzi-Lega et al.<sup>47</sup> (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs).

**Table 16 Summary of ICERs for a woman presenting at 30 weeks' gestation (level 2 hospital), including QALY losses to the mother for 10 years in case of infant mortality**

Test	Versus treat-all				Versus fFN 50 ng/ml			
	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (per QALY)	Incremental costs	Incremental QALYs	ICER (per QALY)
<i>Actim Partus</i> <sup>a</sup>	£5,055	22.016	-£1,116	-0.016	£69,970*	-£346	-0.009	£38,203*
<i>PartoSure</i> <sup>b</sup>	£4,895	22.019	-£1,276	-0.013	£97,656*	-£506	-0.006	£81,896*
<i>fFN 10 ng/ml</i> <sup>a</sup>	£5,690	22.029	-£481	-0.003	£159,834*	£289	0.004	£74,566
<i>fFN 50 ng/ml</i> <sup>a</sup>	£5,401	22.025	-£770	-0.007	£111,815*	£0	0.000	-
<i>fFN 200 ng/ml</i> <sup>a</sup>	£5,159	22.012	-£1,012	-0.020	£51,471*	-£242	-0.013	£18,971*
<i>fFN 500 ng/ml</i> <sup>a</sup>	£5,004	21.995	-£1,167	-0.037	£31,821*	-£397	-0.030	£13,337*

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>, <sup>b</sup> Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.

**Table 17 Summary of ICERs for a woman presenting at 30 weeks' gestation (level 2 hospital), including lifetime QALY losses to the mother in case of infant mortality**

Test	Versus treat-all				Versus fFN 50 ng/ml			
	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (per QALY)	Incremental costs	Incremental QALYs	ICER (per QALY)
<i>Actim Partus</i> <sup>a</sup>	£5,055	22.027	-£1,116	-0.025	£43,956*	-£346	-0.014	£24,938*
<i>PartoSure</i> <sup>b</sup>	£4,895 †	22.035 †	-£1,276	-0.018	£72,145*	-£506	-0.006	£81,847*
<i>fFN 10 ng/ml</i> <sup>a</sup>	£5,690	22.048	-£481	-0.005	£104,733*	£289	0.007	£41,821
<i>fFN 50 ng/ml</i> <sup>a</sup>	£5,401	22.041	-£770	-0.011	£66,924*	£0	0.000	-
<i>fFN 200 ng/ml</i> <sup>a</sup>	£5,159	22.023	-£1,012	-0.030	£34,228*	-£242	-0.018	£13,418*
<i>fFN 500 ng/ml</i> <sup>a</sup>	£5,005	22.000	-£1,167	-0.052	£22,421*	-£397	-0.041	£9,798*

**Key:** ICER, incremental cost effectiveness ratio; fFN, fetal fibronectin; QALY, quality adjusted life years; <sup>a</sup> Bruijn et al.<sup>45, 46</sup>, <sup>b</sup> Hadzi-Lega et al.<sup>47</sup> for comparison with treat-all, indirect comparison between Bruijn et al. and Hadzi-Lega et al. for comparison with fFN 50 ng/ml (Bruijn et al. was used as the reference study in this case); \* ICER represents the South-West quadrant in cost-effectiveness (i.e. a reduction in both costs and QALYs); † Inferred total cost and QALYs for PartoSure obtained by applying relative differences vs Actim Partus found using Hadzi-Lega et al. to Bruijn et al.