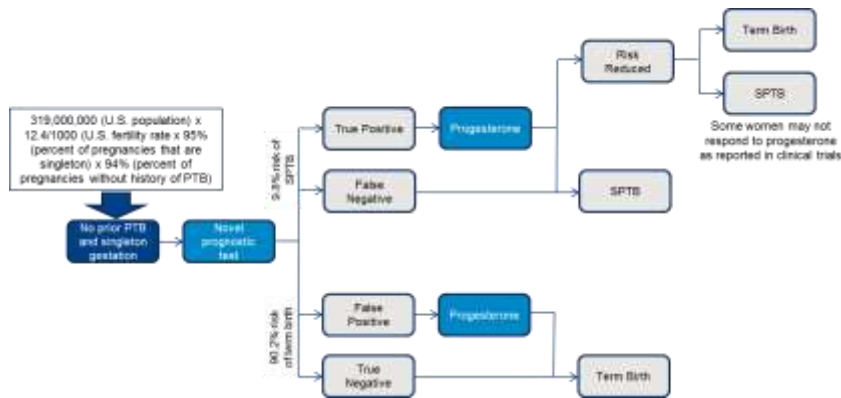


Supplemental Digital Content 1: **Prognostic** Arm Patient Flow

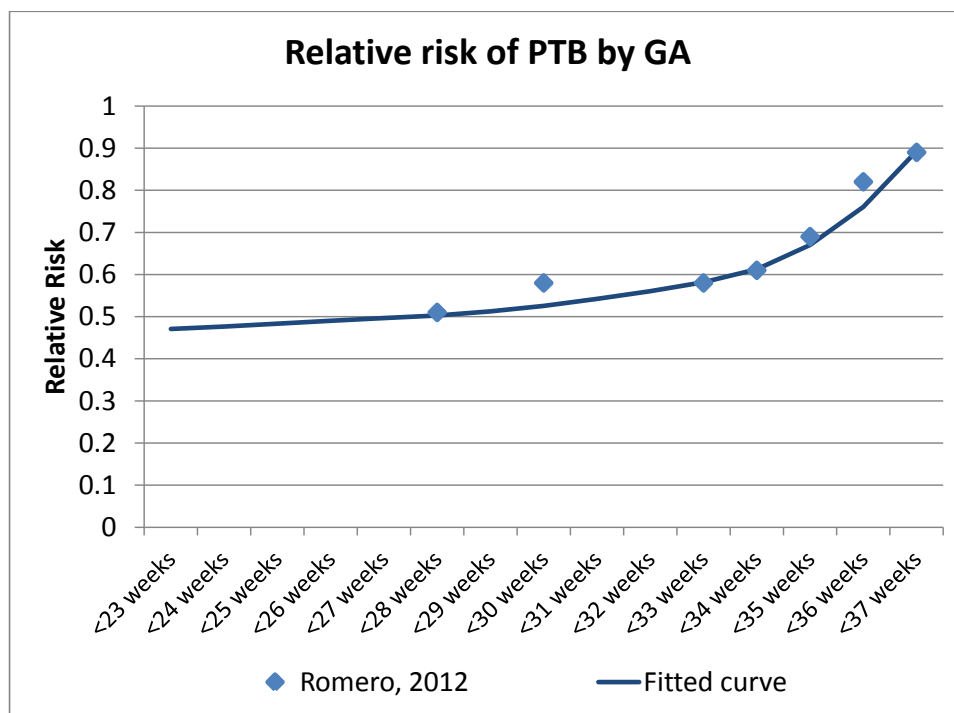
Figure 1: Model schematic showing impact of test results for the novel **prognostic test**



Supplemental Digital Content 2: Relative Risk Data

Relative risk data at certain time points in gestation were available from the Romero meta-analysis. These data were used to fit a week-by-week curve for the relative risk of spontaneous preterm birth with vaginal progesterone therapy.

Figure 2: Curve fit of relative risk of birth (reported – Romero [2012]¹ vs. estimated)



¹ Romero (2012).

Supplemental Digital Content 3: Outcomes Data

Similar to relative risk data, clinical outcomes data were available only for certain time points in gestation. These data were also curve fitted to generate estimated week-by-week rates in the model population

Figure 3: Curve fit for rate of vision loss²

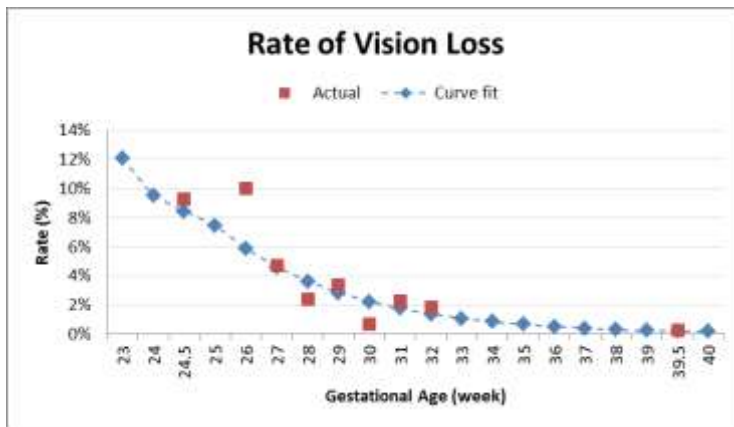
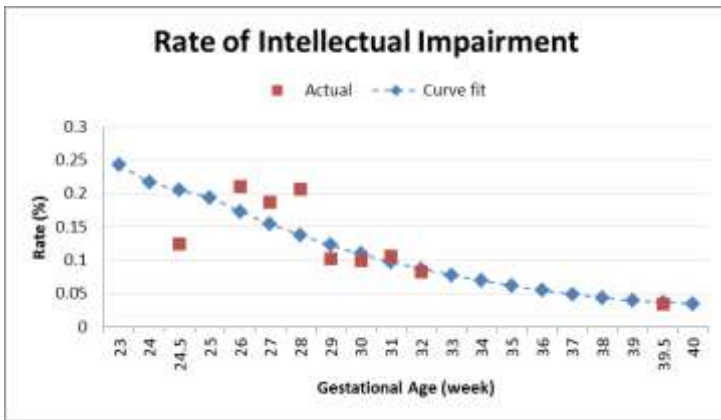
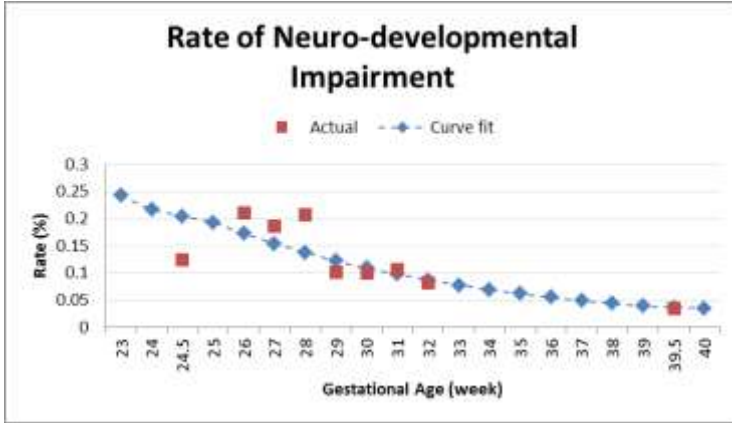


Figure 4: Curve fit for neurodevelopmental impairment^{2,3}

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² Larroque (2008).



Comment [GU1]: Delete – same chart as above

Figure 5: Curve fit for cerebral palsy²²

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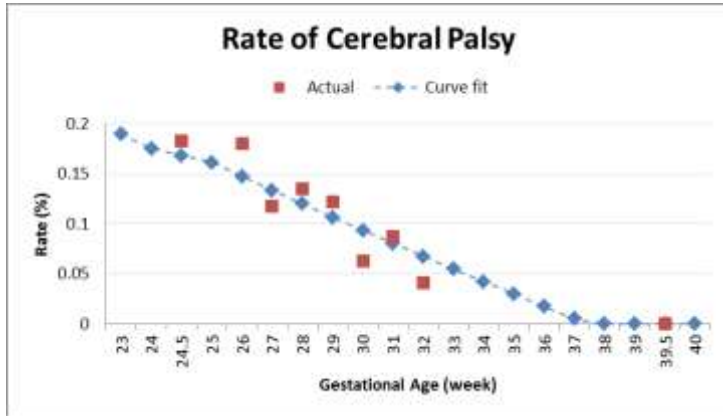
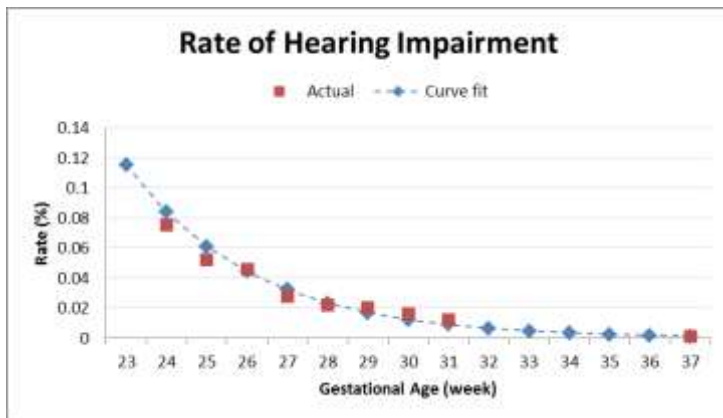


Figure 6: Curve fit for hearing impairment³



³ Van Dommelen (2015).

Figure 7: Curve fit for respiratory distress⁴

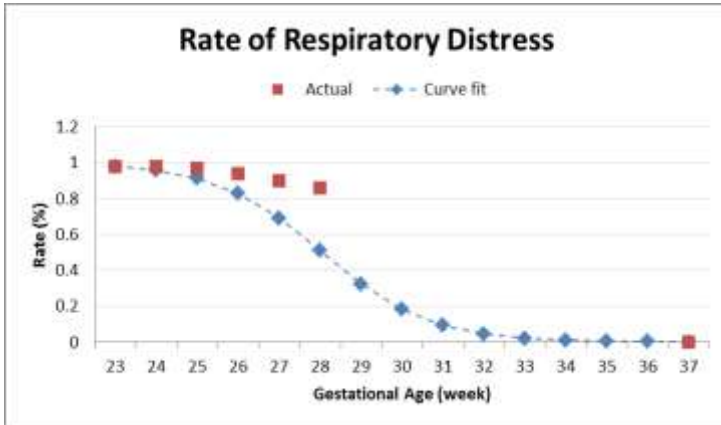
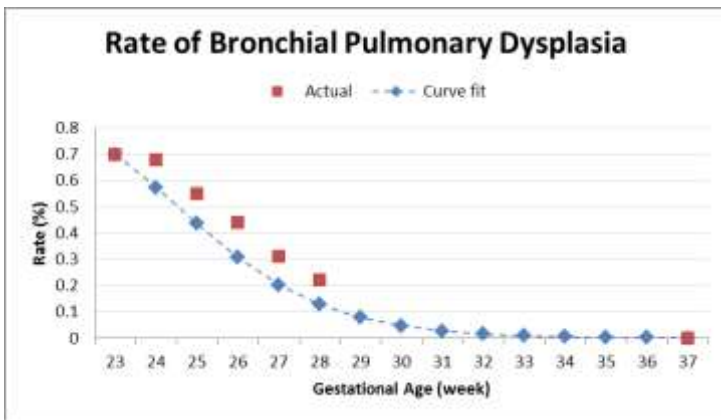


Figure 8: Curve fit for bronchial pulmonary dysplasia⁴⁴



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⁴ Stoll (2010).

Figure 9: Curve fit for intraventricular hemorrhage⁴⁴

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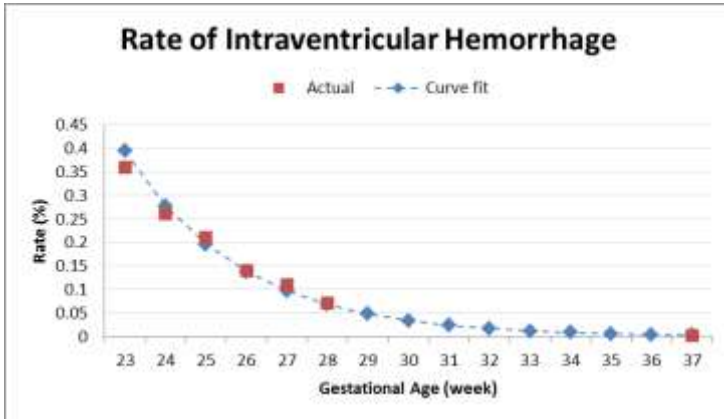
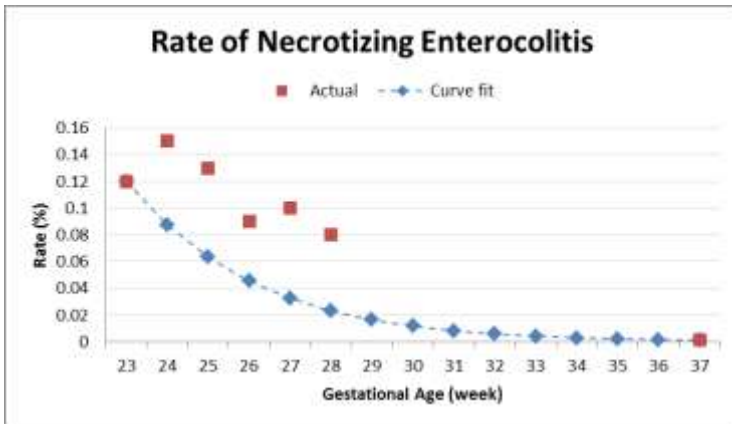


Figure 10: Curve fit for necrotizing enterocolitis⁴⁴

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Supplemental Digital Content 4: Cost data

Acute costs by gestational age were available from Phibbs (2010). These data were inflated to 2015 for the model. Average costs per preterm infant for the following items were also available

- First-year rehospitalization costs⁵
- Indirect medical costs (early intervention, snapshot of 1-year education costs, snapshot of 1-year lost productivity costs)⁶

The assumption was made that all costs in the model would follow the same distribution from the average by gestational age as that reported for acute costs.

⁵ Underwood (2007).

⁶ IOM Report.

Supplemental Digital Content 5: Univariate Sensitivity Analysis

The cost of vaginal progesterone was varied within the range provided in Cahill (2010) with dollar values inflated to 2015 (\$240–\$375, with a base of \$307).

The following inputs were varied $\pm 20\%$ because the data source did not provide confidence intervals for these data points.

- U.S. population⁷
- Incidence of pregnancy per 1,000⁸
- Percent of pregnancies that are singleton^{8a}
- Rate of spontaneous preterm birth^{8b}
- Percent of women with a history of preterm birth⁹
- Test sensitivity¹⁰
- Test specificity^{10a}

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⁷ US Census Bureau.

⁸ CDC (2013).

⁹ Petrini (2005).

¹⁰ Hypothesized performance.

- Cost of diagnostic test.¹¹
- Percentage of women with a response to vaginal progesterone that is analogous to that reported in clinical trials (accounts for additional nonresponders)¹²

Week-by-week inputs listed below were varied $\pm 20\%$ based on the average as described in the example for mortality that follows.

Inputs:

- Mortality
- Mortality by 30 days
- Acute cost
- First year rehospitalization costs
- Early intervention costs
- Snap shot of 1-year education costs
- Snap shot of 1-year lost productivity costs
- Length of stay
- Intellectual impairment
- Vision impairment
- Hearing impairment
- Respiratory distress
- Bronchial pulmonary dysplasia
- Intraventricular hemorrhage
- Necrotizing enterocolitis
- Cerebral palsy
- Readmission rates

Example (mortality)

The average mortality for births between 23 weeks and full term was calculated as 11%.

A distribution factor for each gestational age was calculated as the base mortality rate at that gestational age (e.g., 57% at 23 weeks) divided by the average mortality (11%).

The average was then varied $\pm 20\%$ in the univariate sensitivity analysis and multiplied by the distribution factor to determine the corresponding week-by-week mortality rate as shown in the table below.

This analysis assumes that the varied outcome (e.g., mortality, acute cost, vision impairment, etc., will always follow the same distribution as it does in the base case scenario, but allows the week-by-week inputs to vary by the same amount for each outcome rather than independently.

Table 1: Example of univariate inputs (mortality rate)

Comment [AQ2]: AU: Please check Table 1 for accuracy.

¹¹ Market-based assumption aligned with current costs for non-invasive prenatal tests.

¹² Expert opinion.

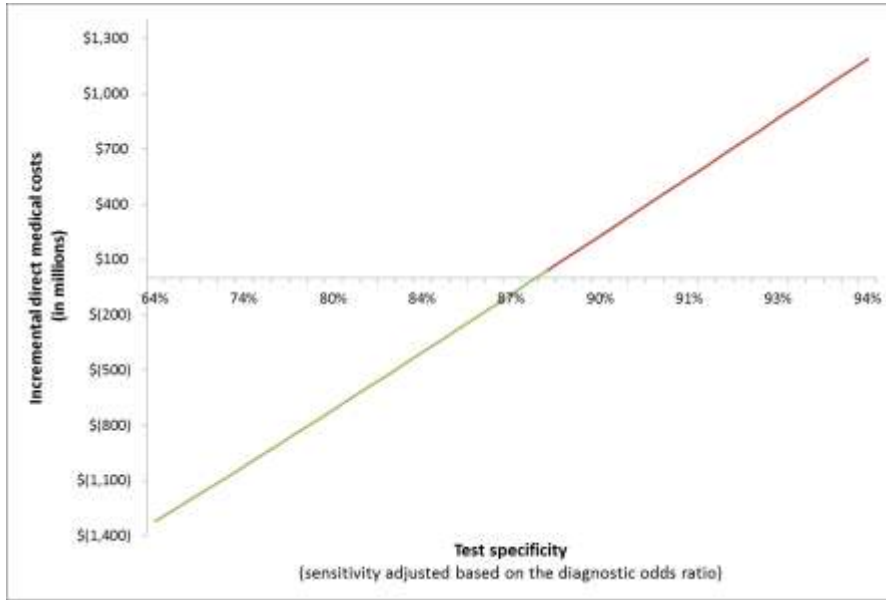
GA (wk)	Base value mortality rate	Distribution factor = (base value at GA/average)	Lowest value for univariate analysis ^a	Highest value for univariate analysis ^a
23	57.0%	5.33 (= 57.0/11%)	45.6% (= 9%, ^b 5.33)	68.4% (= 13%, 5.33)
24	34.1%	3.19	27.3%	41.0%
25	22.8%	2.13	18.2%	27.3%
26	14.6%	1.37	11.7%	17.6%
27	10.4%	0.97	8.3%	12.5%
28	5.5%	0.51	4.4%	6.6%
29	4.2%	0.39	3.4%	5.1%
30	3.2%	0.30	2.6%	3.8%
31	2.6%	0.25	2.1%	3.2%
32	1.8%	0.16	1.4%	2.1%
33	1.5%	0.14	1.2%	1.8%
34	1.1%	0.10	0.9%	1.3%
35	0.8%	0.07	0.6%	0.9%
36	0.6%	0.05	0.4%	0.7%
Full term	0.2%	0.02	0.2%	0.3%
Average	11% ^b		9% (=11%, ^b 0.8)	13% (=11%, ^b 1.2)

Abbreviation: GA, gestational age.

^aValues at each gestational age are therefore varied between the low and high ranges, for example, 45.6 to 68.4% at 23 weeks.

^bBaseline average is varied $\pm 20\%$.

Supplemental Digital Content 6: Threshold analysis for prognostic test specificity



Comment [GU3]: Added chart per reviewer comments