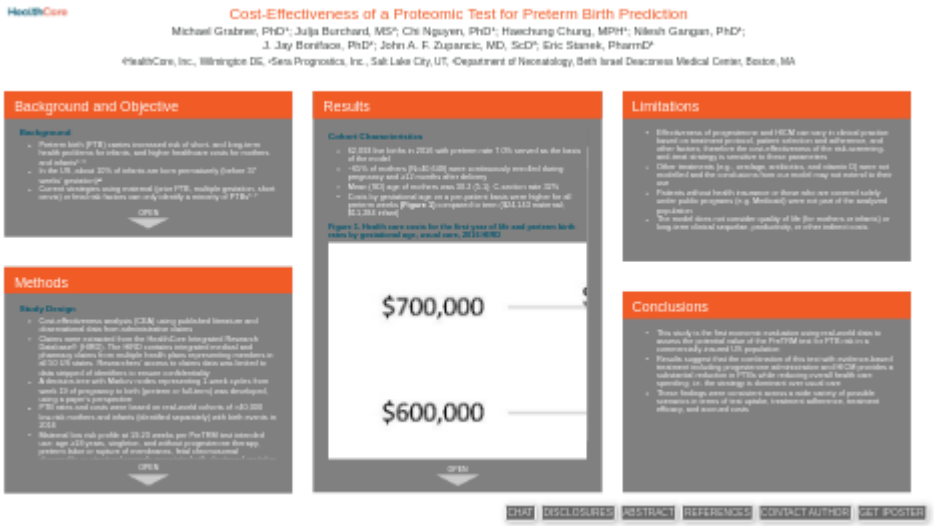
Cost-Effectiveness of a Proteomic Test for Preterm Birth Prediction



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PRESENTED AT:

BACKGROUND AND OBJECTIVE

Background

- Preterm birth (PTB) carries increased risk of short- and long-term health problems for infants, and higher healthcare costs for mothers and infants[1–3]
- In the US, about 10% of infants are born prematurely (before 37 weeks' gestation)[4]
- Current strategies using maternal (prior PTB, multiple gestation, short cervix) or fetal risk factors can only identify a minority of PTBs[5–7]

Objective

- We evaluated the cost-effectiveness of a risk-screening-and-treat strategy, compared to usual care, for a population of commercially-insured pregnant women in the US without known risk factors for PTB
- The strategy included a novel PTB prognostic proteomic blood test (PreTRM®, Sera Prognostics) administered once in the 19th or 20th week of pregnancy[8–9] followed by treatment with a combined regimen of multi-component high-intensity case management (HICM) and vaginal progesterone for the remainder of the pregnancy for women assessed as high-risk

METHODS

Study Design

- Cost-effectiveness analysis (CEA) using published literature and observational data from administrative claims
- Claims were extracted from the HealthCore Integrated Research Database® (HIRD). The HIRD contains integrated medical and pharmacy claims from multiple health plans representing members in all 50 US states. Researchers' access to claims data was limited to data stripped of identifiers to ensure confidentiality
- A decision-tree with Markov nodes representing 1-week cycles from week 19 of pregnancy to birth (preterm or full-term) was developed, using a payer's perspective
- PTB rates and costs were based on real-world cohorts of >40,000 low-risk mothers and infants (identified separately) with birth events in 2016
- Maternal low risk profile at 19-20 weeks per PreTRM test intended use: age ≥18 years, singleton, and without progesterone therapy, preterm labor or rupture of membranes, fetal chromosomal abnormality or structural anomaly associated with shortened gestation
- Inclusion/exclusion criteria were further applied to ensure sufficient medical and pharmacy enrollment coverage

Comparators

- Usual care could include low-frequency use of progesterone or other tests and treatments
- Risk-screening-and-treat assumed vaginal progesterone 200mg/day; low-dose aspirin; and HICM consisting of up to two additional visits to a maternal-fetal-medicine specialist, up to two additional transvaginal ultrasounds, and up to 10 additional nursing calls;[8-10] all from weeks 22 up through a maximum of 36, depending on gestational age at delivery; and only in high-risk women (PreTRM-estimated PTB risk 2x population level)
- We assumed the effect of the treatment began at week 23, to allow a 4-week time lag between the decision to test, test and reporting turnaround time, time to initiation of preventive measures, and their earliest possible impact on PTB risk
- Assumptions on test performance and treatment effectiveness were derived from published literature and expert opinion. Key parameters of the model are described in **Table 1**

Table 1. Key model input

	Base case value	Range (lower-upper)	Source
Number of live births (Jan-Dec 2016)	62,093	NA	HIRD
Number (%) of preterm births under usual care	4,360 (7.0%)	NA	HIRD
Proportion of women opting to be tested	0.85	0.70-1.00	Expert opinion
Characteristics of PreTRM® test			
Sensitivity*	0.75	0.5-0.83	Saade 2016;[12] data on file
Specificity*	0.74	0.49-0.82	Saade 2016;[12] data on file
Cost (one-time)	$745	$395-1,000	Expert opinion
Proportion of women identified as high-risk opting to receive treatment	0.90	0.60-1.00	Expert opinion
Characteristics of treatment for high-risk pregnancies			
Proportion of treated women who adhere to the treatment	0.80	0.60-1.00	Expert opinion
Cost of progesterone (weekly)	$26	$20-50	Average wholesale price for 200mg/day. Lower bound represents generic oral progesterone.** Upper bound based on average of branded oral and vaginal formulations
Cost of high-intensity case management (weekly)	$54.2	$34.2-58.2	CMS physician fee schedule for office visits and transvaginal ultrasounds (2019), plus generic cost of low-dose aspirin
Effectiveness of treatment (risk ratio for preterm birth reduction)	0.13-0.68; depending on gestational week	0.01-0.83, depending on gestational week	Analysis of published literature (references available from presenting author upon request)

CMS = Center for Medicare and Medicaid Services; HIRD = HealthCore Integrated Research Database.

Usual care assumes no testing and minimal progesterone use.

*Sensitivity and specificity are modelled jointly

**Based on expert opinion, we assumed the majority of vaginal progesterone use is via suppository or direct insertion of an oral progesterone formulation.

Study Outcomes and Analyses

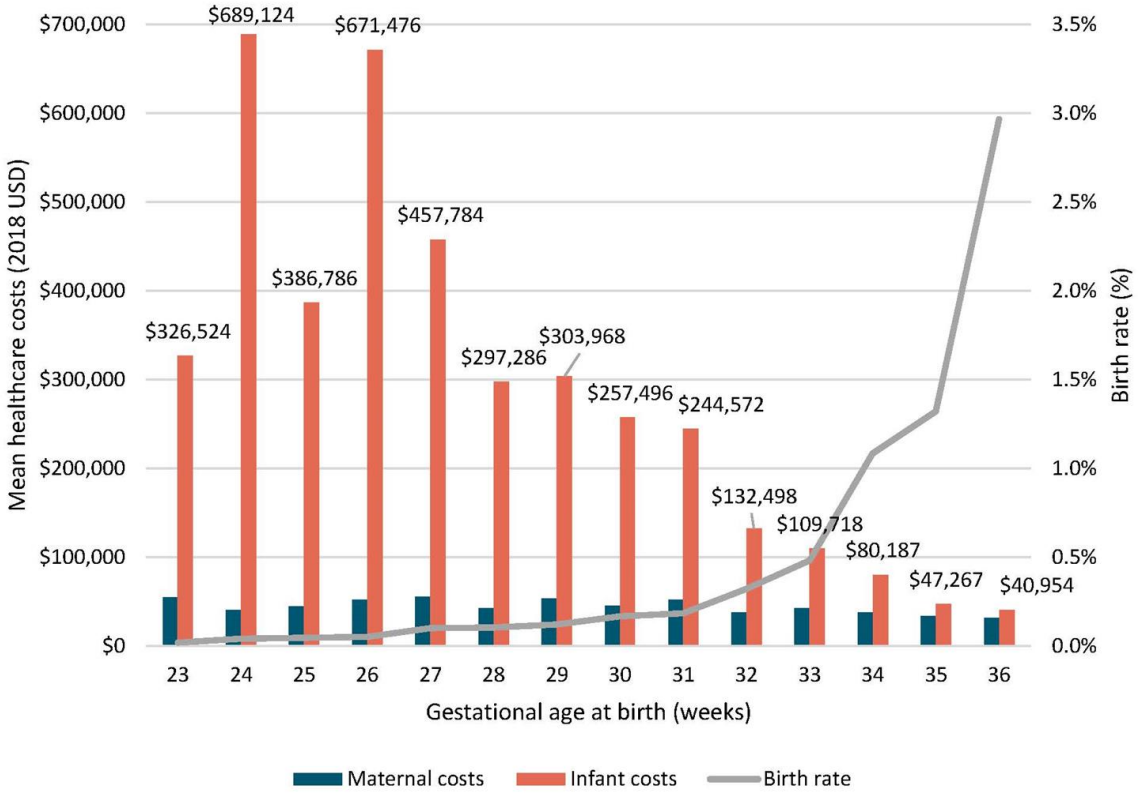
- Direct healthcare costs (medical and pharmacy claims for the payer and patient combined), adjusted to USD 2018
  - Time horizon: from pregnancy start to 12-months post-delivery in mothers and 30-months from birth in infants
  - Mothers: all-cause costs including prenatal, delivery hospitalization, and post-natal
  - Infants: all-cause neonatal, routine well-child and illness medical care
  - Costs for HICM and progesterone were taken from public sources
- The primary effectiveness metric was the number of PTBs (<37 weeks); secondary outcomes included utilization-based metrics such as neonatal-intensive-care-unit (NICU) admissions
- Incremental Cost-Effectiveness Ratio (ICER) = costs of adopting the risk-screening-and-test strategy minus costs for usual care, divided by the difference in total PTBs
- Health outcomes and costs were not discounted given the short time horizon
- Uncertainty was explored via scenario, one-way, and probabilistic sensitivity analysis (PSA)

RESULTS

Cohort Characteristics

- 62,093 live births in 2016 with preterm rate 7.0% served as the basis of the model
- ~65% of mothers (N=40,649) were continuously enrolled during pregnancy and ≥12 months after delivery
- Mean (SD) age of mothers was 30.2 (5.1); C-section rate 32%
- Costs by gestational age on a per-patient basis were higher for all preterm weeks **(Figure 1)** compared to term ($24,143 maternal; $11,284 infant)

Figure 1. Health care costs for the first year of life and preterm birth rates by gestational age, usual care, 2016 HIRD



Cost-effectiveness

- In the base-case analysis, the risk-screening-and-treat strategy dominated usual care with 870 fewer PTBs (20% reduction) and $54 million less in total cost ($61,581 net savings per prevented PTB; $863 net savings per pregnant woman)
  - Risk-screening-and-treat is therefore a dominant strategy (improved outcomes at lower cost vs. usual care)
- Reductions were also seen for neonatal-intensive-care-unit admissions (10%), overall length-of-stay (7%), and births <32 weeks gestation (33%)
- Risk-screening-and-treat remained dominant in scenario analyses **(Table 2)** and one-way sensitivity analysis **(Figure 2)**, except when lower treatment effectiveness was assumed. Nevertheless, cost per PTB prevented in this case ($3,989) remains favorable for decision-makers with a willingness-to-pay threshold of ≥$4,000 per prevented PTB. Cost per pregnant woman is $0.06 in this scenario.

- The strategy was cost-saving in all PSA simulations **(Figure 3)**.
  - As the PSA did not include treatment effectiveness as a parameter, a separate PSA was conducted in a low-effectiveness scenario. Under this assumption, the risk-screening-and-treat strategy remained dominant in 32% of the 10,000 simulations, and was >80% likely to be cost-effective with a willingness to pay of $30,000 per prevented PTB

Table 2. Model results for base case and scenario analyses

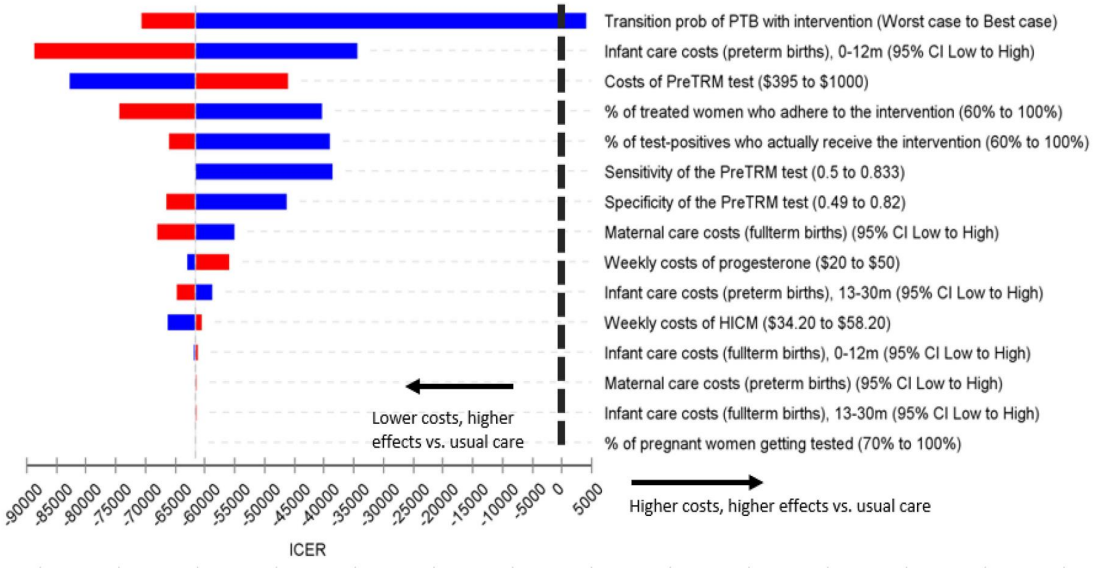
	Usual care	Risk-screening-and-treat strategy	Incremental difference	Savings per prevented PTB*	Savings per pregnant woman
Base case					
Cost (USD)	$2,611m	$2,558m	-$53.6m	$61,581	$863
Number of preterm births	4,360	3,490	-870		
Scenario 1: Lower treatment effectiveness					
Cost (USD)	$2,611m	$2,613m	$1.7m	$3,989 (ICER)	-$0.06 (cost/ pregnant woman)
Number of preterm births	4,360	3,924	-436		
Scenario 2: Higher treatment effectiveness					
Cost (USD)	$2,611m	$2,518m	-$93.6m	$70,722	$1,508
Number of preterm births	4,360	3,036	-1,324		

*Equal to the absolute value of the ICER. In Scenario 1, where incremental costs are positive, there are no savings and the number presented equals the actual ICER. Costs presented in 2018 USD. Incremental costs = risk-screening-and-treat strategy costs minus usual care costs. Risk-screening-and-treat is dominant (cost-saving and at least 1 preterm birth prevented) in the base case and all scenarios except Scenario 1.

PTB = preterm birth; m = million

Additional scenarios, not reported in this table, examined an alternate infant cost definition where only costs from infants who were fully enrolled in their health plan over the 30-month follow-up time period were utilized, and the effects of truncating the modelling timeframe to the first 12 months after birth to observe a shorter-term impact. In all these scenarios the risk-screening-and-treat strategy remained dominant

Figure 2. Univariate sensitivity analysis, base case

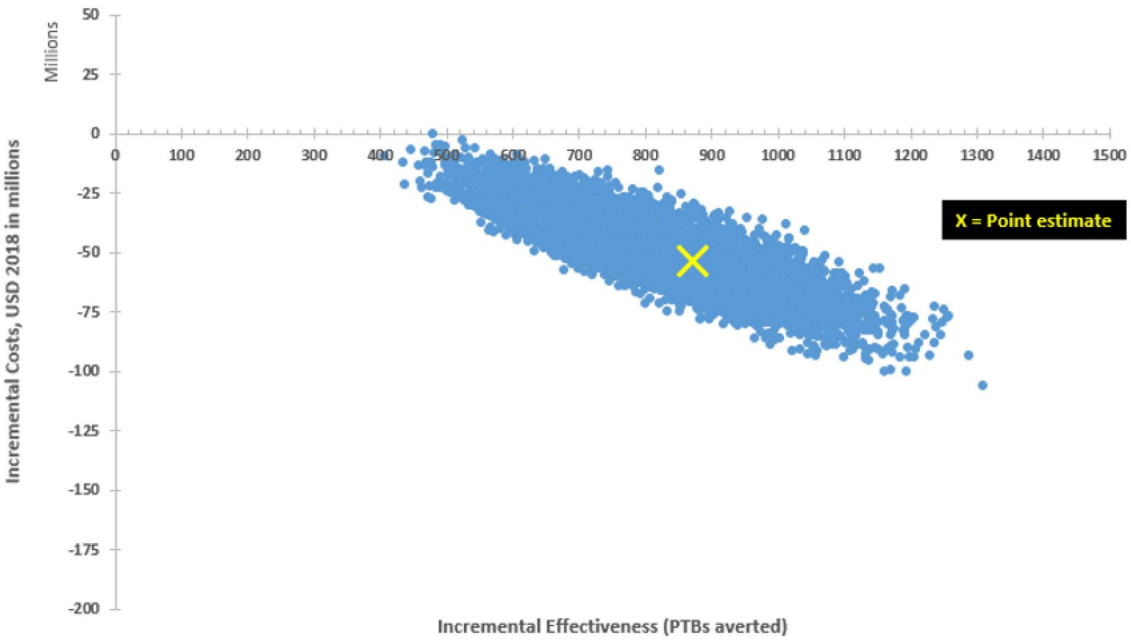


The tornado diagram ranks input parameters by their influence on the incremental cost-effectiveness ratio (ICER), from highest to lowest

HICM = high-intensity case management

PTB = preterm birth; CI = confidence interval (95%)

Figure 3. Probabilistic sensitivity analysis, base case



Each blue dot in the ICER scatter plot (lower panel) represents one of the 10,000 PSA simulation outcomes. The scatter plot is wedge-shaped with all mass in the second quadrant. All dots below the x-axis represent cost savings. In the base case, all simulations are associated with cost savings and PTB reductions.

PTB = preterm birth; PSA = probabilistic sensitivity analysis

LIMITATIONS

- Effectiveness of progesterone and HICM can vary in clinical practice based on treatment protocol, patient selection and adherence, and other factors; therefore the cost-effectiveness of the risk-screening-and-treat strategy is sensitive to these parameters
- Other treatments (e.g., cerclage, antibiotics, and vitamin D) were not modelled and the conclusions from our model may not extend to their use
- Patients without health insurance or those who are covered solely under public programs (e.g. Medicaid) were not part of the analyzed population
- The model does not consider quality of life (for mothers or infants) or long-term clinical sequelae, productivity, or other indirect costs

CONCLUSIONS

- This study is the first economic evaluation using real-world data to assess the potential value of the PreTRM test for PTB risk in a commercially-insured US population
- Results suggest that the combination of this test with evidence-based treatment including progesterone administration and HICM provides a substantial reduction in PTBs while reducing overall health care spending; i.e. the strategy is dominant over usual care
- These findings were consistent across a wide variety of possible scenarios in terms of test uptake, treatment adherence, treatment efficacy, and accrued costs

DISCLOSURES

•Study funding was provided by Sera Prognostics Inc., the maker of the PreTRM® test, to HealthCore Inc.

•Michael Grabner, Chi Nguyen, Haechung Chung, Nilesh Gangan, and Eric Stanek are employees of HealthCore, Inc., an independent research organization that received funding from Sera Prognostics Inc. for the conduct of the study

•Julja Burchard and Jay Boniface are employees and stockholders of Sera Prognostics Inc.

•John Zupancic is a consultant to Sera Prognostics Inc.

ABSTRACT

OBJECTIVES: Preterm birth (PTB) carries increased risk of health problems for infants as well as higher healthcare costs for both infants and mothers. We evaluated the cost-effectiveness of a risk-screening-and-treat strategy, compared to usual care, for a population of commercially-insured pregnant US women without known risk factors for PTB. The strategy included a novel PTB prognostic test (PreTRM®) in the 19th-20th week of pregnancy and treatment with vaginal progesterone and high-intensity case management for the remainder of the pregnancy for women assessed as high-risk.

METHODS: A decision-tree with Markov nodes representing 1-week cycles from week 19 of pregnancy to birth (preterm or full-term) was developed, using a payer's perspective and time horizon from pregnancy start to 12-months post-delivery in mothers and 30-months from birth in infants. PTB rates and costs were based on real-world cohorts of >40,000 mothers and infants with birth events in 2016, as identified in administrative claims from the HealthCore Integrated Research Database®. Estimates of test performance and treatment effectiveness were derived from published literature. Uncertainty was explored via scenario, one-way, and probabilistic sensitivity analysis (PSA).

RESULTS: In the base-case analysis, the risk-screening-and-treat strategy dominated usual care with 870 fewer PTBs (20% reduction) and $54 million less in total cost ($863 net savings per pregnant woman). Reductions were also seen for neonatal-intensive-care-unit admissions (10%), overall length-of-stay (7%), and births <32 weeks gestation (33%). Treatment effectiveness had the most influence on cost-effectiveness estimates per one-way sensitivity analysis, followed by infant care costs and test costs. The risk-screening-and-treat strategy was dominant in the majority of PSA simulations and model scenarios.

CONCLUSIONS: Use of a novel prognostic test during pregnancy to identify women at risk of PTB combined with evidence-based treatment can reduce total costs and prevent preterm deliveries and their consequences in a representative population of commercially-insured US women.

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