ValidationInstitute

2022 Validation Report

Review for: Sera Prognostics

Validation Achieved: Savings

Valid through: March 2023

Company Profile

Category:	**Obstetrics**
Website:	www.seraprognostics.com www.pretrm.com
Public or Private:	Public
Year Established:	2011
CEO:	Gregory Critchfield MD, MS
Company contact:	Shawn McGinnis, mcginnis@seraprognostics.com

Description:

Sera Prognostics is a leading health diagnostics company dedicated to improving the lives of women and babies through precision pregnancy care. Sera's mission is to deliver early, pivotal information in pregnancy to physicians, enabling them to improve the health of their patients, resulting in reductions in the costs of healthcare delivery. Sera has a robust pipeline of innovative diagnostic tests focused on the early prediction of preterm birth risk and other complications of pregnancy. Sera's precision medicine PreTRM® Test reports to a physician the individualized risk of spontaneous premature delivery in a pregnancy, enabling earlier proactive interventions in women with higher risk. Sera Prognostics is located in Salt Lake City, Utah.

Company Profile

Preterm birth is defined as any birth before 37 weeks' gestation and is the leading cause of illness and death in newborns. The 2021 March of Dimes Report Card shows that more than one in ten infants is born prematurely. Prematurity is associated with a significantly increased risk of major long-term medical complications, including learning disabilities, cerebral palsy, chronic respiratory illness, intellectual disability, seizures, and vision and hearing loss, and can generate significant costs throughout the lives of affected children. The annual health care costs to manage short- and long-term complications of prematurity in the United States were estimated to be approximately $25 billion for 2016.

The PreTRM® test is the only broadly validated, commercially available blood-based biomarker test that provides an early, accurate and individualized risk prediction for spontaneous preterm birth in asymptomatic singleton pregnancies. The PreTRM® test measures and analyzes proteins in the blood that are highly predictive of preterm birth. The PreTRM® test enabling physicians to identify, during the 18th or 20th week of pregnancy, which women are at increased risk for preterm birth, enabling more informed, personalized clinical decisions based on each woman's individual risk. The PreTRM® test is ordered by a medical professional.

Claim Assertion for Validation

Despite an unexpectedly low rate of spontaneous preterm birth of 3.5% in the control group in the study, the following differences were seen between the PreTRM-screened arm and the control (unscreened) arm in the study:

- The authors reported 23-80% reductions in preterm delivery rates occurring before 37, 35 and 32 weeks of pregnancy. These reductions were seen in either spontaneous deliveries alone or in any preterm deliveries, which also includes medically indicated preterm deliveries. While the company believes that these reductions across different levels of prematurity are encouraging, the study was not adequately powered to evaluate whether these rate reductions were statistically significant.
- A statistically significant reduction in median NICU (newborn intensive care unit) length-of-stay for spontaneous preterm deliveries admitted to the NICU from 45.5 to 6.8 days (an 85% reduction)
- A statistically significant reduction in median NICU length-of-stay for any preterm delivery admitted to the NICU (includes spontaneous preterm delivery and medically-indicated preterm delivery) from 36.7 to 7.6 days (a 79% reduction)
- Statistically significant faster rate of discharge from the NICU for spontaneous preterm deliveries, any preterm deliveries, and all deliveries, respectively
- A reduction in total NICU number of days incurred in preterm infants admitted to the NICU from 619 to 172 (a 72% reduction)

Claim Assertion for Validation

- A reduction in total neonatal hospital number of days incurred in preterm infants from 700 to 204 (a 71% reduction)
- In infants affected by any degree of impairment associated with prematurity (mild, moderate, severe or neonatal death), severe morbidity/mortality was reduced from 14/70 (20.0%) in the control arm to 5/73 (6.8%) in the screened arm (a relative reduction of 66%).
- Screening 1000 women would cost roughly $900,000. The typical commercial payer pays $4000/day for the NICU. A reduction of almost 500 NICU days/1000 yields a savings approaching $2,000,000.
- On the cost side, that savings does not include the costs of an intensive prenatal care program or the possibility of perinatal admissions. The savings side does not include avoided costs in the first year(s) of life following discharge from the NICU, or lost work time or stress-related spending for parents whose child is in the NICU.

Method / Calculation / Examples

The below is reprinted in full from Sera Prognostics. We have reviewed both the original study and the write-up below. The study design is as close to an RCT Gold Standard as can be found in population health services. The Validation Institute stands behind this design and directional outcome with its Credibility Guarantee.

The PREVENT-PTB study, conducted at Intermountain Healthcare, in Salt Lake City, Utah, enrolled 1,208 pregnant patients from May 2018 through February 2019, who were 18 years or older, with a singleton pregnancy in the 19th or 20th week of gestation, and with no history of prior preterm birth and normal cervical length at or before the time of enrollment. Of the 1,181 women ultimately randomized and for whom outcome data were available, 589 pregnancies were in the PreTRM test-screened arm, and 592 served as controls not having access to the test. Patients whose PreTRM test result risk met or exceeded twice the population risk were deemed “higher risk,” and were offered a group of proactive interventions. These included weekly contact with a care management nurse, two preterm prevention clinic visits, cervical length monitoring, weekly injection of 17-alpha-hydroxyprogesterone caproate, daily administration of low-dose aspirin, and the administration of corticosteroid treatment if patients indicated clinical signs or symptoms of imminent delivery. Patients in the screened group found not to be at higher risk by the PreTRM® test received standard obstetrical care. The control group did not receive the PreTRM® test and received standard obstetrical care only. Due solely to limited financial

Method / Calculation / Examples

resources at the time, the trial was stopped early, prior to data unblinding. As a result of early termination, the trial enrolled 1,208 patients, short of the originally projected enrollment between 3,000 – 10,000 patients required in order to provide sufficient statistical power to evaluate the study's originally conceived primary outcome of spontaneous preterm delivery before 37 weeks. However, a number of pre-defined non-primary outcomes of major neonatal clinical importance were sufficiently powered to demonstrate the positive impact of the test and treat strategy, and revealed consistent benefit across different neonatal outcomes (without correction for multiple testing, as pre-specified). These outcomes included measures of length of stay in neonatal intensive care unit (NICU) and overall hospital length of stay, among others.

Findings & Validation

As noted above, despite an unexpectedly low rate of spontaneous preterm birth of 3.5% in the control group in the study, the following differences were seen between the PreTRM-screened arm and the control (unscreened) arm in the study:

- The authors reported 23-80% reductions in preterm delivery rates occurring before 37, 35 and 32 weeks of pregnancy. These reductions were seen in either spontaneous deliveries alone or in any preterm deliveries, which also includes medically indicated preterm deliveries. While the company believes that these reductions across different levels of prematurity are encouraging, the study was not adequately powered to evaluate whether these rate reductions were statistically significant.
- A statistically significant reduction in median NICU (newborn intensive care unit) length-of-stay for spontaneous preterm deliveries admitted to the NICU from 45.5 to 6.8 days (an 85% reduction)
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Findings & Validation

- A reduction in total NICU number of days incurred in preterm infants admitted to the NICU from 619 to 172 (a 72% reduction)
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A rigorous clinical and economic analysis using actual claims data from a broad population of Anthem affiliated health plans to assess the potential value of the PreTRM® test-and-treat strategy.

The study conservatively modeled the PreTRM® strategy, consisting of testing and proactive evidence-based interventions, within Anthem claims data from individual and employer-sponsored plans, and showed both improved neonatal outcomes and reduced immediate and long-term treatment costs associated with premature birth, when compared to routine care. These results were published in the peer-reviewed journal ClinicoEconomics and Outcomes Research in an article entitled “Cost-Effectiveness of a Proteomic Test for Preterm Birth Prediction.”

The study analysis was conducted by Sera in partnership with HealthCore, using claims data of more than 40,000 pregnant women and infants who were members of individual and employer-sponsored Anthem health plans.

Findings & Validation

The analysis evaluated the PreTRM® test-and-treat strategy by modeling the application of the PreTRM® test during weeks 19 or 20 of pregnancy, and assessed the benefit of proactive interventions consisting of more intensive case-management and monitoring, as well as pharmacologic interventions for women identified as higher-risk by the test, whereas usual care was assumed for any women without higher PreTRM® risk.

Key findings of the analysis include:

- 20% reduction in preterm birth <37 weeks' gestation
- 33% reduction in births <32 weeks' gestation
- 10% reduction in neonatal intensive care admissions
- 7% reduction in overall hospital length-of-stay
- $863 net savings ($1,608 gross savings) per pregnant woman, a $54 million reduction in total costs over the study population

Proposition:

- Screening 1000 women would cost roughly $900,000. The typical commercial payer pays $4000/day for the NICU. A reduction of almost 500 NICU days/1000 yields a savings approaching $2,000,000.
- On the cost side, that savings does not include the costs of an intensive prenatal care program or the possibility of perinatal admissions. The savings side does not include avoided costs in the first year(s) of life following discharge from the NICU, or lost work time or stress-related spending for parents whose child is in the NICU.

Limitations

The word “directional’ was chosen for the “Findings” because no matter how rigorous the study design, real-world messiness often results in outcomes that don’t measure up to what is found in the studies.

For instance, the fact that women volunteered to enroll before being assigned implies that those who test positive would almost certainly be compliant, and a robust prenatal program would be offered to them.

And the physicians in both arms were aware of PreTRM.

The other limitation, as noted in the publication itself, was that the study was terminated early due to financial constraints. It is very possible that had the study size been larger, the differential NICU days of care would have been smaller.

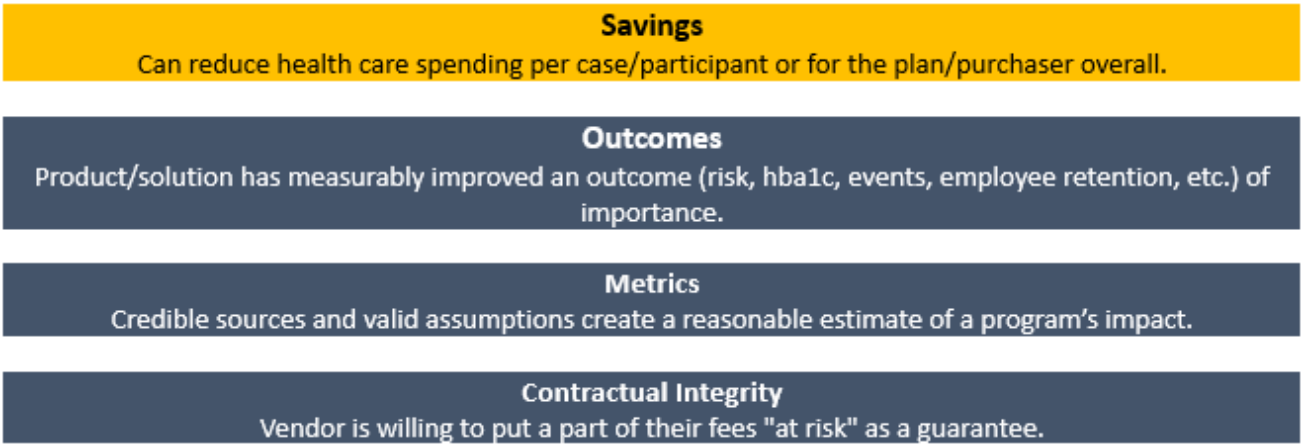
Works Cited

This study was published in the American Journal of Perinatology (AJP), https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0041-1732339
The citation is CC BY-NC-ND 4.0 · Am J Perinatol
DOI: 10.1055/s-0041-1732339

ClinicoEconomics and Outcomes Research- Cost-Effectiveness of a Proteomic Test for Preterm Birth Prediction

Validation and Credibility Guarantee

Sera Prognostics' PreTRM® achieved validation for Savings. Validation Institute is willing to provide up to a $25,000 guarantee as part of their Credibility Guarantee Program. To learn more, visit https://validationinstitute.com/credibility-guarantee/.

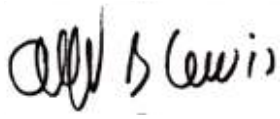


VALIDATION INSTITUTE
500 West Cummings Park
Woburn, MA 01801

Validation Expiration: March2023

CERTIFICATE OF VALIDATION

Applicant:	**Sera Prognostics** 2749 East Parleys Way, Suite 200, Salt Lake City, UT 84109
Product:	PreTRM®
Claim:	On the cost side, that savings does not include the costs of an intensive prenatal care program or the possibility of perinatal admissions. The savings side does not include avoided costs in the first year(s) of life following discharge from the NICU, or lost work time or stress-related spending for parents whose child is in the NICU.
Validation Achieved:	**Validated for Savings**
Validation Award Date:	September 2022



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About Validation Institute

Validation Institute is a professional community that advocates for organizations and approaches that deliver better health value - stronger health outcomes at lower cost. We connect, train, and certify health care purchasers, and we validate and connect providers delivering superior results. Founded in 2014, the mission of the organization has consistently been to help provide transparency to buyers of health care.

Validation Review Process

Validation Institute has a team of epidemiologists and statisticians who review each program. The team focuses on three components:

- Evidence from published literature that a similar intervention had similar results.
- The reliability and credibility of the data sources.
- The rigor of the approach to calculating results.

To achieve validation, the program has to satisfy each of these components. VI's team then summarizes the review into a report which is publicly available. Details of VI's review are available with the program's permission.