Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Methods

Details of Certification Procedures

Care providers and research personnel were trained and certified in the correct use of the STAN S31 and adherence to the STAN guidelines for intervention during a pilot study that preceded the randomized trial. Neoventa provided initial on-line training and certification (per FDA requirements). Two levels of certification are required by Neoventa and the FDA prior to any provider being able to manage patients with the STAN system. For the purposes of this study, two additional, more stringent levels of oversight were used in this trial. The four levels are:

- Certified Provider: completed an on-line training course and passed an on-line test on the background physiology, technical aspects and safety, and examples of use of the system. This level is the minimum required by the FDA for anyone responsible for patient care.
- Credentialed Provider: must have been previously certified and then have completed an on-line clinical case study test comprised of 5 clinical cases set by Neoventa. This level was required by the FDA for any care provider involved in making management decisions around whether to continue observation or to initiate some intervention.
- Authorized Provider: This third level of certification was designed specifically for this study and was applied to the care provider who was the final decision maker in the care of a patient on the STAN trial. To obtain this certification, providers had to be "credentialed" and then appropriately manage 2 patients on an open STAN system using STAN guidelines under proctor supervision (see below). Only a proctor could "authorize" a provider. "Authorization" status required annual renewal.
- Proctor: At each delivery hospital site there was at least one (and up to four) proctor(s). Proctors completed certification and credentialing as above, and then used the STAN monitor in 5 patients' labors. A STAN expert (provided by Neoventa) reviewed the 5 cases and determined if proper procedures were followed. The results were forwarded to the protocol subcommittee who conferred proctor status and monitored the annual renewal of that status. Proctors were required to ensure that an authorized provider was always available to manage a STAN trial patient and to substitute if an authorized provider became unavailable.

Each delivery hospital participated in the pilot phase consisting of enrollment and management of at least 50 patients with STAN. Three members of the protocol subcommittee reviewed all STAN tracings and determined whether management was consistent with STAN guidelines and the study protocol. If so, the hospital was permitted to start the randomized trial. If guidelines were not followed adequately, providers received remedial training and under supervision, enrolled additional patients until satisfactory management was demonstrated.

All research study staff responsible for reviewing the study eligibility criteria and randomization completed a training course on the interpretation of fetal heart rate monitoring prior to the start of the trial. Specific attention was directed to the latest NICHD classification.

Two centralized practical training sessions were conducted, which included didactic instruction as well as hands-on training with the study equipment. Additional training was performed at each site by educators from Neoventa.

The data coordinating center presented regular reports to the protocol subcommittee, the study investigators, and the Data and Safety Monitoring Committee. These included:

- Quarterly Reports – Reports detailing recruitment, data quality, incidence of missing data and adherence to study protocol by clinical center, were provided quarterly to the protocol subcommittee and all other members of the steering committee.
- Data and Safety Monitoring Committee Reports – For every meeting of the DSMC, a report was prepared which included patient recruitment, baseline patient characteristics, center performance information with respect to data quality, timeliness of data submission and protocol adherence, in addition to safety and efficacy data. The reports also included adverse events, loss to follow-up and outcome variables as described in the study protocol.
- Ad hoc reports – Whenever protocol adherence or performance concerns were identified by the protocol subcommittee or data coordinating center concerning a specific clinical center, specific reports were produced, and a process for resolving or improving the specific concerns was agreed upon following discussions with the specific center.
- Review for appropriate labor management – While recruitment was on-going, the protocol subcommittee reviewed management of labors in the open arm, to assess whether the providers acted in response to the fetal ECG ST information (or lack thereof) in accordance with the labor management guidelines. Each labor was reviewed independently by two subcommittee members, who were provided with the fetal heart rate tracing and the type and timing of all labor interventions. They were masked to neonatal outcome. Whenever the two members disagreed, the case was reviewed by the entire subcommittee and a consensus decision was reached. A list of cases that were not in accordance with the labor management guidelines were provided to the staff at the clinical center, and additional training was conducted.

Eligibility

Inclusion Criteria

A woman must meet all of the following criteria to be considered for enrollment in the trial.

1. Singleton, cephalic pregnancy with the intention of a vaginal delivery. A twin pregnancy reduced to singleton (either spontaneously or therapeutically) before 20^0 weeks gestational age is acceptable.
2. Gestational age at randomization at least 36 weeks, 1 day. No upper limit is specified.
3. Cervical dilation of at least 2 cm and no more than 7 cm. A patient with cervical dilation less than 2 cm may be screened but the patient must have documented cervical dilation of at least 2 cm before randomization. The 7 cm upper limit will ensure an adequate amount of time for monitoring and will allow inclusion of patients in the active phase of labor.
4. Ruptured membranes. A patient with intact membranes may be screened and consent may be requested, but membranes must be ruptured and the Goldtrace fetal ECG electrode must be in place before randomization.

Exclusion Criteria

If a woman meets any of one of the following criteria, then she is ineligible for enrollment in the trial.

1. Planned cesarean delivery
2. Need for immediate delivery
3. Absent variability or sinusoidal pattern at any time, or a Category II fetal heart rate pattern with absent or minimal variability in the last 20 minutes before randomization. The categories are specified in the 2008 NICHD guidelines on electronic fetal heart rate monitoring.
4. Inability to obtain or maintain an adequate signal within 3 trials of fetal ECG electrode placements
5. Occurrence of any ST event during attempt to obtain adequate signal
6. Patient pushing in the first stage of labor
7. Known major fetal anomaly or fetal demise
8. Previous uterine surgery (except dilation and curettage). This includes previous cesarean delivery.
9. Placenta previa on admission (any degree) because of the likelihood of cesarean delivery. This does not include low-lying placenta.
10. Maternal fever ≥ 38°C or suspected chorioamnionitis at any time since admission to Labor and Delivery
11. Active HSV infection, because of the likelihood of cesarean delivery and fetal infection with fetal ECG electrodes
12. Known HIV or hepatitis infection
13. Other maternal or fetal contraindication for using the STAN monitor, such as fetal arrhythmia, fetal coagulation disorder, or use of transcutaneous electrical nerve stimulation analgesia, or for using a fetal ECG electrode
14. Enrollment in another labor study which may affect the interpretation of the fetal heart rate or affect the decision on how or when to deliver
15. Participation in this trial in a previous pregnancy
16. No certified or authorized provider available

Figure S1. STAN™ Clinical Guidelines Checklist Showing Definitions and Management Suggestions

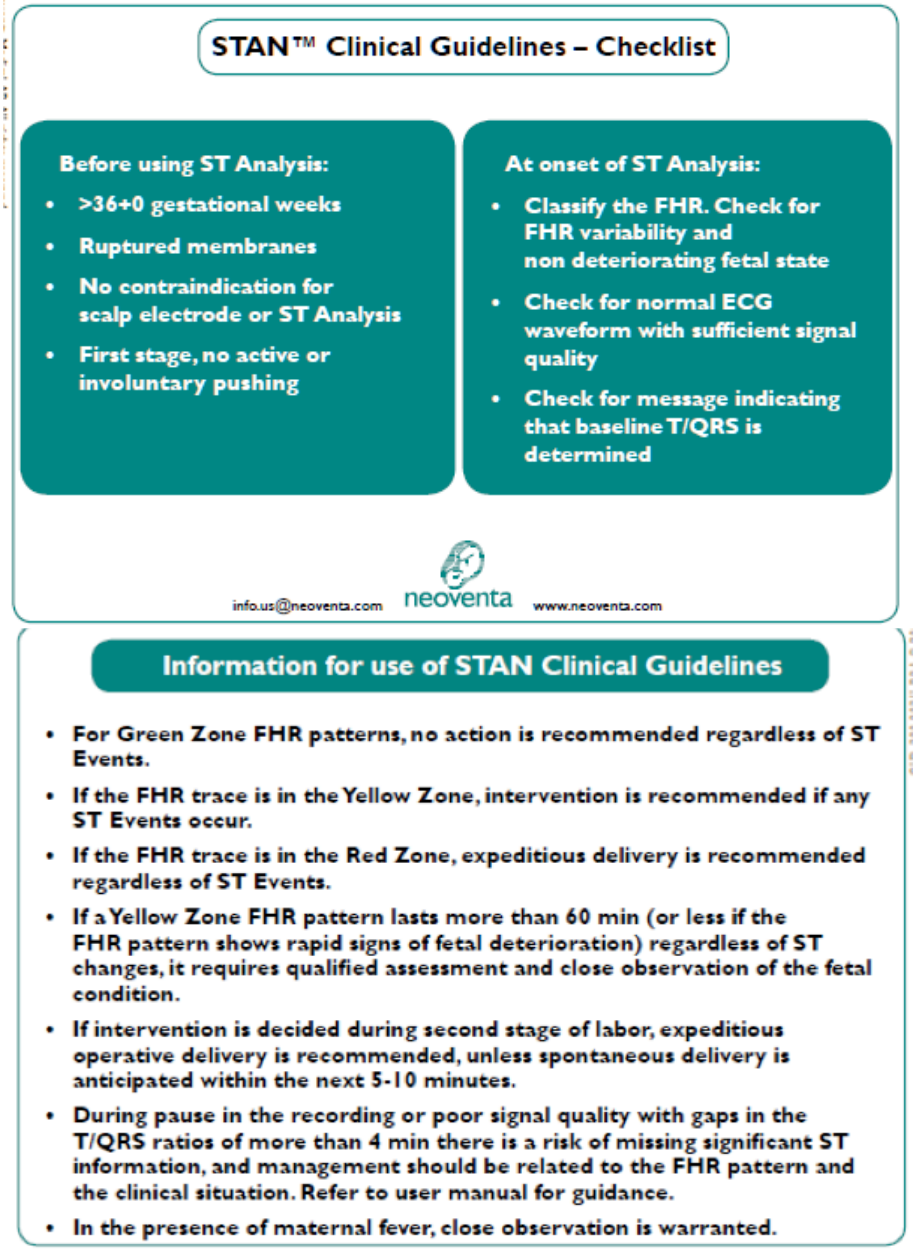
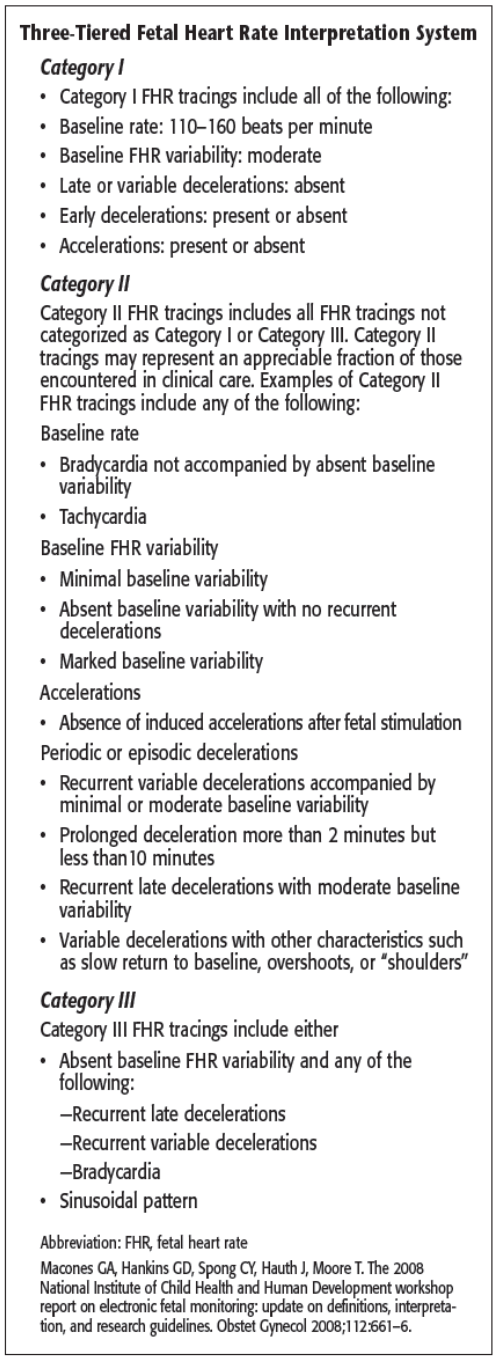


Figure S2. NICHD Three-Tiered Fetal Heart Rate Classification System



Three-Tiered Fetal Heart Rate Interpretation System

Category I

- Category I FHR tracings include all of the following:
- Baseline rate: 110–160 beats per minute
- Baseline FHR variability: moderate
- Late or variable decelerations: absent
- Early decelerations: present or absent
- Accelerations: present or absent

Category II

Category II FHR tracings includes all FHR tracings not categorized as Category I or Category III. Category II tracings may represent an appreciable fraction of those encountered in clinical care. Examples of Category II FHR tracings include any of the following:

Baseline rate

- Bradycardia not accompanied by absent baseline variability
- Tachycardia

Baseline FHR variability

- Minimal baseline variability
- Absent baseline variability with no recurrent decelerations
- Marked baseline variability

Accelerations

- Absence of induced accelerations after fetal stimulation

Periodic or episodic decelerations

- Recurrent variable decelerations accompanied by minimal or moderate baseline variability
- Prolonged deceleration more than 2 minutes but less than10 minutes
- Recurrent late decelerations with moderate baseline variability
- Variable decelerations with other characteristics such as slow return to baseline, overshoots, or "shoulders"

Category III

Category III FHR tracings include either

- Absent baseline FHR variability and any of the following:
  - –Recurrent late decelerations
  - –Recurrent variable decelerations
  - –Bradycardia
- Sinusoidal pattern

Abbreviation: FHR, fetal heart rate

Macones GA, Hankins GD, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretation, and research guidelines. Obstet Gynecol 2008;112:661–6.

Figure S3. Subgroup Analyses for Effect of Study Intervention on Primary Outcome

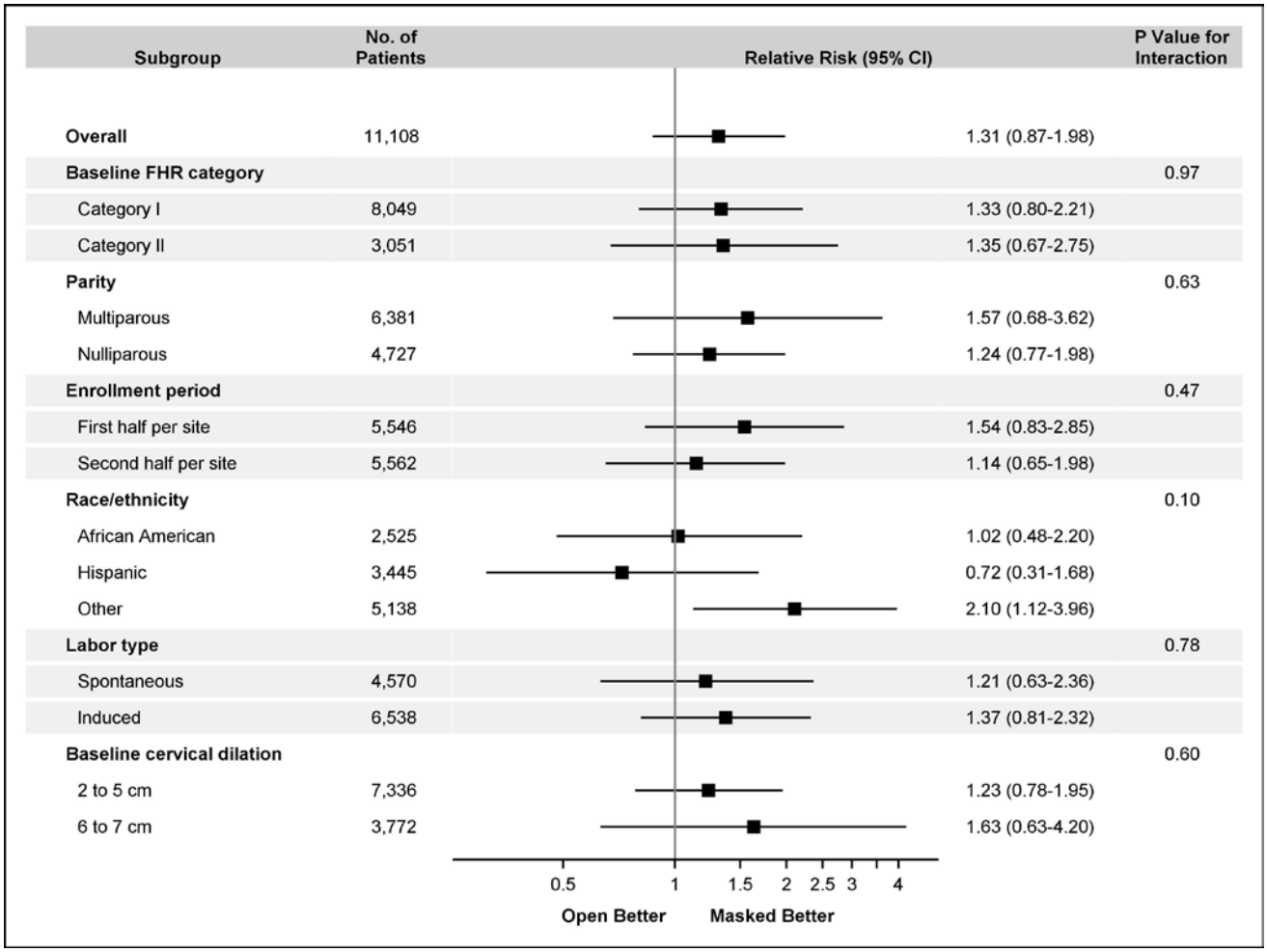


Figure S4. Subgroup Analyses for Effect of Study Intervention on Cesarean Delivery

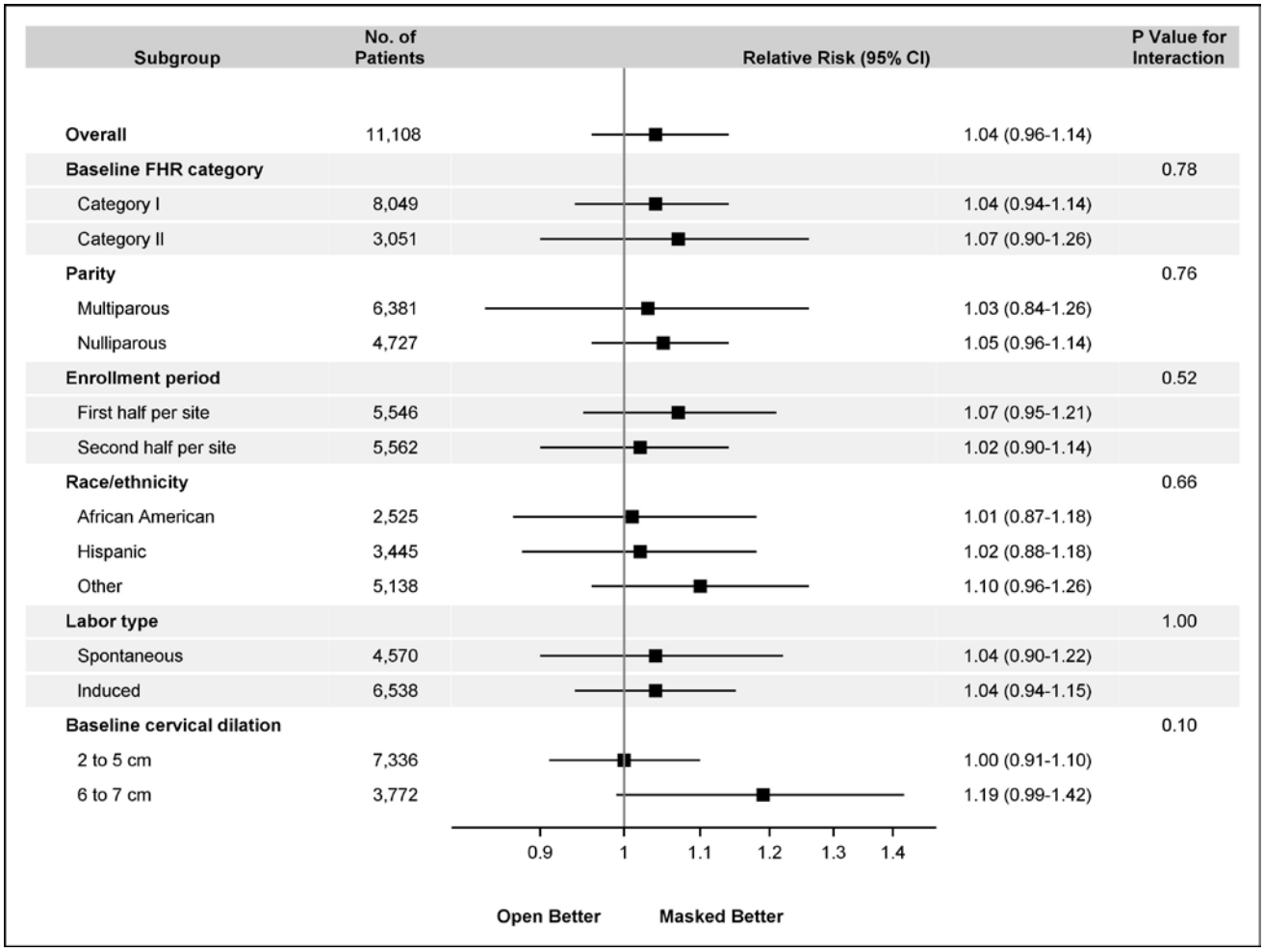


Figure S5. Subgroup Analyses for Effect of Study Intervention on Cesarean or Operative Vaginal Delivery

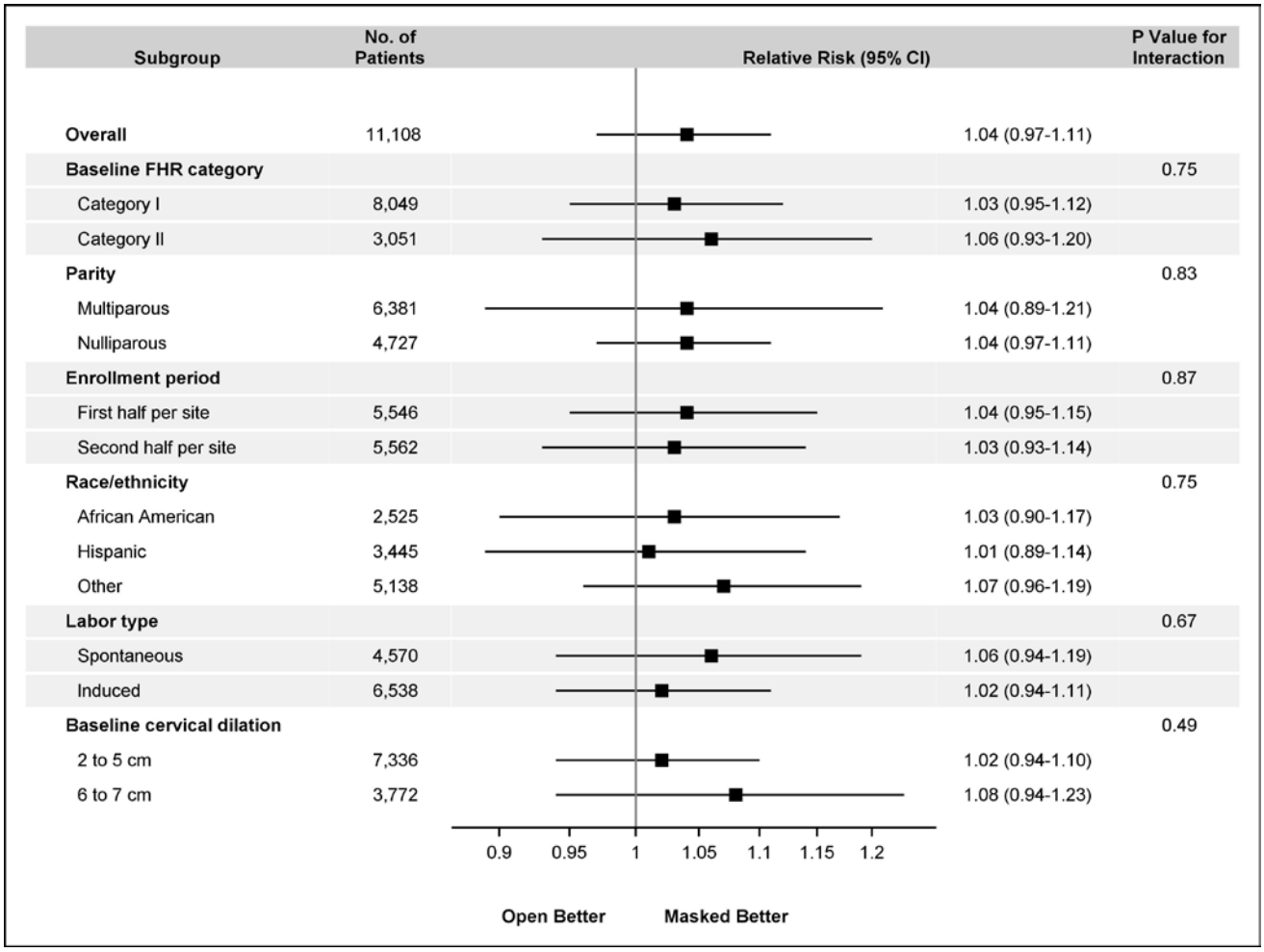


Table S1. Additional Adverse Events

Event*	**Open arm (N = 5532)**	**Masked arm (N = 5576)**
	number (percent)	
Blister on mother's thigh at skin electrode site	0 (0.0)	1 (0.02)
Laceration at fetal ECG electrode site	2 (0.04)	1 (0.02)
Bleeding at fetal ECG electrode site	4 (0.07)	0 (0.0)
Infection at fetal ECG electrode site	2 (0.04)	3 (0.05)
Neonatal sepsis	3 (0.05)	6 (0.11)
Any additional adverse event	*11 (0.20)*	*10 (0.18)*

* Adverse events in addition to those listed in Tables 2 or 3 in the main body of the paper.

Table S2. Management of Open Arm Patients with Regard to STAN Guidelines

			General reason not within guidelines	
Delivery type	Not within guidelines	Within guidelines	Despite STAN guidelines, expeditious delivery did not occur	Delivered when STAN guidelines indicated that labor should continue
Spontaneous vaginal	44 (3.8)	1120 (96.2)	44 (100)	0 (0)
Forceps/vacuum	28 (8.5)	301 (91.5)	15 (53.6)	13 (46.4)
Cesarean	91 (9.7)	843 (90.3)	36 (39.6)	55 (60.4)
All reviewed	163 (6.7)	2264 (93.3)	95 (58.3)	68 (41.7)

Data presented as no. (%). Percentages calculated as the proportion within each delivery type

Table S3. Outcomes for Per Protocol Analyses

Outcome	Open Arm* (N = 5364)	Masked Arm* (N = 5744)	Relative Risk (95%CI)	P Value
	number (percent)			
Primary composite outcome†	47 (0.88)	45 (0.78)	1.12 (0.74, 1.68)	0.59
Stillbirth	0 (0.0)	0 (0.0)		
Neonatal Death	2 (0.04)	2 (0.03)	1.07 (0.15, 7.60)	>0.99
5-min Apgar score ≤3	15 (0.28)	8 (0.14)	2.01 (0.85, 4.73)	0.10
Cord artery pH ≤7.05 and base deficit in extracellular fluid ≥12‡	3 (0.06)	8 (0.14)	0.40 (0.11, 1.50)	0.16
Intubation at delivery	39 (0.73)	30 (0.52)	1.39 (0.87, 2.24)	0.17
Seizure	2 (0.04)	5 (0.09)	0.43 (0.08, 2.21)	0.45
Neonatal encephalopathy	3 (0.06)	6 (0.10)	0.54 (0.13, 2.14)	0.51

* Patients were analyzed according to the intervention that they received. One patient allocated to the masked arm was erroneously "re-randomized" to the open arm. Five patients allocated to the open arm were erroneously "re-randomized" to the masked arm, so fetal ECG analysis information was not available to the provider, and in an additional 163 patients the providers did not follow the guidelines for labor management per the device labeling, and were classified to the masked arm.

† The primary composite outcome includes one or more of the following: stillbirth, neonatal death, 5-minute Apgar score ≤3, cord artery pH ≤7.05 and base deficit in extracellular fluid ≥12, intubation in the delivery room, seizures, and neonatal encephalopathy

‡ Data were available for 5201 in the 'per protocol' open arm and 5521 in the 'per protocol' masked arm. Cord artery pH ≤7.05 and base deficit in blood ≥12 occurred in 32 (0.62%) and 41 (0.74%) deliveries in the open and masked arms, respectively; RR 0.83 (0.52, 1.31); p=0.42