UNIVERSITY OF MINNESOTA

Twin Cities Campus

Human Research Protection Program
Office of the Vice President for Research

D528 Mayo Memorial Building
420 Delaware Street S.E.
MMC 820
Minneapolis, MN 55455

Phone: 612-626-5654
Fax: 612-626-6061
Email: irb@umn.edu
http://www.research.umn.edu/subjects/

APPROVAL OF MODIFICATION

May 30, 2018

Todd Thierer

612-625-0653
tthierer@umn.edu

Dear Todd Thierer:

On 5/30/2018, the IRB reviewed the following submission:

Type of Review:	Modification
Title of Study:	Use of an Occlusal Support Device During the Second Stage of Labor
Title of Submission	Modification #2 for Study Use of an Occlusal Support Device During the Second Stage of Labor
Investigator:	Todd Thierer
IRB ID:	1604M86847
Submission ID	MOD00004756
Sponsored Funding:	Sponsor Name: DELTA DENTAL OF MINNESOTA FOUNDATION, Grant Title: Use of an Occlusal Support Device During the Second Stag
Grant ID/Con Number:	CON000000059364;
Internal UMN Funding:	None
Fund Management Outside University:	None
IND, IDE, or HDE:	None
Documents Reviewed with this Submission:	None

The IRB determined that the criteria for approval continue to be met and that this study continues to involve Greater than minimal risk.

Modifications/updates included:

Our study coordinator is leaving and we have a new study coordinator.

You will be sent a reminder from ETHOS to submit a Continuing Review submission for this study. You must submit your Continuing Review no later than 30 days prior to the last day of approval in order for your study to be reviewed and approved for another Continuing Review period. If Continuing Review approval is not granted before 7/30/2018, approval of this protocol expires immediately after that date.

You must also submit a Modification in ETHOS for review and approval prior to making any changes to this study.

If consent forms or recruitment materials were approved, those are located under the Final column in the Documents tab in the ETHOS study workspace.

In conducting this study, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the HRPP Toolkit Library on the IRB website.

For grant certification purposes, you will need the approval and last day of approval dates listed above and the Assurance of Compliance number which is FWA00000312 (Fairview Health Systems Research FWA00000325, Gillette Children's Specialty Healthcare FWA00004003).

Sincerely,
Tricia A Carstedt

IRB Analyst

We value feedback from the research community and would like to hear about your experience. The link below will take you to a brief survey that will take a minute or two to complete. The questions are basic, but your responses will help us better understand what we are doing well and areas that may require improvement. Thank you in advance for completing the survey.

Even if you have provided feedback in the past, we want and welcome your evaluation.

https://umn.qualtrics.com/SE/?SID=SV_5BiYrqPNMJRQSBn

I.1. Introduction and Overview of the Study

I.1.1. Synopsis

Purpose:

- Aim 1: To determine if an Occlusal Support Device (OSD) can reduce the duration of the second stage of labor
- Aim 2: To determine if an OSD can reduce the incidence of labor complications including Caesarian Sections
- Aim 3: To determine if the use of an OSD can improve Apgar scores in newborns.

Design: This is a randomized, intervention trial. Pregnant women who consent to participate will be enrolled; half will be randomized to have fabrication of an Occlusal Support Device (OSD) to be used during the second stage of labor. The other half will have no alteration in their normal pre or perinatal care. Enrollment is expected to take 24 months and subjects will be followed until delivery.

Sample Size: 500 women; all at the UMP Women's Health Specialists Clinic.

Inclusion Criteria:

- Nulliparous women
- Uncomplicated pregnancy
- Singleton pregnancy

Exclusion Criteria:

- Unable to provide informed consent or comply with study protocol,
- High risk and/or complicated pregnancy,
- Have multiple fetuses as diagnosed by ultrasound,
- Have extensive decay or multiple broken/missing teeth that will interfere with the fabrication of an OSD

Study Procedures

Subject Recruitment

We plan to recruit all of our study subjects from the UMP Women's Health Specialists Clinic. During their routine office visit for their pregnancy the participating physician or their affiliated nurse will make those patients who meet the study inclusion criteria aware of this study and ask them if they would

be interesting in hearing more information about the clinical study. Those patients who express a willingness to listen to a description of the study, will have the purpose of and procedures involved explained to them. Each woman will be given an opportunity to ask questions and given time to consider whether they would like to participate. For those women who would like to participate, oral and written informed consent will be obtained. Consenting participants will then be randomly assigned to one of the two study arms.

Study Data:

Baseline data will include the following:

- Maternal age
- Race
- Parity
- Height
- Body weight
- BMI
- Weight gain during pregnancy
- Number of missing teeth
- Overall dental health
- Temporomandibular dysfunction: presence or absence
- Vitals

Dental Visit:

Women who consent to participate in the study and are randomized to the intervention arm of the study will be scheduled for a dental examination. Participants will be seen at the UMP Adult Dental Clinic or Clinics and Surgical Center dental clinic for a general dental exam. Subjects randomized to the interventional arm of the study will also have impressions for fabrication of an OSD. They will be scheduled for a return visit to have the OSD tried in and adjusted if necessary.

Post Delivery Data:

An obstetrical nurse will abstract additional pertinent maternal health and birth information from the subject's medical record during labor including:

Woman:

- Gestational age at delivery

- Estimated fetal weight
- Indications for induction
- Use of oxytocin in labor
- Obstetrical complications
- Obstetrical interventions with indications
- Time of Second Stage Labor
- Use of epidural
- Vitals

Neonate:

- Birth weight
- Apgar score
- Head circumference
- Admission to the NICU and indications

Additionally, all women in the interventional group will be given a satisfaction survey relative to their experience with the OSD:

1- Disliked or refused use
2- not helpful
3- fair
4- helpful
5- very helpful

Outcome measures

Primary Obstetrical Outcomes

- Time of Second Stage of Labor

Secondary Obstetrical Outcomes

- Complications of Pregnancy (C-section)
- APGAR Score of Neonate

I.1.2. Background and Rationale

- Importance

Prolonged labor, especially during the second stage of active expulsive effort (the pushing phase), is associated with increased risk of maternal complications (e.g. tissue trauma, postpartum hemorrhage, intra-amniotic infection). Developing an effective method to assist and maximize maternal expulsion effort should be of

great value in reducing the number of complications, also including cesarean section or instrumental deliveries. Past studies published in the dental literature have shown that specially designed oral appliances that support the dental occlusion may increase the isometric strength of different muscle groups. Increased strength of the neck muscles could improve efficiency of the Valsalva (pushing) maneuver in increasing intra-uterine pressure, and thus decreasing the duration of phase II of labor. It has also been shown that specially designed oral appliances can have an effect on neuro-endocrinology especially the Paraventricular nucleus of the hypothalamus and CRH levels, reducing cortisol levels in athletic stress. CRH having a role in the female reproductive system could be positively affected by the anti-stress properties of certain oral appliances.

- Improvement in scientific knowledge and clinical practice

This project could lead to an increased ability to determine when intervention during pregnancy utilizing an occlusal support device might decrease the incidence of caesarian section and other complications that occur during the second phase of labor.

- Changes based on this project if specific aims are achieved

If results are successful, routine clinical obstetrical care could include the fabrication of an OSD, thus utilizing a minimally invasive technique to positively impact the outcomes of labor.

I.1.3. Study Design

I.1.3.1. Overview. This randomized, controlled clinical trial is designed to determine if the use of an OSD during second stage of pregnancy can reduce the duration of that stage thereby decreasing the risk for complications and lead to improved neonate outcomes. Five hundred women, in their first, second or third trimester of pregnancy, will be randomized into interventional or control arms. After collection of baseline data, approximately half of the subjects will be randomly assigned to have fabrication of an OSD to be worn during the second stage of labor. Subjects randomized to the intervention arm of the study will have a comprehensive dental exam and OSD fabrication.

I.1.3.2. Subject population, study intervention, outcome measures.

Subject Selection and Informed Consent. Potential subjects will be screened at the UMP Women's Health Specialists Clinic. Before a subject is enrolled in the trial, oral and written informed consent will be obtained in accordance with the policies of the respective institution's Human Subjects Protection Program.

Interpreters, for non-English speaking subjects, will be available to assist in the consent process.

Inclusion Criteria. To be eligible for randomization in this study, each subject must:

1. Nulliparous
2. Have an uncomplicated pregnancy
3. Have a singleton pregnancy
4. 18 or older

Exclusion Criteria. Subjects will be excluded from participation if they:

1. Are unable to provide informed consent or comply with study protocol,
2. Are high risk and/or have a complicated pregnancy,
3. Have multiple fetuses as diagnosed by ultrasound,
4. Have extensive decay or multiple broken/missing teeth that will interfere with the fabrication of an OSD

Test group intervention: OSD during second stage of labor. Subjects randomized to the test group will have an OSD fabricated during their first, second or third trimester of pregnancy for use during their second stage (pushing stage) of their labor.

Control group: No deviation from routine pre and perinatal care.

Outcome measures. The outcome measures are as follows.

<u>Primary Obstetrical Outcomes</u>

- Time of Second Stage of Labor

<u>Secondary Obstetrical Outcomes</u>

- Complications of Delivery
- APGAR Score of Neonate

<u>I.1.3.3. Procedures.</u>

Timeline and Enrollment Schedule. Five hundred subjects will be recruited over 24 months.

Subject Recruitment. A flyer will be posted at the UMP Women's Health Specialty Clinic. Any interested women will be directed to the research assistant at the clinic and be given a structured oral presentation of the study and asked to sign a consent form before they are randomized. Women will also be approached by the participating physician asking if they are interested in participating.

Obstetrical Data Collection. At each site, the obstetrical nurse, research assistant or physician will abstract risk factors for premature birth and birth data from the subject's clinic record.

Delivery of Essential Dental Care. Subjects in the intervention arm of the study will be given the opportunity to obtain treatment at the UMP Adult Dental Clinic or at the patient's oral health care provider of choice for abscessed or carious teeth detected during the dental examination.

Subjects will be free to seek dental care outside of the study. Patients will be financially responsible for any care delivered other than an oral exam.

Coordination of Visits. Study dental visits will be scheduled to coincide as much as possible with the subject's routine monthly prenatal visits.

Subject Payment. At the conclusion of the study, subjects will be given a $10 gift card for use at a discount store (e.g., Target, Walmart, K-Mart). The gift card can be used to purchase items but cannot be redeemed for cash.

Data Transmission. The Study Coordinator is responsible for maintaining a supply of case-report forms, and for data quality control. The Coordinator will keep a photocopy of all forms in a secure, locked file cabinet.

I.1.3.4. Statistical considerations.

Statistical Analyses.

The sample size is based on Aim 1. A sample size of 247 per group will have 90% power to detect a mean difference of 12 minutes between groups using a two group t-test at the 0.05 level of significance and assuming a standard deviation of 41.

For aim 2, this sample size of 247 per group will have 86% power to detect differences of a 1.2% Caesarean section rate in the OSD group and a 6.4% Caesarean section rate in the control group using a chi-square test at the 0.05 level of significance. For aim 3, 247 per group will have 90% power to detect a

mean difference in Apgar scores of 0.29 standard deviations using a two group t-test at the 0.05 level of significance.

Given that some patients will not reach second stage labor (e.g. Cesarean section prior to second stage labor), we plan to enroll additional patients to ensure that 247 patients per group reach the second stage of labor.

The planned statistical analyses are designed to address each specific aim. Descriptive statistics will be calculated for demographics, patient characteristics, and outcomes. The distributions and skewness of the continuous outcomes will be evaluated.
Aim 1: To determine if an OSD can reduce the duration of the second stage of labor

Mean duration of second stage labor will be compared between the OSD and control groups using a two group t-test. We will also explore the effect of important covariates (e.g. epidural or oxytocin use) on duration of second stage labor and whether this effect differs by group using linear regression models. Since some women will likely undergo a caesarean section or operative vaginal delivery during second stage labor, time from onset of second stage labor until delivery will be compared between groups using a log-rank test. Women undergoing these procedures will be censored.

Aim 2: To determine if an OSD can reduce the incidence of labor complications including Caesarian Sections

Rates of labor complications (including Caesarian Sections) will be compared between the OSD and control groups using chi-square tests or Fisher's exact tests. Similar to aim 1, we will also explore the effect of important covariates (e.g. epidural or oxytocin use) on rates of labor complications and whether this effect differs by group using logistic regression models.
Aim 3: To determine if the use of an OSD can improve Apgar scores in newborns.

Mean Apgar scores at 1 and 5 minutes will be compared between the OSD and control groups using two group t-tests.

Reporting for Quality Management. The principal investigator (PI) and Study Coordinator have responsibility for monitoring the trial. Dr. Todd Thierer will monitor overall study management, enrollment, and compliance with protocol. He will provide oversight to assure that quality data are collected, and that adverse events are reported in a timely manner.

I.1.4. References

1- Safe prevention of the primary cesarean delivery. Obstetric Care Consensus No. 1. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:693–711

2- The effect of intrapartum dental support use among nulliparous during the second stage of labor – a randomized controlled study. Amir Aviram, Eran Ashwal, Liran Hiersch, Eran Hadar, Arnnon Wiznitzer, Yariv Yogev. The Journal of Maternal-Fetal & Neonatal Medicine : 1-4. Posted online on 19 Mar 2015

3- Neonatal and Maternal Outcomes With Prolonged Second Stage of Labor. S. Katherine Laughon, MD, MS, Vincenzo Berghella, MD, Uma M. Reddy, MD, MPH, Rajeshwari Sundaram, PhD, Zhaohui Lu, MS, and Matthew K. Hoffman, MD, MPH Obstet Gynecol 2014 124:57-67

4- Duration of the second stage of labor while wearing a dental support device: A pilot study. Koji Matsuo, Janna V. Mudd, Jerome N. Kopelman and Robert O. Atlas J. Obstet. Gynaecol. 2009;35:672–678

5- The Effects Of A Customized Over-The-Counter Mouthguard On Neuromuscular Force And Power Production In Trained Men And Women. Courtenay Dunn-Lewis, Hui-Ying Luk, Brett A. Comstock, Tunde K. Szivak,David R. Hooper, Brian R. Kupchak, Ashley M. Watts, Brendan J. Putney, Jay R. Hydren, Jeff S. Volek, Craig R. Denegar, and William J. Kraemer Journal of Strength and Conditioning Research 2012; 26:1085–1093

6- Maternal and perinatal outcomes with increasing duration of the second stage of labor. Allen VM, Baskett TF, O'Connell CM, McKeen D, Allen AC. Obstet Gynecol 2009;113:1248–58.