Use Of An In-Home Non-Stress Test Device For Remote Fetal Monitoring In A Local High-Risk Obstetric Population (Airstrip)

Protocol Summary

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Sponsor:	AIRSTRIP OPERATIONS
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Background and Introduction

In the setting of high-risk pregnancies, non-stress tests (NST) relying on fetal tococardiography technology have been used to help identify potential ongoing fetal compromise that would result in stillbirth/intrauterine fetal demise (IUFD) within seven days after the NST has been completed. The true power of the NST lies in its negative predictive value of 99.85%; its negative predictive value is much lower at 10-40%.[1] Follow-up fetal monitoring for an abnormal NST (called a non-reactive NST) is generally non-invasive, but requires the patient to be evaluated in a medical facility where ultrasound is available or where extended monitoring can be done.[1] NSTs are routinely used for high-risk pregnancies in which there is a higher risk of intra-uterine fetal demise (IUFD) secondary to maternal, fetal, or pregnancy-related complications. Common indications include pre-gestational diabetes, chronic hypertension, previous IUFD, intrauterine growth restriction, fetal gastroschisis, and preeclampsia.[2]

NSTs are generally performed in an in-hospital setting (antepartum unit or triage area) or in an outpatient clinical setting. In order to perform the test a bed, mid-level provider, interpreting physician, and an NST machine must be available. Most clinics and hospitals are limited in the number of NSTs that can be performed at any given time secondary to NST machine and spatial limitations. A few studies looked at remote NSTs using telephone-photograph pairing; the earliest studies were performed in the late 1970s. The majority of these studies were done before the Internet was available to the public and before the routine use of Bluetooth™ and internet-based technologies. The results of these studies are encouraging – indicating the interpretable NST monitoring strips can be obtained in remote locations and transferred to a central location for reading. [2-8]

In additional to feasibility assessments, cost studies (including cost-effectiveness studies) of remote fetal monitoring systems from the late 1980s to the early 2000s have shown decreased costs for at-home fetal monitoring, even when a midlevel provider conducts in the in-home testing. [9-12]

While the majority of these studies have looked at provider applied devices, there are studies that show patients can be taught how to use an NST device reliably and are able to perform the monitoring to a similar level as midlevel providers. [3,6,13,14] Studies of patient satisfaction for fetal in-home monitoring indicate that remote testing is acceptable to patient and associated with a high level of satisfaction.[13,15]

A few studies have looked at differences in outcome between women remotely monitored and a control group. Pan, et al., found that the NST remote group had a higher number of abnormal NSTs and Apgars, but decreased asphyxia compared to women monitored at home via kick counts.[16] Other studies have shown decreased number and length hospitalizations for remote fetal monitoring.[5,13,17] Another study showed decreased anxiety among women receiving remote monitoring done by a midlevel provider compared to conventional prenatal care.[18]

Since the 1970s and even the 1990s, healthcare systems have evolved, as has information technology and mobile health (mHealth) platforms. Newer and more efficient systems of

electronic fetal monitoring have been developed, allowing for remote monitoring of obstetric patients in labor. **No studies in the last decade have validated or evaluated the utility of modern at-home, patient applied, remote NST monitoring systems, nor have any studies looked at the steps required to integrate at-home NST monitoring into an existing medical system.**

The Airstrip® Sense4Baby™ system device is FDA-approved for provider-applied use and is currently undergoing FDA review for home monitoring use. Studies conducted by Airstrip® have shown that it is feasible to obtain interpretable NSTs in a provider-applied setting using the system device. <SOURCE> In their formative study, Sense4Baby™ showed success rates of turning on and interacting with the device, as well as collection of fetal heart tracing (FHT) and tocometric data, in 92.5% of patients (95% Confidence Interval ± 4.4%). Information from the formative study were used to improved the interface and workflow. In their summative study, patient success in following all steps including obtaining FHT and tocometric data was 99.5% (95% Confidence Interval ± 1.85%). <SOURCE, Scripps feasibility data> During this study, the company also found that interpretability of obtained data did not differ significantly between domiciliary and clinical locations.

Significance

Modern in-home NST machines that relay monitoring results through the Internet have been developed, but feasibility and satisfaction studies have not yet been conducted, particularly in high-risk populations. If these types of machines are found to be usable and safe for patients to use and can be integrated with minimal difficulties into the existing healthcare system, use of at-home fetal monitoring may allow patients to save time and money related to travel for NSTs previously only available through healthcare centers. In-home NST use may also be cost-effective for the healthcare system by increasing the capacity and flexibility to conduct NSTs. Based on previously conducted studies, remote monitoring may also be cost-effective in the ability to reduce duration and frequency of inpatient monitoring.

The aim of this present study is to evaluate the feasibility of integrating an at-home NST program into an existing healthcare system, to evaluate the interpretability of NSTs obtained at home within a high-risk obstetric population, to assess the number of abnormal and/or uninterpretable NST episodes incurred in a domiciliary setting, and define the subsequent patient care algorithm. Additionally, we will determine the patient and healthcare provider satisfaction and explore associated costs, benefits, and effectiveness for the healthcare system and patient.

With the results of this study, we plan to perform a larger study with a high-risk population residing remote from the healthcare center.

Purpose and Objectives

Mobile connectivity has the possibility to impact medical care of many patient populations, including pregnant patients. Non-stress tests (NST) for pregnant patients are currently conducted in clinical settings and are not routinely performed remotely. For rural and distant patients, this

means the need to travel for extended periods of time, multiple times per week, in order to receive these tests. Clinical facilities are also limited in the number of patients to whom they can provide clinical care by the physical space available for NSTs.

NST technology has been developed that enables remote NST monitoring. Preliminary data suggests that patients can reliably obtain a NST with self-application and have similar levels of satisfaction compared to patients receiving NSTs within a clinical setting.

We propose to test the Airstrip® Sense4Baby™ NST device in a local high-risk population in order to assess the feasibility of integrating an at-home NST monitoring program into an established health care system, as well as to evaluate patient and provider satisfaction associated with at-home monitoring.

Research questions

Primary Research Questions:

Can the Airstrip® Sense4Baby™ non-stress test device be integrated into an existing health care system in a manner that produces interpretable NSTs and allows timely interpretation and management by the healthcare provider?

If the device can be integrated, what steps are required and what are potential stumbling blocks for integration?

Secondary Research Questions:

-How often do uninterpretable and/or abnormal NSTs occur?

-What is the care algorithm for these types of NSTs and how do these differ from patients receiving NSTs in clinic?

-Are the patients and healthcare providers satisfied with the use of the NST device at home compared to receiving an NST in the specified clinic?

-What is the cost-effectiveness of this approach for the health system and for patients?

Study Population

Age of Participants: Pregnant women ages 18 and older

Sample Size:

At Utah:	60
All Centers:	60

Inclusion Criteria:

Target population: The target population is high-risk pregnant women.

Accessible population: The accessible population is high-risk obstetric patients receiving care throughout the University of Utah Healthcare system and who receive their NSTs at MFDC.

- Singleton gestation
- Estimated gestational age of 32 0/7 -37 6/7 weeks
- Physician order for twice weekly NSTs
- Live within 60 mile radius of the University of Utah University Hospital or a hospital with an obstetric inpatient unit
- Reliable access to and connectivity with wireless Internet
- Reliable for communication and follow-up

Exclusion Criteria:

- Multifetal gestation
- Maternal age less than 18
- Plans to move prior to end of pregnancy
- No or limited access to internet and/or phone

Design

Observational Research
Prospective Clinical Research

Study Procedures

Recruitment/Participant Identification Process:

Participants will be recruited by IRB approved research staff. Patients may be referred by their primary obstetrician, but we will not specifically ask providers to recruit patients.

Flyers and brochures will be placed in public areas throughout our recruitment catchment area including: University of Utah medical school, hospital and hospital clinics, campus boards, restrooms, etc.

We will screen patient appointment logs to determine women who may be eligible for this study. The inclusion/exclusion criteria will be reviewed with each patient's chart. Potentially eligible patients will be identified and invited to enroll upon presenting for a scheduled NST in the University of Utah Maternal Fetal Diagnostic Center.

Informed Consent:

Description of location(s) where consent will be obtained:

Consent will be obtained at clinics within the University of Utah covered entity. This may include: Madsen Clinic, Clinic 4 and the Maternal Fetal Diagnostics Center.

Description of the consent process(es), including the timing of consent:

Pregnant women who meet the pre-screening criteria will be flagged as potential participants. When she comes to her prenatal clinical visit, we will approach her and explain the study. Patients are given a copy of the consent document and the study is explained. We give the patient ample time to read the consent document and ask questions. If she is interested in participating in the study, we will have her sign the consent document at the current visit. If the patient wants extra time to consider whether or not she wishes to participate, additional time will be granted and follow-up will be arranged.

Procedures:

Study Design

Phase I

This initial study is designed as a pilot study of a small group of local high-risk obstetric patients. This will be a prospective single-cohort study.

Patients with physician-ordered twice-weekly NSTs scheduled in the OB Diagnostic Center at University of Utah Hospital will be eligible for enrollment. Study participants will be recruited to use the Airstrip® Sense4Baby™ system machine on a weekly basis until the time of delivery, while also receiving an in clinic NST weekly. Research study personnel will notify the ordering obstetric provider regarding patient participation in this study (via the electronic medical record system and email). Participants will receive an in-clinic NST with the Airstrip® Sense4Baby™ device, will be taught how to use the device, and asked to demonstrate their ability to use the device. If the participant successfully demonstrates use of the monitor, the device will be given to the patient to use at a scheduled time each week. The patient will be given educational materials, including a visuals-enhanced, short quick start guide.

For her remote NST monitoring, the patient will receive a virtual NST appointment. At the time of the scheduled appointment, the patient will apply the monitor and the NST will be read by the mid-level provider staffing the testing center after a thirty-minute strip has been recorded and transmitted to the database. The NST will also be interpreted by the maternal-fetal medicine physician, according to the established workflow. The patient will be notified of

the result by a telephone call from the mid-level provider and appropriate follow-up arranged according to the NST management algorithm developed for this study. If the patient has trouble with using the device at home, the patient will be able to talk with the mid-level provider via telephone to troubleshoot issues.

The patient will also continue to receive an NST in clinic weekly, allowing each patient to serve as her own control in terms of NST interpretability, frequency of non-reactive NSTs, and satisfaction. Weekly on-site visits will also allow for educational opportunities and trouble-shooting. These NST schedules will be repeated on a weekly basis until delivery or until the provider discontinues the NST order.

Delivery and maternal / neonatal outcome information will be collected from the electronic medical record. Patients will be contacted after delivery to assess overall satisfaction with the NST at home versus in clinic.

Phase II

Upon completion of phase I enrollment (n=30), a second phase of enrollment will begin. Having demonstrated at-home NST interpretability and feasibility of integration into the healthcare system, the next step will be to use the remote NST testing to demonstrate feasible use in rural/remote settings. This will involve enrollment of up to 30 additional subjects. Inclusion/exclusion criteria, enrollment procedures, and study procedures will be identical to phase I recruitment, with the exception of the following:

1. Participants may receive NSTs up to twice weekly at home.During regularly scheduled obstetric visits (every 1 to 2 weeks depending on gestational age and circumstances), NSTs will be performed on site which will allow for educational opportunities and trouble-shooting.However, we will remove the requirement for once weekly on-site testing at the University of Utah Hospital.

2. The requirement to be within a 60 mile radius of University Hospital will be removed.Instead, the requirement will be to be within a 60 mile radius of a hospital with an obstetric unit.Eligibility will be assessed upon enrollment and the nearest obstetrical hospital will be identified and recorded in the electronic medical record (NST nursing documentation and within the pink “sticky note” within the obstetrical episode). Clinical algorithms will be the same, except the referral hospital for urgent and emergent evaluations will be the closest hospital with an obstetrical unit. The interpreting NST nurse and physician will determine the recommended course of action and will communicate to the patient, per established protocols.The NST nurse and physician will also communicate to the responsible obstetric care provider at the nearest hospital for continuity of care.

Device Specifications and Logistics

NST transmission

NSTs obtained at home will be transmitted via technology included in the system in

conjunction with the patient's home wireless Internet system (Figure 1).

The Sense4Baby™ system measures the physiological parameters, then transmits wirelessly over Bluetooth the measured data to a proprietary application software running on a gateway device (Samsung phone), which then transmits it wirelessly (3G, 4G, or Wi-Fi) to a HIPAA-compliant, web database for storage. A provider, using any web browser on any capable computing platform, can then review the data via a custom web portal once the patient has ended the monitoring session and transmitted the data.

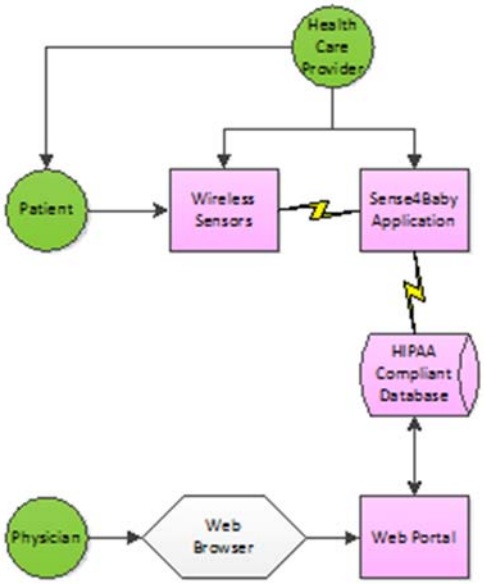


Figure 1: Diagram of information transmission

During the monitoring, the patient will be able to see the results of the monitoring, which can help guide the patient to troubleshoot problems they are having (Figure 2).

Figure 2: Picture of patient-viewable monitor

Figure 3: Image of gateway device with monitoring screen visible

NST data storage

Upon the transmission of the NST data, it is stored on the secure, Sense4Baby™ HIPAA compliant database. The architecture and system design has been developed to ensure that HIPAA guidelines are in place to ensure patient information privacy. Two servers are utilized to enhance security, one server is dedicated to the web portal, and the other server is used to store database information. Access to the portal software is allowed only to authenticated users (via login names and password). Strong password rules (e.g. minimum 8 characters, special characters, renewal after set periods, etc.) are employed. All data communication is encrypted (HTTPS), and all packets containing patient data are de-identified. Data is stored encrypted, and de-identified as well (encryption keys, and identification look-up keys are stored in a separate database, on the same server).

Access to NST storage data

For every site (clinic, doctor's office, hospital, etc.) where the system is deployed (referred to as a "deployment"), a designated Site Administrator will be granted permissions (by Sense4Baby,™ Inc.) to create users and assign them roles (nurse, physician, etc.; the role defines the level of access granted to users) who will be identified via a username (an email is used), and a unique password (which the users themselves create; the Site Administrator does not know this password).

NST troubleshooting

A Quick Start Guide will be provided to the patients and participating healthcare providers. The midlevel provider and the study personnel will be immediately available to help troubleshoot.

Patient and midlevel provider communication and troubleshooting will be facilitated through use of a web-based, HIPAA-compliant video communication solution provided by the University of Utah Department of Telemedicine (Doxy.me). The patient will be trained on how to use this video-based

technology at their initial study visit.

Study Procedures

Patient education

After the patient is screened and enrolled in the study, the patient will be oriented to the Airstrip® Sense4Baby™ system and taught how to use the device – a picture of the device is provided below (Figure 4).

Figure 4: Picture of Sense4Baby™ device in carrier

This instruction will take place in the Maternal Fetal Diagnostic Center (MFDC) by study personnel. The patient will be asked to demonstrate the following manufacturer-evaluated and –recommended steps to ensure the patient can adequately use the system:

1. Turn on and unlock the gateway

2. Connect gateway to internet

3. Start the Sense4Baby™ application

4. Log-in

5. Navigate to the pairing screen

6. Insert the Toco in the dongle (this automatically turns the Central Unit on)

7. Successfully pair the PulseOx

8. Successfully pair the Central Unit

9. Uses adequate amount of transducing gel

10. Position the Central Unit on the abdomen, in a position suitable to hear the Fetal Heart Rate

11. Attach the TOCO on the abdomen in a correct orientation

12. Secure the TOCO (with belt)

13. Secure the Central Unit (with belt)

14. Reset the TOCO to baseline

15. Collect FHR and TOCO data

16. Upload data to server

The patient's first NST will be obtained in clinic via the Sense4Baby™ system. After ensuring appropriate use and attainment of an interpretable, reactive, and reassuring NST, the patient will be discharged to home with the system.

NST appointment flow

At the time of the patient's appointment, the midlevel provider will call the patient to verify the appointment and ensure she is starting the NST. After this verification, the provider will communicate with the patient that he/she will call the patient in approximately 30 minutes to review the tracing and discuss results.

To initiate a monitoring/NST session, the patient will login into the Sense4Baby™ application on the gateway (via authenticated user name and password). She would then connect (pair) the application with the 2 Bluetooth sensors (Central Unit and pulse oximeter), which initiates a monitoring session.

The midlevel provider will utilize the portal to assess the interpretability of the NST strip. If the patient has trouble with the equipment or the midlevel provider identifies problems with the NST session, the patient and provider will troubleshoot accordingly. The individual identifying the issue will call the other. Troubleshooting the equipment will follow the manufacturers suggestions. Troubleshooting the NST strip will follow the created clinical algorithms. After a final disposition is decided, the encounter will be documented and closed.

NST billing

As a standard of care, NST sessions, whether in-home or in-clinic, will be billed according standard NST billing guidelines.

NST session moderating

The midlevel provider assigned to NSTs at the MFDC will log into the Sense4Baby™ portal

after the patient has transmitted the session data and assess the interpretability of the acquired NST. If the acquired data is non-interpretable, the provider will call the patient and ask them to replace the monitoring system and try again for a defined period of time.

NST interpretation

Initial interpretation will be done by the midlevel NST provider. Final interpretation will be completed by the maternal-fetal medicine physician according to established clinical algorithms. The interpretation workflow is identical for on-site and remote NSTs, with the exception that communication with the patient will be done by telephone.

At-home NST follow-up procedure (see associated figure)

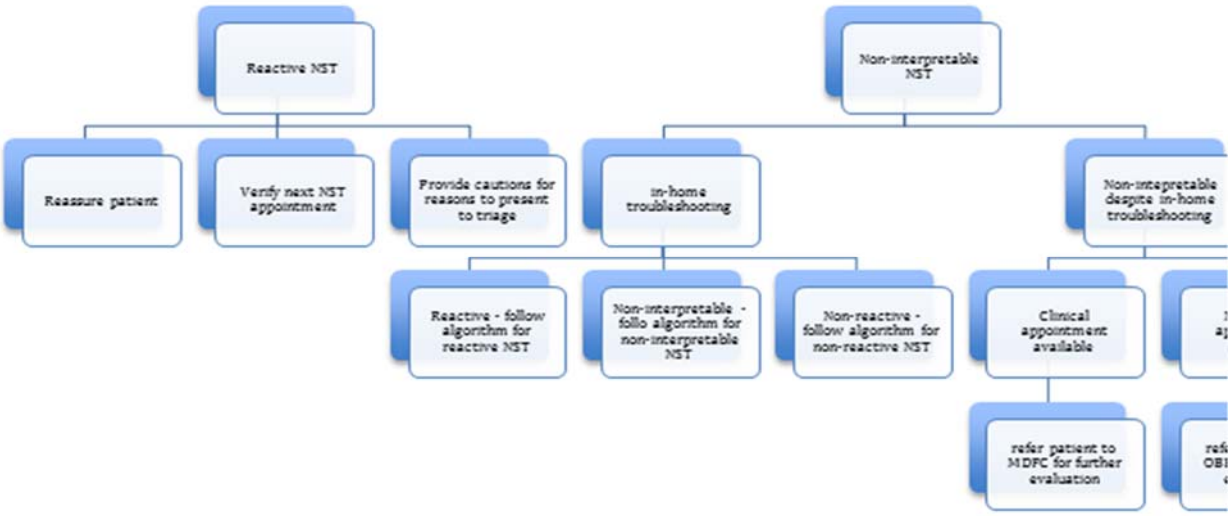
For a reactive NST, the patient will be told that the NST is reassuring and that they should present for their next scheduled in-clinic appointment. For a non-interpretable but overall reassuring NST despite in-home troubleshooting, the patient will be asked to present within the same calendar day to the MDFC or to the Obstetric Emergency Services (OBES) depending on the time of day and the availability of clinic appointments. For a non-reactive NST, the patient will be asked to immediately present to the MDFC or to the Obstetric Emergency Services (OBES) depending on the time of day or the availability of clinic appointments.

Follow-up evaluation of a non-reactive NST will be done in accordance with the clinical standard of care at MDFC and OBES.

To help facilitate any necessary follow-up before the end of the business day, we will strongly encourage participating patients to schedule their off-site NST appointments in the morning.

For an NST considered by the midlevel provider to be urgent according to established national heart rate tracing guidelines (absent variability with recurrent decelerations, sinusoidal pattern, prolonged bradycardia), the midlevel provider will seek immediate physician review by the on-site MFM. If the on-site MFM agrees with the urgent nature of the NST, the midlevel provider will discuss the findings with the patient and instruct the patient to present immediately to the OBES at UUMC or the nearest hospital with an obstetric unit. If the patient is unable to transport herself, an ambulance will be called to transport the patient to the nearest obstetric unit.

Figure 5: Algorithm for actions based on in-home NST interpretation



Data Collection Instrument

A data collection sheet will be developed and utilized in the study. A demographics intake sheet will be used when enrolling patients. Satisfaction questionnaires will be administered to study participants and involved providers. Patient satisfaction questionnaires will be conducted after the second in-home NST, at 2 weeks intervals after the initial survey if the patient is still pregnant, and at 6 weeks postpartum. Provider questionnaires will be conducted at the end of the study after all patients have been enrolled. An additional questionnaire will be administered to providers regarding the accessibility of the NST monitoring segments and interpretability – this will be conducted at the end of the study. Surveys will be built using REDCap. NST documentation within the electronic medical record (EPIC) will be according to the current NST workflow for on-site NSTs; details regarding management of uninterpretable or non-reactive NSTs will be extracted. Obstetric outcomes will be extracted from the patient's electronic medical record (EPIC).

Inclusion/exclusion criteria for which patients were screened out will be collected. Reasons

eligible patients declined study participation will also be collected.

Procedures performed for research purposes only:

Standard of care for this population includes 2 NSTs per week conducted in the out-patien clinic. Participants for this study will have 1 NST completed in clinic and will complete 1 NST at home, per week. Phase II participants may complete both NSTs at home if they n appropriate eligibility criteria. The only difference with home NSTs is that the NST devic patient-applied and the test is conducted at the patient's home. The test itself, and the interpretation, are not different than standard of care testing. Use of the device at home wi not change the patient's standard of care (twice weekly NSTs). The results of the home an clinic testing will be used to inform clinical care in the same way. Inadequate / uninterpretable tracings are a risk for both home and clinic NST monitoring and will requi further assessment per the described algorithms.

Related questionnaires, as described in study procedures section above, are for research purposes only.

Statistical Methods, Data Analysis and Interpretation

Sample size calculations: As this is a pilot study relying mostly on descriptive statistics, we will initially enroll 10 high-risk patients for proof-of-concept and to troubleshoot problems in system logistics. We will then enroll 20 high-risk patients to assess the refined system.

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Variables

Covariates:

- Pregnancy details
- EGA at enrollment
- Indication for NST testing
- Obstetric history
    - Gravida
    - Para
    - Obstetric complication(s)
- Medical comorbidities
- Substance use
    - Blood pressure at each NST appointment
    - Pregnancy outcomes
        - Delivery data
    - Presentation at delivery
    - Infant status – liveborn versus stillbirth (antepartum versus intrapartum)
    - Gestational age at delivery
    - Reason for delivery
    - Mode of delivery
    - Indication for mode of delivery if operative
    - Neonatal gender
    - Birth weight
    - Apgars
        - Highest level of care required for neonate
        - Highest level of care required for patient
        - Maternal days hospitalized after delivery
        - Neonatal days hospitalized after delivery
    - Adverse outcomes/obstetric complications
    - Reason for declining study
    - Demographics
        - Maternal age
        - Maternal BMI
        - Maternal height
        - Maternal weight
        - Race

        - Ethnicity
        - SES indicators
    - Residential zip-code
        - Percent of inhabitants at ___% of the federal poverty level
    - Home rental versus ownership
    - Marital status
    - Employment status
    - Individual annual income
    - Family annual income
    - Family wealth
    - Family size
    - Highest level of education
    - Years of education

Outcome:

- Primary outcome
    - Description of feasibility of integration of NST into healthcare system - Steps required to integrate in home NST monitoring into the current healthcare system
        - Obtainability of NSTs
        - Schedule-ability of NSTs
        - Interpretability
- Secondary outcome
    - NST related
        - Percent of satisfactory NSTs obtained
        - Time required by NST staff
        - Time required by patients
        - Number of abnormal NSTs
        - Length of NSTs
        - Frequency of follow-up needed
        - Frequency of appropriate follow-up according to algorithm
    - Patient satisfaction
    - Provider satisfaction
    - Frequency and type of complications identified

Analysis

Analytic approach

Data analysis will use mostly descriptive statistics – parametric and nonparametric statistics will be used as indicated (*Chi*-squared or Fisher's exact test will be used for nominal/binary outcomes; Student's t tests, Wilcoxin rank sum, or Mann-Whitney U will be used for continuous and ordinal variables as needed).

Data management

Data for this study will be obtained from medical records, as well as from administered surveys

of patients and providers. Study data will be saved in an online encrypted Redcap™ database. Access will be granted only to investigators participating in the study.

Data analysis

We will analyze descriptive and analytic statistics using Stata™ Version 13 (Texas).