Functionality and Acceptability of a Medical Grade, Smartphone based, Fetal Heart Rate Monitor for Self-Administration by Low Risk Pregnant Women

The HeraBEAT USA™ Trial

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1.0 Specific Aims

The coronavirus disease 2019 (COVID-19) global pandemic rapidly changed the standard model of prenatal care in the United States. In response to this pandemic, the Society for Maternal Fetal Medicine (SMFM) and the American College of Obstetricians and Gynecologists (ACOG) recommended integrating telehealth services as appropriate, limiting face-to-face patient contact if clinically possible, and considering alternative methods of providing obstetric care, to decrease the risk of COVID-19 exposure[1–3].

Evidence for integrating home monitoring devices and telehealth services for the provision of prenatal care is limited[4,5] Innovative options for home monitoring of fetal well-being, as a component of virtual or a hybrid prenatal care model is equally negligible. While a few studies have focused on home monitoring of maternal blood pressure, capillary blood glucose, and contraction patterns, [5]few have investigated maternal home monitoring of fetal heart rate, as a component of virtual or hybrid prenatal care.

In addressing this gap, HeraMED designed and tested a medical grade, smartphone fetal heart rate monitor - HeraBEAT USA™ ((HeraBEAT™) - for self-administration at home, under clinical guidance of an obstetric provider.

We propose that HeraBEAT™ self-administered at home by pregnant women, under clinical guidance, will result in accurate monitoring of fetal heart rate, provide peace of mind to patients between prenatal appointments, and enhance the overall prenatal experience of pregnant women.

To evaluate the functionality and acceptability of HeraBEAT™ we plan to:

1. Assess the functionality of HeraBEAT™ self-administered by pregnant women.
    a. Hypothesis: Pregnant women will demonstrate a working knowledge on use of the device, when observed by medical staff, will trouble-shoot appropriately and will rate the device instructions as easy to follow.
    b. Hypothesis: Pregnant women will appropriately self-monitor FHR successfully at home, transmit the data to caregivers, and use the device as prescribed.

2. Assess the acceptability of HeraBEAT™ when self-administered by a pregnant women in the home by assessing the following
    a. Hypothesis: Pregnant women will rate the device as easy to use, easy to interpret, and have minimal disruption in lifestyle as measured by a standardized survey.
    b. Hypothesis: The intervention will reduce the rate of healthcare utilization without impacting maternal safety or the process of care standards specified by the American College of Obstetricians and Gynecologists (ACOG).

2.0 Background and Significance

The current traditional rhythm of prenatal care in the United States assumes dependence on brief face to face visits consisting of low-level physical assessments and the opportunity to communicate about the progress of the pregnancy[6,7]. It has been proven that this method provides benefit to mothers and their fetuses, but the potential that greater benefit could be achieved using 21st century technology has not been widely explored[3,8]. The current COVID-19 pandemic has shifted the method in which obstetric providers plan and provide prenatal care, as global practice changes encourages limited face-to-face interaction, with more reliance on telehealth options for the provision of care[9].

Alternative models for the provision of obstetric care is limited in the literature, but have recently gained traction in obstetric practice, given the current COVID-19 pandemic. A recent systematic review of telehealth interventions to improve obstetric care reported improved schedule optimization for high risk pregnancies, and improved obstetric outcomes for smoking cessation

and breastfeeding[5]. Our randomized, telemedicine integrated, reduced model care – OB Nest – augmented with fetal Doppler and sphygmomanometer home monitoring devices resulted in higher patient satisfaction of care among OB Nest patients while maintaining similar maternal and fetal outcomes when compared to standard prenatal care[10]. Similarly, a study which decreased the frequency of prenatal care and augmented care with a mobile prenatal care App, found no difference in patient or provider satisfaction[11,12].

Despite the rapid growth in a variety of technological advances and innovations in healthcare to support home monitoring[13–17], including home holter monitors, wireless scales for monitoring weight, and home sphygmomanometer for monitoring blood pressure, there has been relatively little research efforts focused on home monitoring devices, self-administered by pregnant women, under the guidance of a clinical team, especially innovative options for home monitoring of fetal well-being. This gap is important as leveraging innovative technological advances and other connected health modalities may allow future re-design of prenatal care, that enhances the overall experience of expectant mothers[18–20] while allowing for rapid adoption during healthcare crises like the current global COVID-19 pandemic.

Recently, the Clinical Excellence Research Center at Stanford University proposed that the costs of delivering prenatal care could be reduced by 2.5% to 13% by using supplemental telehealth innovative tools[8]. Despite the major impact this could potentially have on the delivery of prenatal care, research and investments in this concept has remained limited, and uptake slow, until the recent COVID-19 pandemic.

Consequently, this study proposes to assess HeraBEAT,™ a novel fetal heart rate device, administered at home by pregnant women, under clinical guidance, to augment options for virtual prenatal care.

3.0 Preliminary Research

3.1 Basic Principles of FHR Monitoring

Fetal heart rate monitoring is a method for examining the condition of an unborn fetus in the uterus by noting its heart rate. This is typically done by a manual handheld device in an outpatient setting during routine prenatal care, or continuously, by electronic FHR measurement when pregnant women are admitted for obstetric care. Fetal ultrasound is also utilized to monitor FHR in clinical settings. These methods for monitoring FHR was originally introduced in the 1960s and 1970s, with the hope that it would assist physicians in the diagnosis of fetal hypoxia or abnormal fetal heart[21].

3.2 Doppler FHR Principle

The typical Doppler fetal heart rate monitor is a hand-held ultrasound transducer that uses the Doppler Effect to provide an audible simulation of the heart beat and displays the number of beats per minute. To achieve this, the device is pressed against a pregnant women's abdomen and acoustic waves are then interpreted as FHR. An ultrasound probe is a key component in the system. The probe consists of an oscillator to generate ultrasound frequency (for these applications, the range is 1–3 MHz) followed by an amplifier to condition the sine wave in the order of volts. This waveform is applied to the transmitter transducer to send vibrations through the body and bounce back when the density of the medium changes. Another transducer is then used to receive the bounced vibrations and convert them to electrical signals[21]. Basic FHR Doppler systems are available for outpatient use under clinical guidance. However, self-monitoring of FHR by pregnant women at home is currently not a standard approved use of FHR Doppler devices, although Doppler devices are routinely sold for public consumption.

3.3 Investigational Device

The 'HeraBEAT USA™ (HeraBEAT™) is a wireless Smart Fetal Ultrasound Doppler measuring device designed to be self-administered by pregnant women. The 'HeraBEAT™' device safety and performance claims allow continuous and accurate measurement of fetal heart rate (FHR) and maternal heart rate (MHR) throughout the pregnancy starting at 12 weeks gestation. This study shall evaluate the device performance starting at 20 weeks gestation.

Technologically, HeraBEAT™ is similar to other FHR devices currently on the market in terms of device usage but differ by design in its interface. The HeraBEAT™ device uses a smartphone-based interface, with real time instructions for localizing FHR. The device also measures the maternal heart rate (MHR) and uses this in its algorithm. This is primarily in order to overcome common lay person usage errors such as confusion between MHR and FHR or difficulties locating the FHR due to lack of experience. The data obtained from the device is uploaded to a secure HIPAA compliant cloud-based server for medical providers to review. The intended use, indication for use and contraindications are similar to current medical grade handheld fetal Doppler devices.

The specifications for the HeraBEAT™ are:

- The device will measure fetal heart rate in range of 50-240 BPM.
- The device will measure fetal heart rate with accuracy of ±2 BPM.
- The device will measure fetal heart rate with resolution of 1 BPM.
- FHR value is calculated and displayed every 1 second.
- Device measures FHR and MHR starting at 12 week gestation.
- The device will measure maternal heart rate in range of 45-240 BPM.
- The device will measure maternal heart rate with accuracy of ± 2% or 1 BPM, whichever is greater.
- The device will measure maternal heart rate with resolution of 1 BPM.

- MHR value is calculated and displayed every 1 second.

3.4 Device Components

The 'HeraBEAT™' device is a handheld device consisting of two main units:
1. The HeraBEAT™ sensor device and
2. The HeraBEAT™ smart phone application for iOS/Android (App).

The function of the HeraBEAT™ device is to sense the fetal heart rate signals, process the data and transmit the information wirelessly to the HeraBEAT™ App. The HeraBEAT™ App. receives the digital information from the HeraBEAT™ device, displays the data to the user, saves it for additional use, controls the commencement and termination of the measurement session, and automatically sends the measurement data to a qualified HIPAA compliant cloud server(HeraBEAT dashboard).

The HeraBEAT™ device (Figure 1) is a wireless device, operating on rechargeable battery (low voltage) that communicates with a smartphone via standard low power bluetooth-4 Low Energy (BLE) data link. The HeraBEAT™ device does not contain buttons or switches. Power ON/OFF management is executed via timers and sensing of motion by the accelerometer. The HeraBEAT™ device is managed by an internal Microcontroller (MCU). It controls the battery charger and power management, Blue Tooth Low Energy (BLE) and indicator lights.

Figure 1. Illustration- Left: HeraBEAT™ app. Right: HeraBEAT™ device.

3.5 The HeraBEAT™ Application (App)

The HeraBEAT™ App. (Figure 2) runs on a Smartphone (Android version 6 and above and iOS version 11 and above). The application communicates with the HeraBEAT™ device over Bluetooth low energy (BLE), controls the operation of the device, and receives the FHR and MHR value in real time for displaying numerally and graphically to the user. The application can also record these values for later review and transmission to a healthcare provider.

Figure 2. Representative HeraBEAT™ app screens

3.6 Device Classification

Fetal monitoring devices, including fetal Dopplers, which acquire and display the fetal heart rate and/or uterine contractions, are FDA Class II medical devices.

Table 1: 'HeraBEAT™' system specification

Safety	Complies with	IEC/EN 60601-1, 60601-1-2, 60601-1-11, 60601-2-37
Classification	Anti-electric Shock Type	Class II electrical device when AC/DC adapter connected. Otherwise Internally powered equipment.
	Anti-electric Shock Degree	Type BF equipment
	Degree of Protection against Harmful Ingress of Water	IP22 Protection against falling drops of water when unit is tilted 15°.
Physical Characteristics	Device size	88 x 37 mm, 3.5 x 1.5 inch (Diameter × Height, ±0.08inch
	Device weight	Approximately 4.58 Ounce
Operating Environment	Temperature	From 41°F up to 104°F
	Humidity	From 5% up to 90% RH (non-condensing)
Storage/Transport Environment	Temperature	From -4°F up to 140°F
	Humidity	From 5% up to 95% (non-condensing)
	Light intensity	No direct sun light
	Pregnancy Week	12 to 42

FHR Performance	FHR Measuring Range; Accuracy; Resolution	50 to 240 BPM; ±2BPM; 1 BPM
	MHR Measuring Range; Accuracy; Resolution	45 to 240 BPM; ±2% or 1 BPM, whichever is greater; 1 BPM
Auto Acquisition stop		5 minutes of successful measurement
Recommended Ultrasound Transmission Gel		Aquasonic 100 Ultrasound Transmission Gel, by Parker Laboratories.
Power consumption		< 2 W
Rechargeable Li-ion Battery	Nominal Capacity	3.7VDC, 1250 mAh
	Continuous Work Time	4 hours (with a new battery)
	Power Input	5 V DC, >0.3A
	Charge Time	4 hours
Ultrasound (NEMA/FDA)	Nominal Frequency	2 MHz ±10%
	Ultrasonic Output Power (P)	70mW
	Peak rarefactional pressure (p_r)	0.03 MPa
	Ultrasonic Output Intensity (I_{sata})	≤20mW/cm^2
	Mechanical Index (MI)	0.02
	Thermal index (TIS; TIB)	0.26; 0.7
	Measurement Mode	Continuous Wave Ultrasound Doppler
	Effective Radiating Area of Transducer	4.9±0.5 cm^2
BLE specification	frequency band of transmission	2.4 – 2.5 GHz Channels (2MHZ spacing) 3 Advertising channels @ 2402, 2426, 2480Mh 36 data channels
	frequency characteristics of the modulation	DSSS: GFSK (modulation index = 0.5)
	Maximum RF Input	-10 dBm
	Typical Receive Sensitivity	-94 dBm

	Maximum RF Tx Output Power	+4 dBm

3.7 The HeraBEAT™ Functional Description

The operation of the device starts when the application is open and the HeraBEAT™ device is turned-on:

1. **Step 1:** Achieving Bluetooth (BLE) connectivity between the HeraBEAT™ device and the HeraBEAT App. Pairing is obtained following a onetime PIN code entered by the user. The user is then directed to register and enter her last menstrual cycle (LMP). An estimated fetal gestational age is calculated. Once the application is open, the application automatically searches for and connects to the HeraBEAT™ device.
2. **Step 2:** The user must apply the provided gel to the bottom of the HeraBEAT™ device.
3. **Step 3:** The User presses the "START" command in the HeraBEAT™ App., and is guided to start searching for FHR signals by a built in Guided Search.
4. At this time, the device sends the App. the quality index of the FHR (QFHR), the QFHR index indicate to the application when the location and position of the device over the abdomen is satisfactory and FHR signal is measured.
5. When the QFHR is appropriate, the application instructs the user to hold the position over the abdomen and the device sends the FHR and MHR values for display and recording within the mobile App.
6. **Step 4:** The FHR and MHR measurements stop when either the user presses the "STOP" command or closes the application, or a predetermined time period has been reached.

Complete instructions for use of the HeraBEAT™ are provided in ***Appendix A***.

HeraBEAT™ dashboard layout and specification provided in ***Appendix B.***

The following is a list of HeraBEAT™ safety claims:

- HeraBEAT™ works at low voltage (5V) which is supplied from an internal rechargeable battery (tested per IEC 60601-1).
- HeraBEAT™ device material is isolated and made of electric non-conducting material. In addition, the device does not operate while charging.
- HeraBEAT™ transmits ultrasonic energy, at a maximum intensity of 20mW/cm2, according to IEC 60601-2-37 'Medical electrical equipment – Part 2-37: Particular requirements for the safety of ultrasonic medical diagnostic and monitoring equipment'
- The device turns off if not connected to the mobile application for several seconds.
- All materials are biocompatible and approved for use on skin surface.

- HeraBEAT™ controls the temperature level inside the device to assure that the device temperature remains below the safe temperature limit. In addition, a built-in-test (BIT) is implemented to verify the correct functioning of temperature Sensor.

The device conforms to risk management best practices according to ISO 14971:2007 – Medical Devices – Application of Risk Management to Medical Devices.

4.0 HeraBEAT™ Research Data to Date

A prospective feasibility clinical performance and usability validation study was performed using the 'Compass' (A previous brand name for the HeraBEAT™), Self-Administered Fetal Heart Rate Monitor in Pregnant Women in 2016, at Assaf Harofeh Medical Center and a private OBGYN clinic in Rishon Letzion, Israel. HeraMED Ltd. served as the study sponsor and Michal Feingold, M.D. served as the principal investigator. This study was conducted in compliance with the Israeli Ministry of Health regulations, the ethical principles of the Declaration of Helsinki, and the current Good Clinical Practices (GCP) set forth in EN ISO 14155 (2011) standard.[22]

The study was a prospective, non-randomized, open-label, single center, single arm study, with end-to-end clinical and usability validation to evaluate the performance, usability and safety of the Compass system in pregnant women.

The objectives of this study were to validate the safety and performance of self-operation of the Compass by intended users in realistic use scenarios and conditions. The chosen scenarios represented all steps involved in performing FHR measurement, verifying user's understanding of labeling and instructions for use when using the device, verifying that potential users were able to perform self-selection prior to using the device and evaluate user's subjective perspective/satisfaction.

The study enrolled expectant mothers with confirmed 12 week gestation pregnancy. Twenty five (25) participants were screened and 23 were enrolled, completed and analyzed. Indication for use included expectant mothers ≥18 years, with singleton fetus, gestational ages of 12 weeks or greater and familiar with Smart phone usage. Exclusion criteria included multifetal gestation, maternal history of defibrillation, electro-surgery, and patients with external electrical stimulators, cardiac pacemakers or requiring use of MRI or other high frequency medical equipment.

Primary Endpoint for performance included an evaluation of the ability of participants to self-measure FHR with the device. Primary Endpoints for usability included an evaluation of the following: success rate of the user's ability to self-select the device in accordance with the label; success rate of the user in independently performing critical and essential tasks (objective measure) and user perspective of success (subjective measure, systematically collected) for critical and essential tasks. The Secondary Endpoint for safety included an evaluation by reporting the incidence and severity of all device related adverse events.

The study consisted of a single visit, conducted on one day. Patients were self-selected during the screening process. Usability and performance of the device was evaluated by study personnel.

The feasibility study results were as follows:

- Performance success rate of Fetal Heart Rate detection was 100% (CI 85.2 – 100.00).
- The Pass/Fail success rate for all the usability critical and essential tasks was 100% in the following domains: 1. Self-Selection, 2. Task Performance: Training Material, Handling the Compass, Performing the Procedure, Performing the Switching Off.
- User Perspective of Success was evaluated by a post tasks questionnaire. Each question was evaluated on a scale from 1 to 5 (1. Strongly disagree; 2. Disagree; 3. Neither agree nor disagree; 4. Agree; 5. Strongly agree). Mean scores were calculated for each question. Results ranged from 4.3 to 5.0, indicating that expectant moms agreed or strongly agreed with the ease of use of the device.
- There were no safety issues or adverse events reported. Post-development testing indicated that the Compass System (now HeraBEAT™) was successful in achieving its per protocol efficacy and safety endpoints, usability and performance measures.

5.0 Study Methods

5.1 Overview

Primary Objective

1) To evaluate the functionality of HeraBEAT™ when self-administered by pregnant women by assessing the following:
   a) Study participants' independent use of the device assessed by study personnel observation, including ability of participants to read and follow HeraBEAT™ device instructions, and find fetal heart rate without assistance evaluated using the HeraBEAT™ Independent Device Assessment Form. (***Appendix C***).
   b) Data transmission from the device to the healthcare provider via a HIPAA compliant cloud-based server, assessed by evaluating the data transmitted to the healthcare provider from the HeraBEAT™ US device, including subject' success in finding FHR, time to find FHR, frequency of use, and clinical utility of the FHR/MHR data (***Appendix B***).

Secondary Objective

1) To evaluate the acceptability of HeraBEAT™ when self-administered by a pregnant women in the home by assessing the following:
   a) Patient usability and ease of use assessment as measured by the System Usability Scale (SUS), ***Appendix D***.
   b) Impact on utilization of care as measured by urgent triage and/or emergency care visits for concerns regarding fetal well-being.

5.2 Research Design and Participants

We propose a single center randomized cross-over study in the outpatient obstetric setting at an academic institution in the mid-west, United States to test the functionality and acceptability of HeraBEAT™ for self-administration by pregnant women.

5.3 Participant Selection

This study will recruit low risk pregnant women, with singleton pregnancies, presenting for prenatal care at the Obstetrics and Gynecology Department at Mayo Clinic Rochester. No waivers or exemptions to any eligibility criteria will be permitted. Each criterion will be addressed and documented in the mother's case report form for eligibility assessment. Patients will be recruited as a convenience sample after eligibility is assessed.

5.4 Eligibility criteria

Inclusion Criteria:
1. At least 18 years of age
2. Able to speak, read and understand English
3. Able to provide informed consent (i.e. no impairments or barriers)
4. Owns a suitable iOS or Android device and demonstrates average control and basic understanding of using a smartphone (i.e. download App, operate BT etc.)
5. At least 12 weeks gestation, or following first OB provider visit with pregnancy confirmation
6. Pregnancy documented as low risk

Exclusion Criteria:
1. Any observed cranial or cardiac anomalies on formal ultrasound
2. Multifetal gestation
3. Maternal history of defibrillation
4. Maternal history of electro-surgery
5. Patients with external electrical stimulators, cardiac pacemakers or requiring use of MRI or other high frequency medical equipment
6. Clinical judgment that determines that the pregnancy is at high risk for complications that would require outpatient or inpatient monitoring for clinical care.

5.5 Study Design

As part of current standard of care, pregnant women are initially evaluated by an obstetric physician, nurse practitioner or midwife during the first trimester. During this visit, the study nurse will complete the assessment for eligibility criteria for low risk pregnant women. Upon confirmation of eligibility, the nurse will contact the study coordinator. The study coordinator will approach the patients with study information, ascertain interest in participation, and obtain signed informed consent from those interested.

Between 18 and 20 weeks gestation, all patients complete a fetal sonography assessment for fetal anatomy as part of routine prenatal care. An obstetric provider will review the results with the patient, and confirm that fetal anatomy is normal. Patients with abnormal fetal cardiac or cranial anomalies will be excluded from the study. If the patient interest remains, the study coordinator will confirm ongoing consent and randomize the patient into the study. This will be documented in the appropriate section of the patient's electronic medical records.

Study personnel (obstetric nurses or clinicians) will then provide patients with a study kit, containing the HeraBEAT™ device or a standard fetal Doppler device (based on randomization assignment), discuss the limitations of both devices, and instruct patients on the range of normal fetal heart rate.

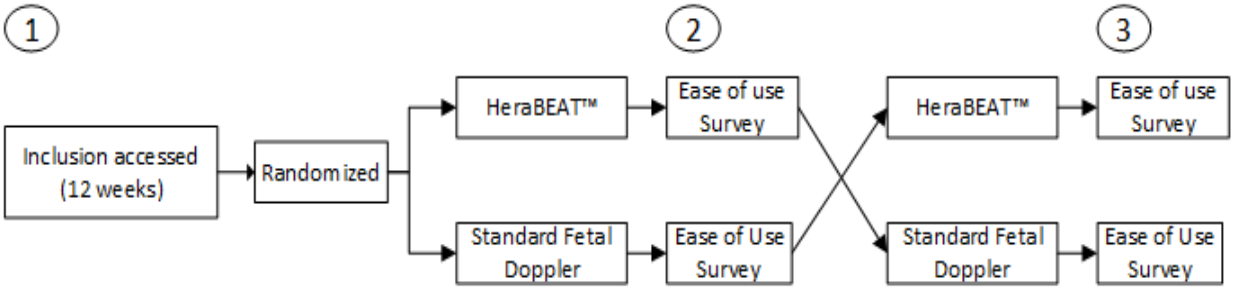
Study personnel will then observe the study subjects' independent self-administration of the devices in the prenatal clinic after patients receive a brief tutorial of the devices operation. Study subjects will be able to refer to the device instructions for use but will not receive assistance or prompts during this testing session. Study personnel will note any mistakes or difficulties by the subjects on the HeraBEAT™ Independent Device Use Assessment Form (Appendix C). Once the observation period is completed, study personnel will document all observations, review and correct any errors made by patients during use of the device, assist patients in confirming accurate use, perform teach back, and provide the study subject with a device for home use. Patients will be instructed to call clinic or Triage with any questions or concerns regarding results of fetal monitoring at home. All calls and recommendations provided will be documented.

5.6 Schema

Patients will be instructed to monitor their fetus once weekly, using their assigned device, from 20 weeks to 36/37 weeks gestation. Patients using the HeraBEAT™ device will have their FHR and MHR data displayed on their App, and uploaded to a HIPPA compliant cloud based server, which can be accessed by the healthcare provider for review (***Appendix B***). Patients using the standard handheld Doppler device will be given a study brochure for recording their weekly data. Patients using the HeraBEAT™ device will be instructed to bring their device during their outpatient clinical appointments, for comparison of MHR and FHR during their routine clinic appointments using methods documented in ***Appendix E*****.**

After approximately 8 weeks of monitoring, patients will complete a System Usability Survey (SUS Survey), ***Appendix D*** to assess ease of use of the device, then crossover to the alternate study product.

Patients who are randomized to HeraBEAT™ from 20weeks gestation to 28 weeks gestation will be given the standard fetal Doppler. Patients who are randomized to the standard Fetal Doppler will switch to the HeraBEAT.™ At the conclusion of each patient device use (28 weeks and 36 weeks gestation), participants will complete the System Usability Survey (Appendix D) to assess ease of use of each device.



1- *Nurse assesses eligibility criteria, ascertains mother's interest, and study coordinator will obtain consent and complete randomization Patients will be given home monitoring equipment after their fetal anatomy sonography is complete, inclusion/exclusion criteria confirmed and Patient Usability Form completed (Appendix C).*
2- *After 8 weeks of use, participants will complete the System Usability Scale (SUS) survey (Appendix D), return the first study device and crossover to the second device. An independent device use assessment (Appendix C) will be assessed by study nursing staff and completed for the second device.*
3- *At the conclusion of 8 weeks of self-monitoring with assigned device, participants will complete the System Usability Scale (SUS) survey to assess ease of use (Appendix D).*

Prior to registering study participants, all eligibility criteria will have been met and fully documented. Mothers will be randomized by the study coordinator after completion of standard informed consent for participation in clinical research including permission to use Protected Health information.

Registration/randomization is available via the Study Data Management System (SDMS), a web application portal framework supported through Mayo Health Sciences Research.

5.7 Intervention

All randomized participants will be assigned to an obstetric physician, midwife or combination of physician/nurse practitioner care team that will supervise care during her pregnancy. All laboratory tests, imaging, and standardized evaluations that ensure the safety of the participant and her fetus will be conducted in both arms of the study as per departmental protocol.

Participants will be instructed to seek care (per routine obstetric precautions) for any concerns regarding fetal wellbeing, irrespective of their FHR on home monitoring devices. No clinical decisions will be solely based on the results of home monitoring data. Data uploaded from the HeraBEAT™ device will be monitored by trained study personnel via the HeraBEAT dashboard : https://hera-med.rmdy.health/CoachConsole/Account/Login . FHR abnormalities will be investigated, using standard obstetric clinical protocols.

All adverse events (AEs) experienced by the subjects while at home or in the clinic will be recorded on the HeraBEAT™ study case report form and evaluated for type of event, severity, whether the AE qualifies as a serious adverse event (SAE), and relationship of the AE to the HeraBEAT™ device use.

5.8 Data Collection

Self-reported responses from surveys will be collected from participants after 8 weeks of use for each device via e-mail (REDCap Survey) or mailed paper surveys. If a participant does not have access to email then the survey will be mailed for completion with a self-addressed envelope with pre-paid postage. Data from the medical record will be abstracted for all participants that are registered in the study to capture demographics, socio-economic status, utilization, standards of prenatal care, delivery outcomes and safety data. The time frame for collection will be from time of enrollment to the 6-8 week postpartum appointment.

Table 2: Outline of data collection by weeks of pregnancy.

Gestational Weeks	12 wks	18-20 wks	24 wks	28 wks	32 wks	36 - 37 wks
Subject interest	X	X				
Subject eligibility	X	X				
Informed consent		X				
Fetal Anatomy Sonography		X				
Independent Device Use Assessment		X		X		
Weekly device use		X	X	X	X	X
SUS Survey				X		X

5.9.1 Participants Demographics

Participant characteristics to be collected at time of enrollment through self-report and medical record review will include: age, race/ethnicity, education level, marital status, BMI, due date, parity, previous miscarriage, previous C-section and insurance.

5.9.2 Participants Reported Outcomes

System Usability Survey: Ease of use will be evaluated using a survey assessing comfort with use, troubleshooting, ease of obtaining FHR, any safety concerns, and whether or not the device was useful for confirming fetal well-being.

Medical device usage: While mothers are using the standard home Doppler they will be asked to track usage information. These metrics will include date of use, user (mother/partner), estimated time to find FHR, and estimated FHR.

5.9.3 Clinical/Practice Important Outcomes

Safety and Healthcare Utilization: Data will be captured from the medical record review and participant's report of any safety concerns. A medical record review will be conducted to capture

all in-office visits within the OB Clinic, all triage visits and any hospitalizations that were prompted by FHR monitoring obtained at home, and recorded on the study case report form.

Patient engagement with remote monitoring devices will be measured by the number of times patients record FHR or both MHR and FHR data. Participant compliance with instructions regarding frequency of device use will be assessed by reviewing the device use statistics gained from information automatically uploaded to the HIPAA compliant cloud storage each time the device is used (***Appendix B*** and https://hera-med.rmdy.health/CoachConsole/Account/Login).

Participants who use the device more often than what is recommended will be re-instructed on appropriate use (once weekly).

6.0 Follow-up Guidelines

All participants will be followed per protocol guidelines and deviations from protocol will be reported to the IRB. If a participant refuses to continue to participate and consent is withdrawn, they will then be considered a withdrawn participant and no further data will be collected through medical review or self-report. Participants withdrawn prior to the end of the study will turn in their device at the time of withdrawal and continue routine prenatal care.

7.0 Stop Guidelines

All enrolled participants may choose to discontinue at any time. Since they will already be assigned to an obstetric provider, no interruption of care will be introduced. Participants may also be asked to discontinue the study if their pregnancy is subsequently diagnosed as high risk, or if cardiac or cranial anomalies are identified on routine fetal sonography.

8.0 Data Analysis Plan

The study will be analyzed according to the intention to treat principle, including all mothers randomized to the study in the arm to which they were randomized, regardless of whether they received the intervention assigned.

Baseline characteristics will be reported in the study results with continuous values being reported as means and standard deviations or median interquartile range as appropriate. Categorical values will be reported as counts and proportion. Two sample t-tests or Wilcoxon-rank sum test and chi-squared tests or Fishers exact test will be used as appropriate. Any baseline imbalances ($p<0.05$) will be explored as a possible confounder to adjust for when the outcome measures are analyzed. We will adhere to the CONSORT guidelines to transparently

report study results and ensure that sufficient information is included to allow for assessment of the study's internal and external validity.

Ease of use will be estimated from the System Usability (SUS) validated questionnaire. These data will be analyzed as a two sample t-test prior to cross over. After cross over we will analyze these data using an ANCOVA adjusting for order of medical devices or as a paired t-test as appropriate.

Within the SUS survey, we will also examine trends within individual questions using chi-square tests. Clinical concerns in FHR will be indicated as a FHR less than 110 bpm or greater than 160 bpm. These data will be analyzed as McNemar's test on the association of the study medical devices with the clinical standard of care. Comparing ease of use metrics will be done using an ANCOVA analysis or generalized estimating equation as appropriate adjusting for gestational age. Additional ad-hoc analysis will be performed using standard techniques appropriate for randomized trials, with each outcome compared between study arms using t-tests for continuous outcomes and chi-square tests for dichotomous outcomes. If there are differences in baseline characteristics between the two study groups, these will be accounted for using ANCOVA or regression models which include an indicator for study arm.

Participants and study clinicians (nurses, obstetric providers) will not be blinded to the intervention after randomization occurs. Study statistician and data analysts will be blinded as to which arm participants were assigned to. Statistical analysis performed by Mayo Clinic Statistician and Ms. Tzippy Shochat, MSc, Statistical Consultant, Rabin Medical Center, Beilinson Hospital, Israel.

8.1 Missing data

We will make every effort to minimize missing data. Trial enrollment, completeness of data collection, and fidelity of follow-up procedures will be reviewed and reported during study team meetings which will be conducted on a monthly basis. As the majority of data collected is part of the standards of care that are routinely collected in the patients EMR and captured directly from the source, the expected missing data will likely be minimal. The study statistician will conduct frequency reports to assess for missing data, and the study team will trouble shoot any problems encountered. We will report rates of missing data for each outcome by study arm, and known reasons for missing data. For data elements that are used to adjust study comparisons we will use multiple imputation to account for any that are missing at random (MAR).

8.2 Sample Size

Difference in ease of use between our standard fetal Doppler and HeraBEAT™ device, as measured by the System Usability Survey (SUS) will be the primary outcome. Approximately 1500 – 2000 expectant mothers receive prenatal care in the obstetric department annually. We aim to recruit 50 participants (50 per arm, with cross-over) for a 99.7% power to detect a 10-point difference in SUS, as this accounts for a withdraw / post-randomization exclusion, estimated as high as 10% (assuming a proportion of expectant mothers to withdraw participation after being enrolled or found to not meet criteria after the fact).

9.0 Potential Limitations

9.1 Conflict of Interest

Obstetric Study Personnel, Abimbola Famuyide, MBBS and Yvonne Butler Tobah, MD are participating Mayo Clinic Innovators, with Know-How license agreement, and stock/equity in HeraMED Ltd. They will not be involved in the direct recruitment of patients for this study. They will participate in future manuscripts of research findings.

9.2 Early Termination / Data Safety Monitoring Board

This study will be monitored for early termination due to any validated safety concerns. The existing obstetric safety review board will be utilized. All reported patient safety concerns will be promptly communicated and investigated by study personnel.

9.3 Confidentiality

Protection of subject privacy: The privacy of all study participants will be protected by avoiding the use of names on all research data (field notes, transcribed conference call, meetings, etc).

All research material will be maintained on a secure server at Mayo Clinic and locked in file cabinets, and all material will be destroyed seven years following completion of the study. The following entities will be allowed to access their study data:

- The Study Sponsor
- The Study Monitor
- Representatives of the US Food and Drug Administration

Subjects must give permission for the above access in order to participate in the study.

9.4 Data Management

All study coordinators will be required to use the current version of all documents and forms and adhere to the study schedule. Any paper forms collected will be stored within the Obstetrics Department for 3 years under lock. Survey data will be captured via email from study participants using the REDCap system, which is a HIPAA compliant secure data entry system that allows for validated data entry, edit checks and logs of all data changes. Participants unable or unwilling to use the e-mail surveys will be provided a paper copy. The statistical team will develop the REDCap data capture system for the data collection as well as survey collection. The data can be accessed by the statistical team at any time and downloaded into a statistical software package. The survey's via e-mail will be administered and tracked for completion by the statistical team. The statistical team will coordinate with the study coordinator for the mailing and receipt of surveys where mothers have indicated mailing only. The study coordinator will be responsible for the actual mailing of the survey, where the statistical team will provide information to help them coordinate. In cases where a response is not received

within 10 working days a second survey will be mailed or e-mailed, according to mothers' wishes.

Data generated by the HeraBEAT™ device will not contain any patient identifiers. The HeraBEAT™ device generates a UUID- Unique Identifier for each install. The UUID is available in the app at: Home Screen>Settings>About. The app attaches the UUID to saved measurements, which are in turn uploaded to HeraMED's cloud anonymously. No protected health information (PHI) will be stored in HeraBEAT server (the FHR measurement will contain no identifiable data and only the UUID). The HeraBEAT server is HIPAA compliant. The physical storage is in a secured, HIPAA compliant Azure server (Microsoft Azure Cloud Data Center - US East 2 - 101 Herbert Drive - Boydton). The deidentified data can be accessed only by HeraMED CTO and project manager and RMDY CTO, IT manager and DBA. The DB is encrypted using SQL Server Enterprise TDE. The server system keeps a full audit trail.

The Mayo Clinic research team will have secured access to the measurement data via a web-based dedicated service (HeraBEAT Dashboard):

https://hera-med.rmdy.health/CoachConsole/Account/Login

All data, documents, and analysis findings will be password protected and backed up on a routine basis. The data will be stored within the secure system for seven years following completion of the study.

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