Study Title: Neonatal Sleep Intervention to Improve Postpartum Hypertension

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Document: Study Protocol and Statistical Analysis Plan

Study Protocol and Statistical Analysis Plan

This study is a randomized controlled trial at Magee-Womens Hospital in which individuals with a hypertensive disorder of pregnancy are randomized to the neonatal sleep intervention (the SNOO responsive bassinet), or usual care of safe sleep education in the postpartum period.

Inclusion and Exclusion Criteria. Individuals meet inclusion criteria if they are ≥18 years old, have a singleton, full-term (37 weeks or greater weeks of gestation), live birth of a non-anomalous fetus, a diagnosis of gestational hypertension or preeclampsia by ACOG criteria, are enrolled in the Connected Care (formerly known as Vivify) institutional remote monitoring program, and are willing to undergo randomization and use the SNOO for their neonate. Individuals will be excluded if they are <18 years old, non-English speaking, having chronic hypertension, pre-gestational diabetes, cardiac disease, kidney disease, or liver disease, have an infant admitted to the NICU, intend to use the SNOO prior to study enrollment, are not willing to be randomized, or are not willing to use the SNOO. Individuals who meet criteria will be approached during their postpartum admission. If the participant agrees to enroll in the study, she will be consented and randomized at that time. Randomization will occur via permuted blocks with randomly varying block sizes by a web-based data entry system.

Study Overview. Those randomized to the intervention will be oriented to the use of the SNOO (see Figure 1) and instructed to have their neonate sleep in the SNOO as often as they can, with the understanding that some sleep does occur outside of bassinets. The SNOO is a commercially available device which is a responsive bassinet for neonates, and designed to respond to the infant's cries and automatically respond by emitting engineered white noise sounds and providing a rhythmic rocking motion. The infant is also swaddled to remain securely back-down. The SNOO automatically increases the sound and motion if the infant is still crying. However, if the infant does not settle within 3 minutes, the SNOO shuts off and alerts adults for additional assistance. Parents can also modify the SNOO settings to meet the baby's need for sound and/or motion.

Figure 1: SNOO responsive bassinet

Participants receiving the SNOO will be also asked to download and use the SNOO Smart Sleeper mobile application using either their own name and email address (if they are comfortable) or a study-provided ID and email address. This mobile application provides daily sleep reports while the SNOO is in use, alerts the parents that the infant requires additional attention if the infant does not settle after 3 minutes of crying, and allows the parents to customize the sound and/or motion level the infant receives.

Participants both groups will both receive:

- Standard of care safe sleep education during their postpartum admission, including a handout on safe sleeping from the UPMC Healthwise educational database
- Routine postpartum management of their hypertensive disorder of pregnancy, which at Magee-Womens Hospital, consists of enrollment in the Connected Care remote monitoring program.
- BP cuff and a scale with instructions on their use

For both groups, participants will be requested to record vital sign parameters into the Connected Care institutional remote monitoring program through 6 weeks postpartum. There is one main study visit at 6 weeks postpartum, and one brief study visit at 4 months postpartum which will be conducted through video calls. Participants will complete an infant sleep log and a maternal sleep log for the 7 days leading up each of the planned study video visits. At each video visit, participants will be asked to take their weight and blood pressure. At the first video visit, a questionnaire will be administered which includes:

- Pittsburgh Sleep Quality Index (PSQI): 19 questions of subjective sleep quality
- PROMIS Sleep Disturbance Questionnaire: 27 questions regarding sleep quality
- Epworth Sleepiness Scale (ESS): 8 questions to assess daytime sleepiness

- Edinburgh Postnatal Depression Scale (EPDS): 10 questions to identify individuals at risk for postpartum depression
- Generalized Anxiety Disorder 2-Item (GAD-2): 2 questions to screen for generalized anxiety disorder
- Perceived Stress Scale 4 (PSS-4): 4 questions to assess stress level
- Breslau 7-Item (Breslau-7): 7 questions to screen for post-traumatic stress disorder
- Survey questions to assess demographic information, reproductive history, current health status, BP medications, infant feeding method, and SNOO use

Participants will be compensated up to $60 paid on a VINCENT card. They will receive $50 after completing the 6 week postpartum research visit, and $10 after completing the 4 month postpartum research study visit.

See a visual representation of the study design in Figure 2:

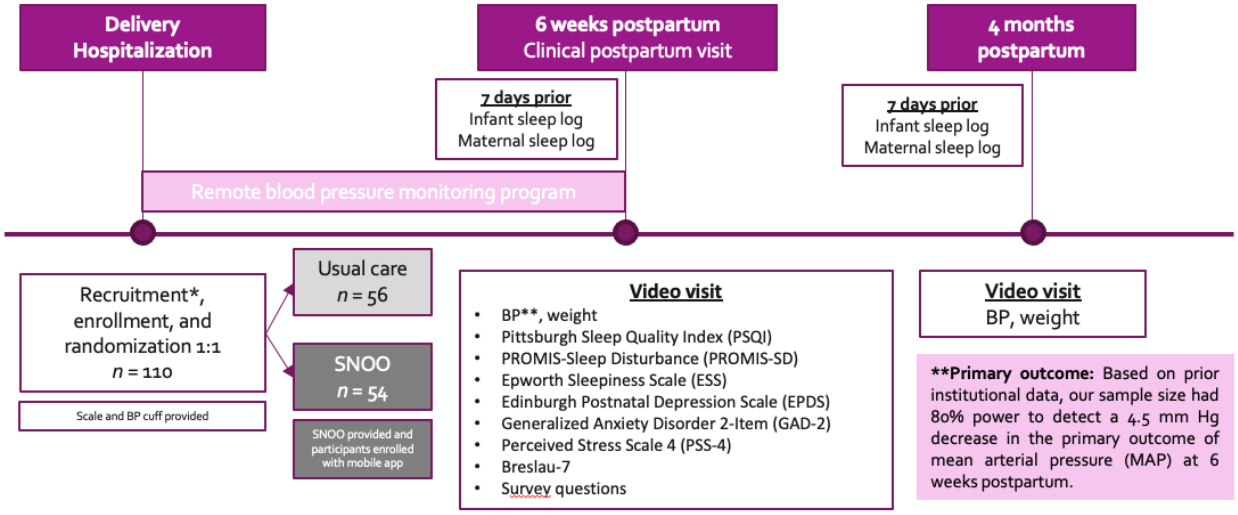

Figure 2: Study Design

Outcomes. The primary outcome is mean arterial pressure (MAP) at 6 weeks postpartum. Secondary outcomes include MAP at 1 week and 4 months postpartum; systolic and diastolic BP at 1 week, 6 weeks, and 4 months postpartum; antihypertensive medication use at 1 week, 6 weeks, and 4 months postpartum; Stage 1+ Hypertension or antihypertensive medication use at 1 week, 6 weeks, and 4 months postpartum; maternal weight and body mass index at 1 week, 6 weeks, and 4 months postpartum; subjective sleep quality at 6 weeks postpartum using the PSQI, PROMIS, ESS; objective sleep assessment using sleep log data at 6 weeks and 4 months postpartum; and mood assessment at 6 weeks postpartum using the EPDS, GAD-2, PSS-4, and Breslau-7.

Sample Size Calculation. In current remote monitoring patients without a history of chronic hypertension, the mean MAP at 6 weeks (among 1,007 individuals) was 94 ± 8 mmHg. With 1:1 randomization, 2-sided t-test with independent means, a sample size of 100 individuals total (50 per arm) would give an 80% power to detect a 4.5 mm Hg decrease in MAP. Additionally, for our secondary outcomes of systolic and diastolic BP at 6 weeks postpartum, we would be powered to detect a 6 mm Hg decrease in systolic BP and a 5 mm Hg decrease in diastolic BP with an alpha of 0.05, which would be a clinically meaningful outcome.

Statistical Analysis. Statistical analysis was performed using the intention-to-treat principle, with all randomized participants included in the analysis. All statistical was performed using Stata (StataCorp LLC, version 17.0, College Station, Texas, USA). Two-sample two-sided t-tests and Mann-Whitney U tests were performed to assess the differences between two groups of continuous, normally-distributed and non-normally distributed variables, respectively. Pearson's chi-square or Fisher's exact tests were performed to assess the differences between two groups of categorical variables. An alpha level of 0.05 was set for all statistical analyses. Pre-specified subgroup analyses include breastfeeding status, postpartum SARS-CoV-2 status, and a per-protocol analysis.