PROJECT TITLE:

Yoga in the NICU (YIN) for Parents: A Randomized Clinical Study

PRINCIPAL INVESTIGATOR:
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Contents

1. Objectives

1.1. Purpose, specific aims, or objectives:

The purpose of this proposal is to test the efficacy of yoga as a mind and body intervention to decrease stress, anxiety, and depression in parents of critically ill neonates hospitalized in the Seattle Children's and University of Washington neonatal intensive care units (NICUs). Specific aims include developing a randomized controlled pilot study to elucidate the optimal research strategy with which to implement mind and body interventions for parents of NICU patients. We will ultimately use these data to plan a multicenter Randomized Controlled Trial (RCT) to evaluate the short and long-term effects of yoga practice on NICU parents, the parent-child interaction, and child outcomes.

1.2. Hypotheses to be tested:

We hypothesize that a combined program of breath work, physical practice and meditation will decrease parental stress, anxiety, and depression in the NICU, improve parent-child bonding, and through this, child, and family outcomes.

2. Background

2.1. Relevant prior experience and gaps in current knowledge:

Preterm infants are often critically ill and require prolonged hospitalization in neonatal intensive care units (NICUs). The care of these infants is often regionalized, so that they can get the specialized treatment needed in centers with expertise in delivering this care. An unintended consequence of regionalization is the physical and emotional isolation parents experience when they stay with their hospitalized child far from family, friends, and work. As a result of these stressors, loss of parental control, autonomy, and concern for their child's wellbeing, nearly half of NICU mothers develop anxiety, depression, or posttraumatic stress disorder, and this may persist for years.

Helping parents to cope with the birth and hospitalization of a preterm infant is critical for the parents' health and wellbeing, as well as for the optimal development of their child, as parental anxiety and depression may affect parent-child bonding and result in altered child development. The practice of yoga, which encompasses physical postures (asana), but also includes breathing techniques (pranayama), and meditation (dhyana), has proven benefits in many areas of medicine and wellness including stress management, mental and emotional health and promoting sleep. Given the positive effects on both physical and emotional health, these mind and body techniques are promising as a therapeutic modality by which parental stress, anxiety and depression could be reduced.

There are gaps in our knowledge as previous studies of yoga have not occurred in hospital settings and have not included subjects in an acute state of distress such as parents of critically ill hospitalized neonates. Furthermore, in the current COVID-19 environment it is important to explore ways to make yoga interventions available to families by remote access, and to test whether this approach is successful.

Faculty advisors of this project have extensive prior experience with design and completion of multicenter trials involving newborn infants in NICUs across the United States. To allow us to evaluate the use of yoga as a means for helping parents cope with hospitalization of their newborn infants, we have enlisted a team of yoga practitioners including a registered prenatal and postnatal yoga teacher (Leanne Matullo), UW NICU RN, yoga teacher and NICU parent advocate (Rebecca DeBoer, RN). Faculty advisor Dr. Sandra Juul is also a certified Yoga and

Meditation teacher and will provide guidance in the design of the yoga intervention for NICU parents.

2.2. Relevant preliminary data:[2]

This is the continuation of a prior project: Yoga in the NICU Pilot Study see 2.4.

Surveys were completed by both NICU parents (n=31) and hospital stakeholders (n=140) to assess the feasibility and desirability of a yoga intervention for NICU parents. Preliminary data for Aim 1 suggest that NICU parents struggle primarily with stress and anxiety compared with depression. Parents with an infant hospitalized at UW NICU or SCH NICU primarily cope with the admission through social support (e.g., talking with friends and family), though mindfulness and meditation activities are considered important as well. A small percentage of hospital stakeholders surveyed had concerns about the safety (22%) and liability (14%) of a yoga intervention for parents, however most stakeholders had few concerns.

We were pleased to learn through our survey data that hospital stakeholders strongly view an intervention of yoga for NICU parents to increase parent satisfaction and confidence. Overall, there was overwhelming support from both parents and stakeholders in both institutions for a yoga intervention for parents of NICU babies.

2.3. Scientific or scholarly background:

See 2.1

2.4. Prior approvals:

Yoga in the NICU Pilot Study approved (exempt status) by UW IRB ID# STUDY00010722

3. Study Endpoints[3]

3.1. Primary and secondary endpoints:

Goal would be to enroll parents of NICU inpatients from UWMC and SCH into the study on a rolling basis for 4-6 months or until we have enrolled a total of 20 parents to the intervention and 20 parents to the control groups spanning both institutions. The intervention lasts for a duration of 6 weeks.

3.2. Primary or secondary safety endpoints:

N/A

4. Drugs, Devices and Biologics[4]

4.1. Manufacturer and name of all drugs, devices and biologics:

N/A

4.2. Description and purpose of all drugs, devices and biologics:

N/A

4.3. Regulatory status of all drugs, devices and biologics:[5]

N/A

4.3.1. Drugs or Biologics:
☐ IND Exempt. Explain:[6] N/A
☐ IND.

4.3.2. Devices:
☐ IDE Exempt. Explain:[7] N/A
☐ Abbreviated IDE / Non-Significant Risk. Explain:[8] N/A
☐ IDE / Significant Risk.

4.4. Plans to store, handle, and administer any study drugs, devices and biologics so they will be used only on subjects and be used only by authorized investigators:
N/A

5. Procedures Involved

5.1. Study design:[9]

This will be a randomized controlled pilot study to elucidate the optimal research strategy with which to implement mind and body interventions for **parents** of NICU patients, at 2 sites (University of Washington NICU and Seattle Children's Hospital NICU) comparing: 1) control group 2) yoga intervention (i.e: breathing exercises + meditation +postures).

Parents will be enrolled in the study after day 10 of infant admission to NICU and begin participation by day 14 of NICU admission (see Recruitment methods section 19).

The non-birth parent will be invited to participate in this study and may participate without the birth parent. If both parents are participating the partner would be randomized to the same group (control or intervention) see randomization section 5.2. In the circumstance that the birth parent declines participation and non-birth parent consents to participation, we will still obtain consent from parents to access infant medical records, however we will not obtain birth parent EPDS scale (see section 5.2)

If an infant is transferred from UWMC to SCH as part of their clinical care, a parent enrolled initially at UWMC may continue participation in this study while infant is admitted at SCH.

Control group: Parents will experience usual care including all available parental support as practiced in the specific site NICU. We will utilize a 'waitlist' control model for this project, whereby the parents randomized to control group will have unlimited access to the online platform hosting the yoga intervention following the completion of the study period.

Intervention group: In addition to usual care, the parents randomized to the intervention group will be provided a yoga mat and participate in 30-min online led yoga sessions done at least twice weekly at the parent's pace using a secure, virtual platform (website). There will be 6 total yoga classes (one introduced per week for a 6 week period). Each yoga session will be divided into three components, which will vary in duration based on a curriculum designed *specifically* with the post-partum state of mothers in mind:

- **Yoga postures (Asana)** = low impact gentle postures meant to be done individually
- **Breathing techniques (Pranayama)** = deliberate modifications of breath such as rapid

diaphragmatic breathing, slow/deep breathing, alternate nostril breathing, breath holding
- **Meditation (Dhyana)** = guided meditation

The goal of this project is to conduct a pilot study to both allow optimization of engagement for a future definitive study, and to obtain empirical estimates of effect sizes and variability within the target study population.

5.2. Research procedures:[10]

Screening: see section 19

Randomization: The parent(s) who consent to participate in the study will be randomized using a 2x2 computerized block randomization (www.sealedenvelope.com/simple-randomiser/v1/lists). Participants will be stratified by NICU into two groups A) usual care B) yoga intervention. At the time of consent, the study coordinator will be **blinded to the randomization**, and the parent will be presented with a sealed envelope that identifies group A (control) and group B (intervention).

When both parents from the same family are eligible and interested in study participation, both will be consented and then randomized to the same group and followed separately with outcome surveys. Since parental outcomes are likely correlated. Prior to randomization we will ask parents to designate one parent as the primary study participant. Outcomes of the parent designated as the secondary study participant will be included in exploratory analyses that appropriately accounts for potentially correlated outcomes.

Intervention Group: Parents will receive an information sheet (see 'Welcome Packet YOGA GROUP' in "other attachments") explaining the practice of yoga, meditation and breathing exercises, FAQs about the study including how to access an electronic tablet while in the unit (if parent is unable to supply their own device), instructions on how to access study website and Zoom. Parents will also sign the study consent form and HIPAA authorization, receive a personal yoga mat, ear-pods (if needed), and details regarding compensation for the study (see 23.1). Participants have the opportunity to keep the ear-pods and yoga mat at the conclusion of the study. Parents in the intervention group will receive usual care for parent support offered in site NICU and be enrolled in a 6-week virtual yoga curriculum (see description in 5.1). They will also be asked to periodically fill out questionnaires throughout the study.

Control Group: Parents will sign the study consent and HIPAA forms. Information will be provided regarding the waitlist control model (see 5.1), and details about the compensation for the study (see 23.1). Parents in the control group will receive usual care for parent support offered in site NICU. They will also be asked to periodically via email to fill out identical questionnaires as the intervention group throughout the 6-week study period.

In general, a participating non-birth parent may skip self-report items that are considered not applicable, however there should be very few items that cannot be answered by either parent.

SELF-REPORT SURVEYS:

Yoga in the NICU Introduction Survey: demographic survey completed on a smart device at the time of enrollment. This survey (see supplemental materials) will include basic demographic data including age, ethnic background, race, education level, employment status, assessment of household food insecurity (measure of SES), assessment of prior mental health treatment (in the past 12 months before delivery of premature baby), assessment of yoga practice prior to and during pregnancy (for either birth parent or participating partner). We will also collect a personal email address where subsequent study surveys will be sent directly from REDCap.

To further assess parental stress, anxiety and depression, participants in both arms of the study will complete the following surveys (see supplemental materials)

1. *Depression, Anxiety, Stress Scale (DASS21):* to assess baseline participant depression, anxiety, and stress with these three self-report scales. Each of the three scales contains 7 items divided into subscales with similar content (depression, anxiety, and stress). Scores for depression, anxiety and stress are calculated by summing the scores for relevant items.
   - Two-times: at enrollment and conclusion of study

2. *Parental Stress Scale: Neonatal Intensive Care Unit* (PSS:NICU) a 26-item self-report scale designed to measure the degree of stress experienced by parents during hospitalization related to alterations in their parental role, the appearance and behavior of their child, and sights and sound of the unit.
   - Three times: at study start, midpoint (3 weeks) and at the conclusion of the study

3. *Postpartum Bonding Questionnaire* (PBQ) a 19-item self-report scale evaluating two factors involved in parent-infant bonding.
   - One time: at conclusion of the study

4. *Course Completion Survey* filled out by all participants at the conclusion of the study. There will be specific questions in this survey directed through branching logic to parents in the intervention group relating to safety and adverse events as well as parent opinions about the yoga intervention.

To address the baseline level of **post-partum depression** in the parent population, we will obtain individual responses and composite scores of *Edinburgh Postnatal Depression Scales* (EPDS) that have been administered by the unit Social Worker (as a regular part of parental NICU care). EPDS are entered by SW and stored in the infant EPIC chart (at UWMC) or the maternal chart (at SCH) (see section 5.4). For non-birth parent participants, or those participants who have not received a baseline EPDS by the unit social worker, the study coordinator will administer the EPDS (see other attachments) at the time of enrollment as part of this research study. The EPDS has been validated for use in male partners (Matthey S, et. al. *Journal of Affective Disorders* (2001)). In the circumstance that birth parent declines participation and non-birth parent consents to participation, we will not obtain birth parent EPDS scale.

Video and Web-based Resources: A study website will be designed using the www.rise.com (team url = nest) platform, a secure, user friendly, and engaging virtual platform for creating courses, guides and training content. Rise is easy to navigate, adaptable for all devices (mobile, tablet, PC), and supports multimedia activities. Study website will be designed to accommodate the 6-week study period (see webpage screen shots in supplemental materials). Yoga sessions (30 min each) will be pre-recorded and uploaded as links on the study website (see sample files in supplemental materials). A tablet device will be made available for use in the building (UWMC/SCH) for those parents who do not have a suitable personal device.

- UWMC: 9 tablets available for parents to borrow courtesy of NICU
- SCH: 3 tablets have been made available for parents to borrow courtesy of Child Health, Behavior and Development (CHBD) and Seattle Children's IT

Parental response and adherence to the online program will be assessed throughout the study period by tracking participation of the yoga sessions on the website (rise.com)

Zoom check-ins: There will be optional weekly virtual (Zoom) 'check-in sessions' available for

participants in the intervention group to speak directly with a yoga instructor in real time to ask questions. A recurring date/time will be selected by study coordinator, and yoga instructors will sign up to host sessions using a google document available in a shared drive. The study coordinator will substitute if a yoga instructor is unavailable, and relay questions from participants to the instructor via email. For Spanish speaking participants logging into the zoom session, we will call a Certified Language Interpreter (CLI) remotely (see other documents for CLI access) to interpret Q&A session.

5.3. Data sources that will be used to collect data about subjects:[11]

Electronic medical records will be reviewed (EPIC) at both institutions (University of Washington and Seattle Children's Hospital). REDCap database will be used to maintain demographic data and collect survey data from parents in intervention and control groups

5.4. Data to be collected, including long–term follow–up data:[12]

Infant Demographics: gestational age (weeks), birth weight (g), postnatal age at enrollment and discharge (days)

Infant characteristics: Apgar score (5 min), inborn (n), multiparous birth (n), primary and secondary diagnoses (BPD, NEC, PDA, RDS, GI/GU, cardiac, other), IVH (grade), mechanical ventilation at study start (y/n), length of assisted ventilation (days), length of stay (days), any breastfeeding at discharge (y/n)

Parent Demographics: age, ethnicity, race, highest level of education, employment status, marital status, other children at home, mode of delivery (vaginal/c-section), experience with yoga before and during pregnancy

Parent characteristics: Edinburgh Postnatal Depression Scale scores (located in the infant EPIC chart (UWMC) or the maternal EPIC chart (SCH), or administered by study coordinator at time of enrollment)

Parent study data: YIN Introduction Survey, EPDS (if not administered by unit social worker) DASS21, PSS:NICU, PBQ, post-study questionnaire, participation in yoga intervention (tracked on rise website): sessions started (n), duration of participation (min)

6. Data and Biospecimen Banking[13]

6.1. Complete list of the data and/or biospecimens to be included in the bank:[14]

- N/A

6.2. Location of data and/or biospecimen storage:[15]

N/A

6.3. List of those with direct access to data and/or biospecimens in the bank:

N/A

6.4. Length of time data and/or biospecimens will be stored in the bank:

N/A

6.5. Procedures for protecting the confidentiality and privacy of the subjects from whom the data and/or biospecimens were collected:[16]
N/A

6.6. How the data and/or biospecimens will be made available for future use:

6.6.1. Who can request data and/or biospecimens from the bank:
N/A

6.6.2. Format in which data and/or biospecimens will be provided:
N/A

6.6.3. Process for investigators to request data and/or biospecimens:[17]
N/A

6.6.4. Restrictions on future use:[18]
N/A

6.6.5. Plan for providing data results from banked data/biospecimens:
N/A

7. Sharing of Results

7.1. Plan to share results with subjects/others:[19]
No. Results will be analyzed with the goal of publication in a medical or research journal.

8. Study Timelines

8.1. Duration of an individual subject's participation in the study:
6 weeks

8.2. Duration anticipated to enroll all study subjects:
4-6 months

8.3. Estimated date for the investigators to complete this study:
Anticipate completing the study period Jan 2022. Anticipate completion of data analysis May 2022, anticipate manuscripts Sept 2022.

9. Study Population[20]

9.1. Inclusion criteria for each subject population (e.g., patients, parents, providers):

- NICU inpatients born <32 weeks gestation at birth and/or <1500g, OR estimated length of stay ≥ 6 weeks
- Parents of current NICU inpatients born <32 weeks gestation at birth and/or <1500g OR estimated length of stay ≥ 6 weeks
- Parents with any level of experience with yoga (none to regular practitioner)
- Parent age ≥ 18 years
- Parent speaks and reads in either English or Spanish

9.2. Exclusion criteria for each subject population:

- Expected length of stay of NICU inpatient < 6 weeks
- Parent only speaks or reads in a language other than English or Spanish
- Parent plans to relinquish child
- Child or parents are too unstable as assessed by the Attending Physician

9.2.1. Justification if subjects who use a language other than English or subjects with a parent/legally authorized representative (LAR) who uses a language other than English, will be excluded from the research:[21]

The goal of this pilot study is to generate data to support a parent mindfulness intervention of yoga, breath work, and meditation to reduce stress, depression, and anxiety of parents with infants hospitalized in the NICU. Based on the small sample of parent participants, the inclusion of multiple languages to this study population may confound our research or render appropriate analysis of the data impractical. Further limitations of including a population that uses a language other than English or Spanish include lack of appropriate validated instruments, surveys, or assessments published in other languages to determine parental stress and parent-child bonding for NICU parents.

To improve equity within this project the PI (Dr. Sara Neches) is submitting this modification of the current IRB to include Spanish speaking parents. The results of this pilot study will be used to generate a universally accessible parent mindfulness intervention that is inclusive of all ethnicities and languages with the goal to be inclusive of every parent in the NICU regardless of their language of care.

9.3. Populations with special considerations, involved in the study:[22]

☒ Children/Teenagers[23]
Risk assessment specific to this vulnerable population and additional safeguards:[24]
Neonates admitted to the NICU at University of Washington and Seattle Children's Hospital are subjects, parents of neonates are participants.

☐ Children who are Wards of the State[25]
Risk assessment specific to this vulnerable population and additional safeguards:
N/A

☐ Adults Unable to Consent [26]
Risk assessment specific to this vulnerable population and additional safeguards:
N/A

☒ Individuals who use a language other than English[27]
Anticipated language(s) for subjects and their parent(s)/LAR:
All study documents (e.g consent forms, study information sheets, posters), self-report scales, and the study website have been translated into Spanish using the company TransPerfect (official translation certification will be attached in other documents). Given the small sample size of parents participating in this pilot study, the yoga videos will be available on the study website with Spanish subtitles. We are currently working on

obtaining grant funding for the yoga videos to be recorded with Spanish language voice over.

Process to ensure study information is available throughout the research to individuals who use a language other than English:[28]

Study coordinator or her designee will plan to enroll parents using translated study consent forms with in-person interpretation or via video or voice interpreter. Zoom sessions for parents to ask questions of a yoga instructor will also be assisted by a telephone interpreter.

☐ Neonates of Uncertain Viability or Non–Viable Neonates[29]

Risk assessment specific to this vulnerable population and additional safeguards:

N/A

☐ Pregnant Women[30]

Additional safeguards:

N/A

☐ Prisoners[31]

Additional safeguards:

N/A

☐ Economically or educationally disadvantaged persons[32]

Additional safeguards:

N/A

10. Number of Subjects

10.1. Total number of subjects to be enrolled locally:[33]

At least 20 parents of NICU inpatients, 20 NICU inpatients

10.2. Total number of subjects to be enrolled across all participating sites:[34]

20 parents (and potentially their partners) randomized to control group (10 from UWMC and 10 from SCH)
20 parents (and potentially their partners) randomized to intervention group (10 from UWMC and 10 from SCH)

10.3. Number of screened subjects versus the actual number enrolled in the research:[35]

All infants at UWMC and SCH NICU will be screened if born <32-weeks gestation and/or <1500g or LOS estimated >6 weeks

10.4. Power analysis:

According to research by Pace et al. (2016) the proportion of parents with low birthweight infants hospitalized in NICUs who endorsed anxiety approached 50%. Smaller studies of parents of very low birthweight infants have shown rates of depression in mothers and fathers ranging from 30-60% (Meyer, EC et al (1994), Davis, L (2003), Mackley, AB, 2010). The study population in Aim 1 (NICU parents) reported a higher level of baseline anxiety and stress (~60%) regarding having an infant in the NICU.

Based on this information, and an anticipated 20-30% decrease in stress and anxiety with yoga practice, we will need a sample size of 16 parents enrolled in each group to see a power of 0.80 at an alpha level of 0.05. Given this information, and the possibility of attrition of study participants, we will plan to enroll 20 parents in control and 20 parents in intervention group for this pilot study.

11. Withdrawal of Subjects

11.1. Anticipated circumstances under which subjects will be withdrawn from the research without their consent:

N/A

11.2. Procedures for orderly termination:

N/A

11.3. Procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection and withdrawal from data/biospecimen banking:

Parents may withdraw from the study at any time. Data will be retained for analysis even if participant withdraws. Parents will only receive compensation for the portion of the study completed.

12. Risks to Subjects

12.1. Reasonably foreseeable risks to subjects (include each study population, each arm, and optional procedures):

Infants: risks related to breach of confidentiality due to improper use of personally identifying medical information. To minimize these risks as much as possible, personally identifying information will be stored in the secure manner described in 15.1 below, and only de-identified aggregated data will be used in the analysis.

Parents:
Control group: Parents will receive usual care available for parental support. There are minimal risks associated with filling out the research questionnaires (depression, social anxiety, parental-child bonding, NICU related stress).

Intervention group: Parents in the intervention group will receive usual care for parent support. There are minimal risks associated with filling out the research questionnaires (depression, social anxiety, parental-child bonding, NICU related stress). There is minimal risk of physical injury in the yoga intervention group, as parents will be performing low impact postures designed with the specific physical limitations of post-partum mothers in mind.

Edinburgh Postnatal Depression Scale scores of parents in both control and intervention groups will be accessed from the infant or maternal charts (or administered separately if not administered by social worker or if non-birth parent is participant), thus there are risks related to breach of confidentiality due to improper use of personally identifying medical information.

12.2. Procedures with unforeseeable risks:

N/A

12.3. Procedures with risks to an embryo or fetus should the subject be or become pregnant:
N/A

12.4. Risks to others who are not subjects:
N/A

12.5. Procedures performed to lessen the probability or magnitude of risks:
Risk of breach of confidentiality will be minimized by storing personally identifying information in the secure manner described in 15.1 below, and only de-identified aggregated data will be used in the analysis.

Instructions of how to minimize risks of physical injury will be explained prior to performing physical postures, and during each session. There will be weekly virtual check-in sessions for participants to ask questions in real time to a yoga instructor.

13. Potential Benefits to Subjects

13.1. Potential benefits that individual subjects may experience from taking part in the research:[36]
Decrease parental stress, anxiety, and depression in the NICU, helping parents cope with the birth and hospitalization of a preterm infant, improve parent-child bonding.

14. Data Analysis/Management

14.1. Data analysis plan, including statistical procedures:
All data will be collected in REDCap spreadsheets and analyzed using STATA 17.0 statistics and data analysis software using appropriate statistical tests. Additional assistance with statistics will be provided by the Institute of Translational Health Sciences (ITHS) Research Services at the UW.

14.2. Quality control procedures for collected data:[37]
Data will be reviewed by study mentors for accuracy

15. Confidentiality and Privacy[38]

15.1. Procedures to secure research records[39], data, and/or biospecimens during storage, use, and transmission:
Record ID, identifying info (name, email address), infant demographics, and participant responses to self-report scales will be stored in a UW REDCap database. Note that any EPDS administered to either birth parent or non-birth parent as part of this study will be linked to the participant by their record ID number. There will be no identifying parent information on any paper forms. Results of EPDS will then be entered by the study coordinator into a secure REDCap form according to participant record ID.

Links to study surveys will be sent to participants directly from REDCap via email and data. Infant medical record numbers and surname will be saved on a password protected file in the Seattle Children's computer server. There will be no patient identifying information associated with the study website.

When using Zoom the following actions will be taken to protect participant confidentiality and privacy: (1) Use the latest version of Zoom available; (2) Make the meeting private; (3) Require a password for meeting entry; (4) Disable private chat. There will be no audio and/or video recording of zoom sessions.

15.2. Steps that will be taken to protect the privacy interests throughout the study:[40]

Yoga sessions are accessed with any smartphone, tablet or PC using the virtual platform, and can be done at the bedside or in the privacy of the parent's lodging or home. Access to the rise website is secure with unique participant username and password. Location of participation is at the discretion of the participant.

15.3. Location where the data and/or biospecimens will be stored:

REDCap database and statistical software. See 15.1 above

15.4. Length of time data and/or biospecimens will be stored:

1 year following the conclusion of the study to allow for analysis and publication

15.5. Individuals with access to data and/or biospecimens:

Sara Neches, MD (Principal Investigator), Sandra Juul, MD PhD (faculty Mentor)

15.6. Process for the transmission of data and/or biospecimens outside Seattle Children's:

15.6.1. List of data and/or biospecimens that will be transmitted:

Data will not be transmitted outside of Seattle Children's server except for de-identified data being moved to statistical software package for analysis.

15.6.2. Individual(s) who will transmit data:

Sara Neches, MD (principal investigator)

16. Provisions to Monitor Data to Ensure the Safety of Subjects[41]

16.1. Plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe:[42]

Principal Investigator Sara Neches will evaluate self-report data collected in both arms of the study weekly, and report to clinical social worker at specific NICU site regarding any individual parent with concerning symptoms of depression, anxiety or stress that may not have previously been identified.

16.2. Data reviewed to ensure safety of subjects:

Depression, Anxiety, and Stress Scale (DASS21), Parental Stressor Scale: NICU (PSS:NICU), Postpartum Bonding Questionnaire (PBQ).

16.3. Safety information collection procedures:

Individual REDCap surveys will be assigned directly to parents via email. Data will be stored in a longitudinal secure REDCap database.

16.4. Frequency of cumulative data review:

weekly

16.5. Conditions that trigger an immediate suspension of the research:
N/A

17. Use of Social Media

17.1. Types of social media to be used and how:

Study website: https://rise.com (team url = nest)
Parents will be invited to the website, provided a username and prompted to create a unique password. There will be no patient information on the website, and no means for synchronous communication. There will be a means of asynchronous communication (email) between the participant and PI during the study for questions or concerns.

Zoom video conferencing: UW HIPAA secure zoom account
A recurring zoom meeting will be scheduled weekly for parents to communicate directly with a yoga teacher. See 15.1 for privacy related to zoom

17.2. Measures in place to protect the privacy or confidentiality of subjects:[43]

No identifying information regarding the patient (infant) will be shared during this study. Weekly zoom check-ins will be voluntary and for parents participating in the yoga intervention only, no names or patient information will be disclosed during these meetings.

17.3. Types of communications that will be submitted to the IRB for review:[44]

Email communication with parents will be directed through REDCap and limited to periodic requests to fill out REDCap surveys during the study period, emails containing gift card links, and reminder emails.

17.4. If user-generated content will be active, how it will be monitored and what actions will be taken to ensure subject safety and study integrity:

No user generated content

18. Research Related Injury[45]

18.1. Available compensation in the event of research related injury:
N/A

19. Recruitment Methods[46]

19.1. When, where, and how potential subjects will be recruited[47]:

University of Washington and Seattle Children's Hospital: All infants born <32 weeks gestation and/or <1500g or with a length of stay estimated to be >6 weeks, and who has been admitted to the University of Washington NICU or Seattle Children's NICU will be screened for eligibility by principal investigator (Sara Neches).

A screening form (see other attachments) will be maintained on REDCap to document patients screened, reasons for eligibility/ineligibility, reasons for nonparticipation of eligible parents. A recruitment log (see other attachments) will be maintained in a password protected database located on the Seattle Children's server containing MRN of enrolled infant, record ID of parent participant and date of consent for data collection purposes. PI will send secure email with names of patients who meet inclusion criteria to weekly attending of record for final approval to contact (re: patient/parent stability). PI or representative (resident/fellow or APP caring for infant) will make first contact with parent with a standardized bedside conversation or phone

call to explain study. If family is interested in more information PI will meet family in person in the NICU at least 10 days after admission. Following consent, the introductory survey and first set of self-report scales will be completed during enrollment process.

Participants in the intervention group will be guided on how to log into the study website, and will be instructed to respond to emails with links for self-report scales to be completed throughout the study period. Participants in the control group will be instructed to respond to emails with links for self-report scales to be completed throughout the study period. The first week of intervention will begin on the Monday after enrollment or 10-14 days after infant admission to the NICU.

Note that UWMC is a birth hospital, thus 10 days after admission will likely be 10 days of life. Infants are typically referred/transferred to SCH NICU from other NICUs, and thus 10 days after admission may reflect different ages. The inclusion criteria for both institutions will be the same.

19.2. Steps that will be taken to protect privacy during the recruitment process:[48]
Site enrollment log will be maintained in a password protected database located on the Seattle Children's server. Screening form will be maintained by the site PI on a secure REDCap database, and will contain the following information: Record ID, screening date, mother/father, eligibility (yes/no), attending approval to enroll (y/n), whether they were enrolled, and if not enrolled, the reason why. If the parent is enrolled as a study participant, document that consent was obtained, and the study ID number. MRN numbers of infants will be stored on a separate recruitment log in a password protected excel sheet on the Seattle Children's server. MRN number is required to access infant demographic information.

19.3. Sources of subjects:[49]
All parents of infants born <32 weeks gestation or <1500 grams will be screened by study coordinator.

Subjects will be recruited by screening of the electronic medical record (EPIC) at the University of Washington and Seattle Children's NICUs

19.4. Methods that will be used to identify potential subjects:
See 19.1

19.5. Materials that will be used to recruit subjects:[50]
A Study poster will be used to inform staff, faculty, and parents about the study. Posters will be available in the NICU Attending office and NICU Staff lounges and staff bathrooms at both institutions to increase awareness of the study

19.6. Recruitment methods not controlled by Seattle Children's:
N/A

20. Consent/Assent/Permission[51]

20.1. Consent/assent/permission process:[52]
The Attending health care provider will approve the research coordinator to meet and discuss the study with potential subjects. If either parent is interested in learning more about the study,

the research coordinator or investigator will be notified so they can discuss the study with the parent and seek consent in person. Investigators will only approach a family after infant's attending heath care provider gives permission and family indicates that they are interested in further information about the study. The parent may withdraw from study at any time. Investigator will retain the original signed document, and a copy will be provided to the subjects. Consent for participation must be obtained after the baby is at least 10 days of age (UWMC) or has been admitted at least 10 days (SCH). An identical consent form will be presented by the research coordinator to both control and intervention groups reviewing the practice of yoga, meditation and breathing exercise as well as the details of the study.

20.1.1. Alternative way of obtaining consent/assent/permission information for individuals who are not able to receive/access/use the electronic consent system being used or explanation as to why an alternative process is unnecessary:[53]

Consent form will be signed on paper, no electronic consent system will be used. Any initial parent REDCap surveys or demonstration of the study website will be done on iPads made available specifically for parents participating in the YIN study.

20.1.2. Where the consent/assent/permission process will take place:
At the site where infant is admitted (UWMC or SCH NICU) in person with parent(s).

20.1.3. Steps that will be taken to protect privacy during the consent/assent/permission process:[54]
Consent discussion will take place in patient's individual room or private conference room if available, keeping in mind the privacy of the parent and infant.

20.2. Plan for documenting consent/assent/permission:[55]
Consent will be documented in writing on a paper form provided at the time of the consent conversation. REDCap screening form will document date of consent. REDCap randomization form will record date of randomization and outcome of randomization (Group A or B).

20.2.1. Plan to confirm that the individual who provides the electronic signature[56] is the subject (or their parent/LAR), when the signature is not personally witnessed by a member of the study team or explanation as to why such a plan is unnecessary:[57]
Study coordinator will only receive actual signatures of participants on paper consenting forms. NO electronic signature will be used.

20.2.2. If using electronic consent, plan to manage consent documentation over the life of the study in a way that maintains integrity and accessibility:[58]
N/A

20.2.3. If consent/permission will be documented in writing (check one):
☒ "SOP: Written Documentation of Consent (HRP-091)" will be followed.
☐ "SOP: Written Documentation of Consent (HRP-091)" will not be followed.
Process of documenting consent:[59]
N/A

20.2.4. If consent/permission will not be documented in writing (check all that apply, *complete Section 21.13 to request a Waiver of Documentation of Consent*)[60]

☐ A written statement/information sheet describing the research will be provided to subjects.[61]

☐ A written statement/information sheet describing the research will not be provided to subjects. Explain: N/A

☐ A consent script will be used.[62]

20.3. Waiting period available between approach and obtaining consent/assent/permission:
N/A

20.4. Process to ensure ongoing consent/assent/permission:
N/A

20.5. If this box is checked, "SOP: Informed Consent Process for Research (HRP-090)" will be followed: ☒

20.6. If "SOP: Informed Consent Process for Research (HRP-090)" will not be followed, address the following:[63]

20.6.1. Role of the individuals listed in the application as being involved in the consent process:
N/A

20.6.2. Time that will be devoted to the consent discussion:
N/A

20.6.3. Steps that will be taken to minimize the possibility of coercion or undue influence:
N/A

20.6.4. Steps that will be taken to ensure the subject's understanding:
N/A

20.7. **Individuals who use a language other than English**

20.7.1. Presentation of Research Information and Documentation:

☒ Appendix A-10 of the Investigator Manual will be followed[64]

☐ Short form procedures may be used per HRP-091. If so, choose applicable box(es):

☐ Per section 5.5.1

☐ Per section 5.5.2

☐ Appendix A-10 of the Investigator Manual will not be followed. Explanation of procedures not following Appendix A-10:

20.8. **Subjects Who Are Not Yet Adults (Infants, Children, Teenagers)**

20.8.1. Process used to determine whether an individual has not attained the legal age of consent under the applicable law of the jurisdiction in which the research will be conducted (e.g., individuals under the age of 18 years):[65]

Parents under the age of 18 will be excluded from participation. Individuals will be asked their age at the time of enrollment. Since to be included in the study, minors

must be infants in the NICU, no additional process is needed to determine whether they have reached the age of majority.

20.8.2. Parental permission will be obtained from:[66]

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☒ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Neither parent.[67]

20.8.3. Process used to determine an individual's authority to consent to each child's general medical care if permission will be obtained from someone other than parents:[68]

N/A

20.8.4. Assent will be obtained from:[69]

☐ All children.

☐ Some children. Specify: N/A

☒ None of the children. Explain: subjects are neonates, intervention for parents

20.8.5. Procedures for obtaining and documenting assent:

N/A

20.8.6. Plan for re-approaching children who have reached the age of majority to obtain consent:[70]

N/A

20.9. **Cognitively Impaired Adults/Adults Unable to Consent**[71]

20.9.1. Process used to determine whether an individual is capable of consent:

N/A

20.9.2. Individuals from whom permission will be obtained in order of priority:[72]

N/A

20.9.3. Assent will be obtained from:

☐ All of these subjects.

☐ Some of these subjects. Specify: N/A

☐ None of these subjects. Explain: N/A

20.9.4. Process for obtaining and documenting assent:[73]

N/A

20.10. **Waiver or Alteration of Consent/Assent/Permission**[74]

20.10.1. Reasons for requesting a waiver or alteration of informed consent/assent/permission:[75]

N/A

20.10.2. Consent/Assent Waiver/Alteration Criteria justifications:[76]

20.10.2.1. The research involves no more than minimal risk to the subjects because:
N/A

20.10.2.2. The waiver or alteration will not adversely affect the rights or welfare of the subjects because:[77]
N/A

20.10.2.3. The research could not practicably be carried out without the waiver or alteration because:[78]
N/A

20.10.2.4. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format because:[79]
N/A

20.10.2.5. Whenever appropriate, the subjects will be provided with additional pertinent information after participation:
N/A

20.10.3. If the research involves a waiver of the consent process for emergency research, provide sufficient information for the IRB to make it determinations:[80]
N/A

20.11. **Waiver of Written Documentation of Consent/Permission (address one option):**

20.11.1. Option 1:

- The research involves no more than minimal risk to the subjects because:
  N/A
- The research involves no procedures for which consent is normally required outside of the research context because:
  N/A

20.11.2. Option 2:

- The principle risk of a signed consent document would be the potential harm resulting from a breach of confidentiality because:
  N/A
- Both are true:

  ☐ The only record linking the subject and the research would be the consent document

  ☐ The subject or LAR will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

20.11.3. Option 3:

- The research involves no more than minimal risk to the subjects because:
  N/A

- The subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm. Explain:
  N/A
- There is an appropriate alternative mechanism for documenting that informed consent was obtained. Explain:
  N/A

21. HIPAA Authorization and RCW Criteria

21.1. HIPAA Authorization (check all boxes that apply):

- ☐ The study does not involve the receipt, creation, use and/or disclosure of protected health information (PHI).[81]
- ☒ HIPAA authorization will be obtained as part of a signed consent form.
- ☒ The study will access PHI without prior authorization from subjects (including for recruitment purposes – e.g., reviewing the medical record to determine eligibility). *Complete Section 21.2 to request Waiver of HIPAA Authorization*.
- ☐ Subjects will review a written statement/information sheet with the appropriate HIPAA language but will not provide a written signature. *Complete Section 21.2 below to request an Alteration of HIPAA Authorization*.[82]
- ☐ Other. Explain:[83]
  N/A

21.2. HIPAA Waiver/Alteration Criteria: [84]

21.2.1. Reasons for requesting a waiver or alteration of HIPAA Authorization:
Research coordinator or designee will review medical record to determine eligibility for this study.

21.2.2. The use or disclosure of PHI involves no more than a minimal risk to privacy of individuals, based on, at least the presence of the following elements:

21.2.2.1. An adequate plan to protect the identifiers from improper use and disclosure:

Record ID, screening date and parent surname, parent email address will be saved in the screening form, and additional data regarding demographics and characteristics of NICU baby and parent will all be collected and stored in a secure REDCap database. Infant surname and MRN will be stored in a recruitment sheet located in a password protected file on the Seattle Children's Server.

21.2.2.2. An adequate plan to destroy identifiers at earliest opportunity consistent with conduct of research:

Identifiers saved in REDCap and SCH server will be destroyed within one year of collection.

21.2.2.3. Assurances that PHI will not be reused or disclosed to any other party or entity, except as required by law or for authorized oversight of the research:

PHI collected will not be reused or disclosed to any entity, except as it relates to concerns for parent safety (e.g., unit social worker will be

contacted if depression or anxiety scales are concerning and further intervention for parent is advised).

21.2.3. The research could not practicably be conducted without the waiver or alteration of authorization:

Without the waiver, screening for eligibility would not be possible. All parents of infants in the NICU would need to be approached, which would unnecessarily burden those who are ineligible for the research.

21.2.4. The research could not practicably be conducted without access to and use of the PHI:[85]

This research requires the screening of patients in the NICU prior to consent to target the study to the appropriate population.

22. Payments/Costs to Subjects[86]

22.1. Amount, method, and timing of payments to subjects:[87]

Parents participating in both control and intervention groups will receive a total of $50 in gift cards (tango cards) during the course of the study:

- $20 after completing 1 week of intervention, Intro survey, DASS21, first PSS:NICU.
- $10 after completing 3 weeks of intervention and second PSS:NICU
- $20 after completing 6 weeks of intervention, second DASS21, third PSS:NICU, PBQ, course competion survey

Distribution of tango cards will be done via email by the study coordinator and tracked in both a REDCap form and an excel sheet using participant randomization number and record ID (see other attachments)

Each family or pair of participants (partners) may receive only one set of gift cards totaling $50. This will be made clear in the study consent form and parent information sheets.

22.2. Reimbursement provided to subjects:[88]

22.3. Additional costs that subjects may be responsible for because of participation in the research:[89]

Free WiFi is available for participants if logging into the study website from UWMC, SCH, Hotel Nexus, or the Ronald McDonald house. Study coordinators are unable to determine if free WiFi will be available if participants log into the study website from another location not listed above.

23. Community-Based Settings[90]

23.1. Site(s) or location(s) in the community where the research team will conduct the research:

N/A

23.2. Composition and involvement of any community advisory board:

N/A

23.3. For research conducted outside of the organization and its affiliates:[91]

23.3.1. Site-specific regulations or customs affecting the research:

N/A

23.3.2. Local scientific and ethical review structure:

N/A

24. Resources Available

24.1. Qualifications (e.g., training, education, experience, oversight) of investigator(s) to conduct and supervise the research:[92]

Sara Neches. MD is a current Neonatal-Perinatal Medicine fellow at the University of Washington/Seattle Children's Hospital, and holds a BA in Psychology from Hunter College, The City University of New York. Additionally, she has been a practitioner of yoga for over 15 years. Dr. Neches is supported in this research by Dr. Sunny Juul Professor and Division Head of Neonatology at the University of Washington. Dr. Juul has ample experience in running clinical trials, as she has previously led both single site studies, and multicenter trials. She is the PI of the NINDS funded Preterm Epo Neuroprotection Trial (PENUT; NCT01378273), and multi-PI of the High-Dose Erythropoietin for Asphyxia and Encephalopathy trial (HEAL; NCT02811263). Dr. Juul is also a certified Yoga and Meditation teacher, having taken a 200-hour Yoga Teacher Training in December 2019, and a 20-hour Yoga Philosophy class in May 2020. Dr. Dennis Mayock was an integral part of AIM 1 of the YIN study (to assess feasibility), and serves as a research advisor to Dr. Neches.

24.2. Other resources available to conduct the research:[93]

We plan to recruit a total of 40 parents participants (20 from UWMC NICU and 20 from SCH NICU). Based on a query of NeoData software for the years 2018-2020, there are approximately 10-20 admissions monthly of infants meeting the screening criteria (<32 weeks gestation or <1500 grams) at the UWMC and 5-14 admissions monthly of infants meeting criteria at Seattle Children's NICU.

We need to recruit a total of 20 parents from each NICU site over the 5-month recruitment period. We will begin enrolling parents in the study in Aug 2021 and recruit parents for a total of 5 months (Dec 2021). Sara Neches (PI) will dedicate research time to the intervention as well as the collection and analysis of data. As detailed in the proposal above, research will be conducted using a virtual web-based platform to be accessed by participants in a location determined by the participant but not limited to bedside with neonate at UWMC or SCH NICU, Seattle Children's Chapel and Meditation room as made available by chaplain, hotel or other lodging.

This study poses minimal risk to subjects. Should concerns arise regarding the psychological state of parents throughout the study these concerns will be brought to the attention of the site NICU social worker.

25. Coordinating Center Procedures

25.1. Coordinating center institution:

Seattle Children's Hospital

25.2. If Seattle Children's is the coordinating center:

25.2.1. Process to ensure communication among sites:[94]

Prior to the initiation of recruitment Sara Neches will communicate with attending physicians, APPs at both sites, fellow physicians, site NICU leadership, social workers at both UWMC and SCH to alert staff of project, recruitment methods and study time-period. Sara Neches will remain in direct contact with leadership in both sites and will ensure modifications to the study proposal are accurately reflected in the study materials. Sara Neches will remain in close contact throughout the study time-period regarding recruitment, enrollment, and randomization of participants. General study documents (blank consent form, study packet, mindfulness readings, blank surveys) will be available to all investigators via shared drive.

25.2.2. Process to ensure all site investigators conduct the study according to the IRB approved protocol and report all non-compliance:

Sara Neches will periodically report progress during Dr. Juul's clinical study meeting where individual projects are discussed with full study team. Copies of this IRB will be presented to all site investigators.

25.2.3. Process to ensure all required approvals are obtained at each site:

See 25.2.1.

25.2.4. Process to ensure all sites are informed of any problems and/or interim results:

Besides weekly progress reports through the clinical study group, Sara Neches will plan to check in with NICU leadership of both sites (UWMC and SCH) at the midpoint of the study (Oct 2021) to present interim results and discuss any problems with recruitment or participation.

26. International Center for Harmonization of Good Clinical Practice (ICH-GCP)

26.1. If you have committed to conducting the described study per ICH-GCP, check this box: ☐[95]

- This is generally applicable for contracts with industry-sponsored studies or sponsor protocols. See your contract/agreement or Sponsor Documentation if you are unsure.
- Note that completing GCP training is a separate activity and does not automatically mean that you have committed to conducting the study per ICH-GCP.
  If you check the box, upload a current curriculum vitae (CV) for the PI to the "Other Attachments" section of the "Local Site Documents" SmartForm.

[1] Provide a list of the participating sites (pSITEs). pSITEs are those sites outside Seattle Children's that will rely on the Seattle Children's IRB as their IRB of record. All pSITEs should be listed even if no study procedures will occur at the site. Remove the heading if this is not a study where Seattle Children's IRB will serve as the IRB of record for other institutions.

[2] Include information if this protocol is associated with other IRB-approved studies (e.g. is this application the next part/phase of a previously approved application.

[3] In clinical trials, an endpoint is an event or outcome that can be measured objectively to determine whether the intervention being studied is beneficial. Some examples of endpoints are survival, improvements in quality of life, relief of symptoms, and disappearance of the tumor.

[4] Include information on a drug or biologic in this section if: (1) the study specifies the use of an approved drug or biologic; (2) the study uses an unapproved drug or biologic; (3) the study uses a food or dietary supplement to diagnose, cure, treat, or mitigate a disease or condition; or (4) data regarding subjects will be submitted to or held for inspection by the Food and Drug Administration (FDA). Only include information on a device in this section if: (1) the study evaluates the safety or effectiveness of a device; (2) the study uses a humanitarian use device (HUD) for research purposes; or (3) data regarding subjects will be submitted to or held for inspection by the FDA. Please note that mobile medical applications may meet the definition of a device – see FDA Guidance.

[5] See the Investigator Manual HRP-103 for sponsor requirements for FDA-regulated research.

[6] Explain what IND exemption category applies to the drug and why. Note that a drug is not exempt from an IND unless all criteria for one category are met. See "HRP-306: Drugs" for more information.

[7] Explain what IDE exemption category applies to the device and why. Note that a device is not exempt from an IDE unless all criteria for one category are met. See "HRP-307: Devices" for more information.

[8] Explain why the device is NOT a significant risk device. A significant risk device means an investigational device that: (a) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (b) is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; (c) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (d) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

[9] Be sure to indicate if controls will be included and include information about why control arms are ethically acceptable.

[10] Describe all of the research procedures being performed. Be sure to make it clear which procedures apply to each subject population. When applicable, describe how research procedures differ from standard of care and/or affect standard of care. Describe any audio/video recording that will be involved.

[11] Attach all surveys, scripts, and data collection forms to the "Supporting Documents" page.

[12] Include information about the frequency of data collection.

[13] See HRP-001 - SOP – Definitions for definition of banking. Type N/A if not applicable. If the data is subject to NIH Genomic Data Sharing Policies (e.g. you will submit data to dbGaP, NDAR, FITBIR), indicate here.

[14] If applicable, include a list of identifiers that will be banked.

[15] Be general (e.g., researchers' lab, clinic, etc.)

[16] Generally, data and/or biospecimens should be released in a coded, non – identifiable manner.

[17] Include a description of the process used to verify and document that any required approvals have been obtained prior to release of data/biospecimens from the bank.

[18] You can allow for use for broad purposes

[19] This includes putting results and/or data in the subject medical records.

[20] If your population will differ from the representative population where the study will take place (e.g., race, ethnic group, or gender), provide a rationale for the differences.

[21] Seattle Children's IRB prohibits the exclusion of populations who use a language other than English from research unless there is sufficient justification for the exclusion. In most circumstances, the cost of translation and/or interpreter services will not be considered sufficient justification for the exclusion of participants who use a language other than English in accordance with NIH guidelines. ("Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources." 59 FR 11146, March 28, 1994). See Investigator Manual HRP-103 for additional information.

[22] If you check a box below, be sure to include the additional considerations associated with the population.

[23] Refer to HRP-416 CHECKLIST: Children.

[24] If the study is minimal risk, explain why. Must also include, as applicable: (1) why direct benefits are anticipated, (2) why risks are justified by anticipated benefit and/or the relationship between risk and prospective benefit compared to available alternatives, (3) why risk represents only minor increase over minimal risk, (4) how study procedures are reasonably commensurate with those inherent to the child's actual or expected conditions, (5) whether the interventions/procedures are likely to yield generalizable knowledge about the participant's condition and why it is of "vital importance" to understanding or amelioration of the participant's underlying disorder or condition, and (6) an explanation of what alternative methods/approaches were considered to make the above assessments (as applicable).

[25] This population may be wards of the state or any other agency, institution, or entity. Refer to HRP-416 CHECKLIST: Children, Section 6, for additional guidance on required considerations for this population.

[26] This refers to both cognitive impairments and adults who are incapacitated for any other reason. As applicable, refer to HRP-417 CHECKLIST: Cognitively Impaired Adults.

[27] This includes subjects and their parent(s)/LAR.

[28] Applicable to information conveyed in writing and verbally. For example, your plan could include translating all study documents and having a study team member or interpreter available who can speak the language to answer questions.

[29] Refer to HRP-413 CHECKLIST: Neonates and HRP-414 CHECKLIST: Neonates of Uncertain Viability.

[30] Refer to HRP-412 CHECKLIST: Pregnant Women.

[31] Refer to HRP-415 CHECKLIST: Prisoners

[32] Indicate how you will ensure that there is no coercion or undue influence

[33] A subject is considered "enrolled" when they consent to be in the study.

[34] Only applicable for multisite studies.

[35] i.e., numbers of subjects excluding screen failures.

[36] Payment for participation is not considered a benefit.

[37] For example, data will be double entered, data will be reviewed by another study team member to ensure accuracy, etc.

[38] If your study is multisite and there are differences in how confidentiality will be maintained by the coordination center and our local site, this should be explained in this section (e.g. local site will have samples that are linked to a person's name, but the coordination center will only receive coded samples without any links). Confidentiality regarding use of Social Media will be explained in a protocol section below.

[39] Including the signed consent/assent/permission forms and any information/documentation collected during the consent process.

[40] Privacy refers to persons and their interests in controlling the access of others to themselves. For example, based on privacy interests, people want to control the time and place where they give information, the nature of the information they give and who receives and can use the information.

When providing a response, consider the subject population and nature of the study. For example, persons might not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center that is clearly identified as such by signs on the building.

[41] Applicable for studies that present more than minimal risk.

[42] Include information about who (describe in terms of role or group) will review the data.

[43] This should be specific to the social media you are using for the research.

[44] All communications that are directed towards subjects and specific to a particular study will require prior IRB review and approval. All non-IRB reviewable communications can be described in general terms by category – news stories, relevant publications – and representative examples of each can be provided.

[45] Applicable if the research involves more than minimal risk to subjects. If minimal risk, this section is N/A.

[46] If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) those methods should also be described here.

[47] If the study will enroll or seek permission from individuals who speak a language other than English and recruitment methods will differ for these individuals (e.g., they will be approached by a bi-lingual person outside the study team), be sure your description covers these methods as well.
[48] For example, subjects will be initially approached in a private room or a letter rather than a postcard will be sent when the study name may disclose health information about the potential subject.

[49] For example, medical records, CIS, clinical databases, other study records. If the study will access PHI for recruitment purposes without prior authorization from subjects, please address this in the HIPAA Authorization section below.

[50] Attach copies of these documents to the Recruitment Materials section of the study SmartForm. For printed advertisements, attach the final copy. For online advertisements, attach the final screen shots (including any images). When advertisements are taped for broadcast, send the final audio/video tape to IRB@seattlechildrens.org. You may attach the wording of the advertisement to the SmartForm prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.

[51] "Permission" refers to consent obtained from a parent or LAR.

[52]Address the following in the response, as applicable:

1. How you will ensure that subjects and/or their parent/LAR have sufficient opportunity to discuss and consider whether or not to participate in the research.
2. Speak to the suitability of the intended consent process for the intended audience, taking into consideration the subject's and/or parent/LAR's age, language, comprehension level, and familiarity with technology tools (if applicable).
3. If using an electronic process to send consent information or obtain documentation of consent (e.g., e-signature), identify the process to be used to send the consent information (e.g., e-mail).
4. If using an electronic process (e.g., e-mail), describe the procedures that ensure the electronic process allows subjects/parents/LARs to ask questions they may have before signing (e.g., by in-person discussions, telephone calls, videoconferencing). If conducting a consent conference, describe the method to be used for the conference (e.g., telephone call, video conference), specifying any programs (e.g., Zoom) to be used. If applicable, indicate that the consent discussion will be audio or video recorded and whether recording will occur within any programs being used (e.g., Zoom).
5. If using an electronic process, describe how the subject and/or parent/LAR will navigate the consent materials, including whether the subject/parent/LAR will have the ability to move backwards and forwards within the electronic system and to stop and continue at a later time. Also indicate how long it will take.
6. The availability of study personnel to assist subjects and/or their parent/LAR in using the electronic process, if applicable.

[53] Some study teams are currently considering creative solutions for such individuals; these potential solutions include snail mail, drive through paperwork for consent, and loaner device/hotspots for e-consenting. If no alternative will be made available (meaning these individuals cannot be enrolled), the IRB will look for a sufficient rationale for this exclusion.

[54] For example, the consent discussion will take place in a private room.

[55] Address the following in the response, as applicable:
1. Identify the means of documenting consent/assent/permission (e.g., in writing, verbally, etc.). If obtaining an electronic signature, identify the specific software/application to be used.
2. Include a description of how the consent/assent form(s) will be delivered, including any programs (e.g. REDCap) to be used.
3. Include a list of any information about the individual that will be collected during the assent/consent/permission process.

4. If the research is conducted outside of Washington State, provide confirmation that the electronic documentation of consent is legally effective in that jurisdiction. Note, the study team's location while conducting the study dictates the jurisdiction. For single IRB studies, the participating site's study team location while conducting the study dictates the jurisdiction.

[56] Electronic signature in this context refers to a legally effective electronic signature (e.g., a signature obtained via DocuSign) and does not apply to procedures where a waiver of documentation of consent is requested.
[57] Indicate "N/A" if not obtaining an electronic signature. Researchers are encouraged to consider the risks and benefits of the research when determining whether it is necessary to verify the subject/parent/LAR identity. For example, consider how likely it is that someone other than the subject would provide the consent. Social behavioral minimal risk research will not typically warrant identity verification.
[58] For example, consent forms will be downloaded as soon as they are full executed and saved electronically in a location accessible to the study team.

[59] This section describes the ways in which the procedures will not follow Seattle Children's SOP.

[60] See "HRP-411: Waiver or Written Documentation of Informed Consent" for further information.

[61] An information sheet template (HRP-502D) can be found in the Click IRB Library and should be attached to the consent form of the study SmartForm. For internet research, the information sheet can be translated to an on-line format, if desired.

[62] The IRB sometimes requires a script if you are having the consent conversation over the phone rather than in person. Templates for a consent script are available on the IRB website on the Participant Recruitment page and should be attached to the study SmartForm.

[63] This section describes the way(s) in which the processes for this study will not follow Seattle Children's SOP.

[64] Note the Short Form Consent may only be used when certain conditions are met. See HRP-091 for requirements for Short Form consent form use.

[65] For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children." The age of majority in Washington is 18; however, sometimes younger children have ability to consent for certain types of care (e.g. sexual reproduction/health; mental health; drug/alcohol treatment). For research conducted outside of the state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." If the sites in other states in the study are conducting their own IRB review, you do not need to worry about this--type N/A. If you are conducting research and are actively recruiting participants outside of Washington who are NOT coming to SCH to give consent and who will be covered under SCH IRB approval, this section should be addressed in your protocol.

[66] For minimal risk studies and greater than minimal risk studies that offer a prospect of benefit, the IRB generally requires one parent to provide permission for the child to participate.

[67] If parental permission will not be obtained, please address this in the Waiver or Alteration of Consent Process below.

[68] See HRP-013 for more information.

[69] The IRB generally follows the following guidelines for written assent: children 7-12 should provide written assent on the "simple" assent form (HRP-502G); children 13-17 should provide written assent by co-signing the parental permission form (HRP-502A). The IRB will consider other assent scenarios (e.g. verbal assent for some or all

children; not requiring assent for some or all children; or waiving assent): please provide details about the plan for your study. See HRP-090 and HRP-416 for more information on waiving assent and when assent is not necessary.

[70] See Appendix A-13 of the Investigator Manual HRP-103 for requirements for re-consent at age 18. If you think you meet the conditions for a waiver at 18, please address this in the Waiver or Alteration of Consent Process below.

[71] See "HRP-417 Cognitively Impaired Adults" for further information.

[72] For example: durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child. If you are following HRP-013 in order to make this determination, simply state that in this section. For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative." For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." If the sites in other states in the study are conducting their own IRB review, you do not need to worry about this--type N/A. If you are conducting research and are actively recruiting participants outside of Washington who are NOT coming to Washington to give consent and who will be covered under SCH IRB approval, this section should be addressed in your protocol.

[73] The IRB may allow the person obtaining assent to document assent on the consent document.

[74] Provide justifications/explanations for each subject population for which a waiver/alteration is being requested.

[75] For example: consent/parental permission will not be obtained, required information will not be disclosed, the research involves deception, waiver for participants who turn 18, waiver for information collected about a non-present parent, or other waivers as necessary.

[76] The IRB needs to make all the waiver findings and key to this determination is that the IRB understand why it is not practicable to do the research without a waiver of consent. You need to provide a rationale in order for the IRB to consider whether the waiver criteria are met. See "HRP-410: Waiver or Alteration of the Consent Process" for further information.

[77] Possible reasons might include: a) you are not collecting information that could put subjects or their families at harm, e.g., affect eligibility for insurance, employability, stigmatization; b) you are not collecting information that would alter or affect the subject's care; c) any publication or presentation of research results would be done in a manner that would never reveal an individual's identity either directly or indirectly.

[78] Possible reasons could be: a) inability to locate families because of the lengthy time period over which the records/samples were created; b) many of the subjects whose records, data, or biospecimens will be used may have died and contacting the families about the research could cause harm and anguish to families; c) all eligible patients must be included in the study for the results to be meaningful.

[79] For example, identifiers are necessary, so that researchers can perform quality checks or identifiers are necessary to link data from multiple sources.

[80] See "HRP 419: Waiver of Consent for Emergency Research" for further information.

[81] PHI is health information that is also identifiable because it includes one or more of the 18 HIPAA identifiers. See Investigator Manual HRP-103 for the list of HIPAA identifiers.

[82] If your study involves using or creating PHI and your only contact with participants is online, you can request an alteration of HIPAA authorization to remove the signature requirement. As an alternative to a waiver of

documentation of consent and an alteration of HIPAA authorization, you must demonstrate that the electronic consent signatures are compliant with applicable state/international law (in Washington, see RCW 19.34.300).

[83] For example: altering HIPAA elements for international research.

[84] Provide justifications/explanations for each subject population for which a waiver/alteration is being requested.

[85] Possible reason could be: the nature of the research is specific to individuals' health and requires access to individuals' health records.

[86] See "HRP-316: Payments" for further information.

[87] Methods of payment include check, ClinCard, gift cards, etc. Provide details on who will be the recipient of the payment (parent or child).

[88] Reimbursement is used when the subject is paid back for travel expenses such as transportation, food, childcare, or lodging. Reimbursement is generally distributed to person who incurred cost (usually parent) and requires receipts to be submitted.

[89] This could include things like fuel/transportation costs, parking, and/or childcare.

[90] Community-based settings may include community clinics, schools, non-profit organizations, etc.

[91] Type N/A if this section does not apply.

[92] Provide enough information to convince the IRB that the principal and/or co-investigator(s) are appropriately qualified to conduct and supervise the proposed research. When applicable, describe their prior clinical experience with the test article or study-related procedures, or describe their knowledge of the local study sites, culture, and society.

[93] For example, as appropriate: (1) Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit? (2) Describe the time that you will devote to conducting and completing the research. (3) Describe the facilities in which the research will be conducted. (4) Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research. (5) Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

[94] Including communication between sites of current study document versions and modifications.

[95] If you check the box, you are required to conduct your study according to the principles outlined at https://www.ich.org/products/guidelines/efficacy/efficacy-single/article/integrated-addendum-good-clinical-practice.html.