Study Title: HARMONY - **H**ealth **A**nd **R**esponse: Digital **M**arkers for **O**utcomes in Peri**N**atal Depression Treatment Stud**Y**
Lay title: HARMONY Study

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Overview: The purpose of this study is to determine if the addition of digital sensing data collected from phones and watches during the early stages of perinatal depression (PND) treatment can better predict treatment outcomes than using self-reported symptoms alone. The overarching goal is to develop a tool to predict the right treatment at the right time for individuals with PND, enhancing clinical decision making and ultimately improving the scalability and accessibility of historically inaccessible PND treatments.

STAND for PND: The UCLA Depression Grand Challenge (DGC) has previously developed a technology-assisted, scalable therapy system called STAND (Screening and Treatment for ANxiety and Depression) for perinatal depression (PND) and has demonstrated in an initial randomized clinical trial that this treatment intervention to be as effective as psychiatrist delivered care for PND. In this study, we will administer STAND for PND for up to 12 weeks as part of study participation. There will be no comparison between our treatment intervention and a treatment as usual condition, as this is not a trial of efficacy. In the STAND for PND treatment model, women with moderate symptoms will be routed to coach-guided, digital cognitive behavioral therapy (CBT) tailored to PND, which has been demonstrated to be an effective treatment approach for PND (e.g., Heller et al., 2019; Pettman et al., 2023; Loughnan et al., 2019). Women with severe depression or suicidality will be routed to clinician delivered CBT, with CBT demonstrated to be an effective treatment approach for PND (e.g., Nillni et al., 2018; Cuijpers et al., 2023; Frieder et al., 2019). Women receiving CBT tailored for PND may be referred to a UCLA clinic for pharmacotherapy if recommended by the clinical team. Symptoms will be regularly monitored in all participants throughout the intervention period.

Digital Sensing in Depression: The DGC also has substantial experience in large-scale longitudinal digital sensing studies, and experience identifying associations between self-report or clinical ratings of depressive symptoms and digital sensing features, including in pregnant and postpartum women.

Digital Sensing in a STAND for PND study: In our previous STAND for PND study, we did not include digital sensing. In this next phase of our research program, we will collect digital sensing data from phones and watches during the first four weeks of study participation. We will enroll up to 250 women during their last trimester or who are in the postpartum period to participate in the 3-month study, which includes treatment provided

through the STAND for PND program of care and during which we will obtain 4-weeks of digital sensing data. See **Figure 1** for an overview of the study design.

We will be testing whether behaviors measured through digital sensing (i.e., digital features) in combination with self-reported depression symptoms will better predict treatment outcomes than the self-reported depression symptoms alone. We are testing the hypothesis that prospective longitudinal assessments using digital devices will enhance our ability to predict outcomes of STAND-PND.

This project is part of a larger program of research that aims to improve clinical decision-making for PND by establishing a clinical care model for PND that fully integrates digital sensing with digital therapy. Demonstrating the feasibility and acceptability of integrating digital sensing in PND care, particularly using the same platform that will be used to provide access to digital therapy content, will prepare the DGC for a full randomized clinical trial.

An additional objective of this program of research is to target low-income mothers from populations that have had limited access to mental healthcare, given that this population is particularly vulnerable to the impact of PND.

For complete study background, aims, and analysis plans, see these sections in the NDMH Biomedical Research Template.

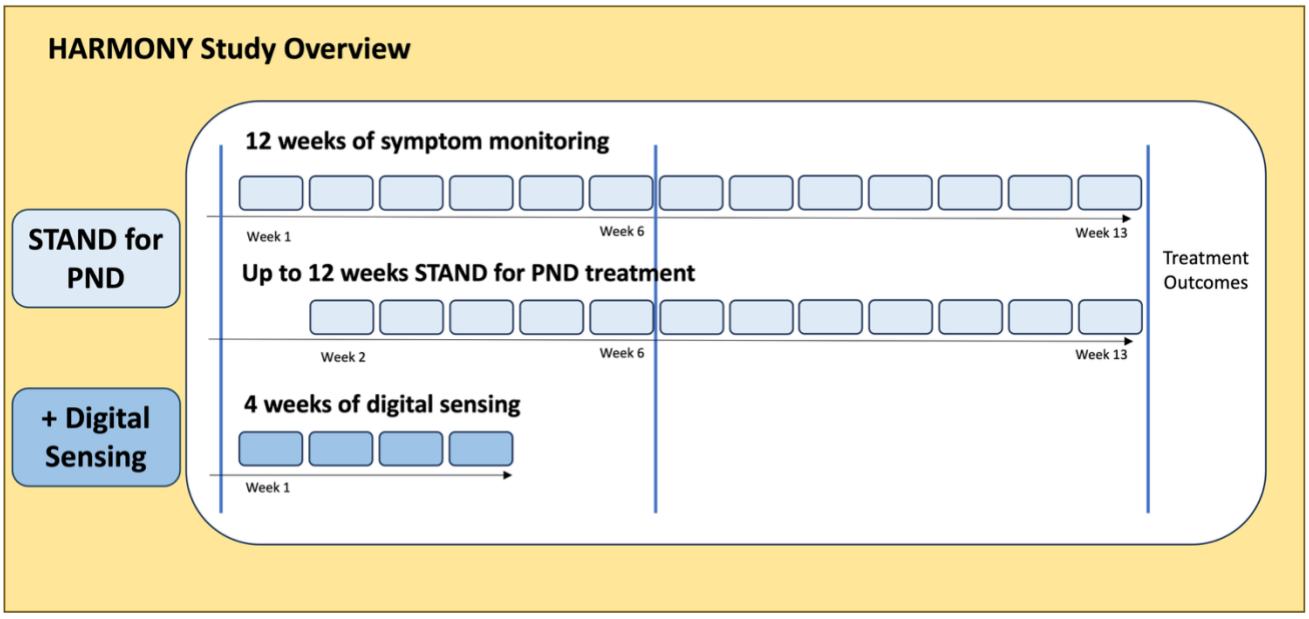

Figure 1: Overview of HARMONY Study research design

Sample: We aim to enroll women who are in their last trimester of pregnancy (28 weeks' gestation) through postpartum period (12 weeks after delivery) and are experiencing moderate-to-severe depression. We estimate needing to enroll 250 women in order to obtain complete data on 200 women. Women will be recruited from participating UCLA Health clinics in the Los Angeles area.

Inclusion Criteria:

- At least 18 years of age
- Able to read and communicate in English
- Between 28 weeks pregnant and 12 weeks postpartum
- Moderate-to-severe depression, as defined by Edinburgh Postnatal Depression Scale (EPDS) score ≥11
- Not currently seeing a provider for mental health care
- Own functioning iOS smartphone (iPhone 11 or newer, iOS 18 or newer) with access to reliable data plan and Wifi)
- Able to read and understand a written informed consent form
- Willingness to participate in treatment through the study and follow all study procedures, including providing HIPAA Authorization for research, installing a study app on personal iPhone, and wearing the provided Apple Watch for at least 20 hours every day in the first four weeks of the study (including while sleeping)

Exclusion Criteria:

- Currently receiving treatment by a therapist or a psychiatrist
- Unstable suicidality (e.g., 2 or more suicide attempts or self-injurious behaviors resulting in hospitalization in the last 6 months)
- Current substance use disorder that interferes with treatment: specifically, patients meeting diagnostic criteria for Substance Use Disorder (SUD) will be eligible for inclusion only if they are able to attend sessions while not under the influence of that substance, with the exception of individuals abusing opiates or freebase cocaine, who will be excluded
- Principal diagnosis of psychosis unrelated to depression (unipolar or bipolar)
- Neurological conditions
- Severe uncontrolled medical conditions (e.g., anorexia nervosa, cardiac conditions requiring continuous monitoring)
- Cognitive impairment (e.g., developmental disability, dementia)
- Previously participated in the UCLA Depression Grand Challenge "New Moms Mood Tracking & Wellbeing Study" (IRB #20-001924)

Study Procedure:

Overview: The anticipated duration of study participation for participants lasts approximately 3 months. See **Table 1** for an overview of the study assessment schedule. After recruitment through one of our various recruitment strategies (defined below), prospective participants can review information on a study webpage, including eligibility requirements, time commitment, and compensation. Interested participants can proceed

to determine eligibility by completing online screening; prospective participants may also complete screening by phone with study staff. If eligible, interested participants can provide written electronic consent to enroll in the study. Information will be collected to issue the participant their Study Kit, which may include the Apple Watch to be worn for the first four weeks of the study, as well as to schedule their remote onboarding session. Participants will complete their remote onboarding session by secure video conference with a member of the study team and complete a series of self-report surveys online. Participants will be informed about the treatment intervention condition to which they have been assigned and be provided with instructions for engaging in the treatment intervention. Participants will receive a link via email or text to complete weekly self-report assessments of symptoms of depression and will additionally be instructed to complete additional self-report surveys after starting their assigned treatment intervention according to the schedule outlined in **Table 1**.

As explained in the remote onboarding session, participants will be asked to install a study app on their personal iPhone, pair the Apple Watch to their iPhone, and wear the Apple Watch for the required amount of time during the first four weeks while engaging in their assigned treatment intervention. Participants will be provided instructions for watch wear and device charging requirements. If a participant already owns their own personal Apple Watch, they can use their personal watch rather than receive one from the study team, so long as the Apple Watch is at least a Watch S8 or newer with watchOS 11 or newer.

Participants may receive reminders to complete their assessments or engage in their assigned treatment intervention by phone, email, or text. Participants may also receive push notifications from the app installed on their iPhone with reminders to complete study assessments or engage in their assigned digital therapy package. Participants will be informed that study staff will monitor data collection and reach out to the participant if assessments are not completed.

With the exception of symptom ratings, which will start weekly after the onboarding session, the remaining assessments are tied to the participant's treatment engagement. As participants may enroll anywhere between the last trimester of pregnancy (28 weeks' gestation) through postpartum period (12 weeks after delivery), baseline assessments will be completed near the point of their onboarding session; these will be sent to the participant prior to the onboarding session and must be completed prior to their first clinical encounter. The remaining assessment time points are relative to treatment initiation (Orientation session for Tier 2, Intake session for Tier 3). Additional surveys will be sent to the participant after the first treatment session, 6 weeks after treatment initiation (mid-point) and 12 weeks after treatment initiation (study end).

For participants who enroll during the last trimester of pregnancy, their assessment and treatment schedule may be shifted by approximately two weeks after delivery. Participants will continue to receive weekly reminders to complete self-report assessments of depression symptoms during this period of time. However, treatment sessions may be paused for approximately two weeks, and the additional self-report assessments will be shifted according to the changes in the treatment schedule. If the

participant delivers during the first four weeks of the study, the end date for digital sensing data collection will also be shifted by two weeks.

	Screening & Enrollment	Baseline	Start of Care	Week 2	Mid-Point	End of Care	Study End
Screening, including EPDS	✓						
Consent	✓						
HIPAA Authorization for Research	✓						
Treatment Assignment	✓						
Onboarding session		✓					
Prescribed Medication History		✓					
Depression symptom severity (EPDS) with suicidality follow-up		✓	Weekly				
Depression symptom severity (PHQ-8)		✓					
Demographics		✓					
Medical Comorbidities		✓					
Medication and Treatment History		✓			✓		✓
Pregnancy History		✓					
Peripartum Survey		✓			✓		✓
Stressful Life Events		✓			✓		✓
Major experiences of Discrimination		✓					
Everyday experiences of Discrimination		✓			✓		✓
Maternal Social Support		✓			✓		✓
Postpartum Bonding Questionnaire		✓*			✓*		✓*
Breastfeeding Difficulties		✓*			✓*		✓*
Sleep Quality		✓			✓		✓
Routines Survey		✓			✓		✓
First Clinical Appointment			✓				
Last Clinical Appointment						✓	
Care Evaluation & Treatment Satisfaction				✓		✓	
Program Feedback							✓
Digital Sensing			✓				

Table 1: HARMONY Study Schedule of Assessments. Week 2, Mid-Point and Study End assessments are scheduled relative to treatment initiation.
*Administered when applicable (i.e., if postpartum)

Recruitment: We will work with clinics throughout the UCLA Health System to identify prospective participants. All prospective participants will be directed to a website, which contains information about a number of research studies being conducted by the UCLA Depression Grand Challenge (DGC), including the HARMONY Study. Interested women can navigate to the HARMONY study landing page to learn more about the treatment intervention being offered, study requirements, time commitment, and compensation. The study webpage will also contain contact information to reach study staff directly, and may include a page with Frequently Asked Questions (FAQs).

Study staff and clinical partners will work to identify prospective participants and share information about the study. This may include sharing information about the study at a clinical encounter and distributing study information for display at participating clinics. This may include having research staff or clinic staff checking the medical record of patients with upcoming appointments to identify if they are potentially eligible, and then contacting them in-person or via myChart message with information about the study.

We will also leverage direct myChart recruitment messages, with the support of the Embedded Clinical Research and Innovation Unit (ECRI), part of the UCLA Center for Smart Health (CSH). The ECRI team can use information in the UCLA medical record to screen for potential participants (e.g., age, sex, primary language) and send recruitment

messages through the myChart patient portal. If they patient indicates an interest via the myChart message, a member of the ECRI team or the study team will respond with information about the study webpage. The recruitment messages will include a link to our study webpage, as well as study team contact information. We will also work with UCLA CareConnect teams to deploy custom smartphrases, such that information about the study can be shared in a patient's after-visit summary if the smartphrase is entered in CareConnect during a clinical encounter.

Recruitment partners include providers and clinic staff at UCLA Health OB/GYN Clinics, the UCLA West Medical Clinic, Inpatient and Outpatient Social Workers, Lactation Consultants, and the MOMS Clinic.

Additional recruitment strategies may be deployed by the study team, including posting IRB-approved recruitment materials in social media channels, sharing with community organizations, and contacting other channels for distribution (e.g., postpartum support groups).

Prescreening: Prospective participants will be directed to our study webpage. Interested prospective participants can proceed with completing prescreening questions online, which includes self-reporting on demographics, eligibility screening items, and completing an online self-report assessment of current depression symptom severity. Interested prospective participants can speak with a member of the study staff or consult online FAQ before proceeding with online eligibility screening. As stated in the eligibility criteria, eligible participants must have a recorded EPDS score of 11 or higher within the previous 7 days in order to be enrolled in the study. If there are delays in obtaining consent and completing enrollment, an EPDS may need to be re-administered to ensure eligibility and tier assignment.

Women will be notified immediately about whether they are eligible to participate in the study; if additional information is needed to determine eligibility (e.g., confirm exclusionary diagnosis), information will be provided to the prospective participant about next steps and expected timeline.

Women who endorse suicidality with intent or means as part of online screening will receive follow-up for risk assessment, as outlined in our Risk Protocol.

Consent and Enrollment: If eligible based on screening, prospective participants will be routed to provide written electronic consent via the REDCap eConsent framework. We have received approval from the Office of Compliance to use this workflow for obtaining consent and HIPAA Authorization for Research. As part of the consent workflow, participants will be presented with 1) the US Bank Focus Blue Program Visa card fees disclosure (described under Compensation below); 2) the California Research Subjects' Bill of Rights; 3) the informed consent form, and 4) the HIPAA Authorization for research. Participants are required to acknowledge #1, and sign #2 through #4 to enroll in the study (with signature provided using their mouse). In the REDCap eConsent framework, participants view each page of the informed consent with the IRB stamp visible on the

embedded pdf. Participants are required to enter their first and last name, provide signature, and enter date and time on the last page of the consent. Participants can then view an online version of the signed consent form and can download a signed copy of the informed consent form as pdf. Following guidance of the Office of Compliance, study staff administering consent forms are required to counter-sign the consent form once it is signed by the participant. Participants can request a copy of their signed consent form from study staff at any time.

After signing consent, participants are considered enrolled in the study. Participants will be routed to a webpage where they can provide information needed for the study team to ship them a Study Kit, which will include the Apple Watch if the participant does not own an eligible watch, printed instructions, and a US Bank Focus Blue Program Visa card. Participants will be also asked to provide the information needed to schedule their remote onboarding session. An email confirmation will be sent to the participant within three business days after completing enrollment. The confirmation email will include instructions for preparing for the remote onboarding session. A separate calendar invite may additionally be sent that includes the video conference link for the onboarding session.

Research Assessments: See the **Table 1** for the schedule of assessments, and the **Appendix** for a detailed list of the measures to be collected.

Baseline (approximately 2 hours, including 60-minute onboarding session and 60-minute self-report surveys):

- Once participants schedule their remote onboarding session, they will receive a link to complete their baseline assessments prior to their onboarding session. Participants are instructed to complete these surveys prior to their onboarding session, and that they must be completed before their first clinical appointment or this session will need to be rescheduled.
- The online self-report assessments that participants will complete at baseline capture information about demographics, depression symptoms (including suicidality), medical and treatment history, history of pregnancy, sleep quality and daily routines, social support, infant bonding, and breastfeeding difficulties (if applicable), stressful life experiences and experiences of discrimination.
- Participants will receive a reminder by text on the business day prior to their remote onboarding session. If participants have not completed their baseline assessments on the day prior to their remote onboarding session, they will also receive reminders from the study team.
- The remote onboarding session will be scheduled for 60 minutes and will be conducted by secure video conference. Study staff will walk participants through steps of making sure their iPhone is updated, their Apple Watch is paired to their iPhone, the steps to install the study app (MyDataHelps) on their iPhone and enroll in the study bundle, agree to data sharing requirements in the study app, and the tasks required during the study schedule. A primary goal of the onboarding session is to ensure that participants are fully informed of the measures to be collected from their iPhone and the provided Apple Watch via

the study app and understand daily wear and charging requirements during the four-week digital data collection period.

- At the onboarding session, study staff will collect information from the participant about previous and current prescribed medication use.
- Study staff will remind participants that they may contacted about missing assessments and will be available for the duration of the study to answer any questions from participants about their use of the study app, Apple Watch, or completion of study tasks.
- Study staff will review the treatment condition to which they have been assigned and help schedule the Orientation or Intake session for participants assigned to Tiers 2 and 3, respectively, during the onboarding session.
- Once all tasks considered part of the baseline assessment are completed, including completion of all baseline self-report surveys and confirmation by the participant of receipt of the US Bank Focus Blue Program Visa card, study staff will issue intake compensation. The same card will be used to issue compensation throughout the study; however, if the participants lose their US Bank Focus Blue Program Visa card, they can request a replacement.

Daily Assessments:

- During the first four weeks of participation in the study, participants will be asked to ensure that the study app remains installed on their iPhone, and to wear their Apple Watch at least 20 hours per day, including while sleeping.
- Participants will be asked to follow charging requirements during this period, which includes charging their devices while on the same Wifi network and while they are Bluetooth connected, for at least two hours each day.

Weekly Assessments (approximately 60 minutes over 13 weeks):

- Participants will be asked to complete a self-report symptom of depression (including suicidality) every week, starting from baseline. This survey is expected to take approximately 5 minutes to complete.

Mid-point Assessments (approximately 30 minutes):

- Participants will be asked to complete a set of self-report assessments 6 weeks after treatment initiation.
- The online self-report assessments that participants will complete at baseline capture information about depression symptoms (including suicidality), changes in medical or treatment history, pregnancy and delivery status, sleep quality and daily routines, infant bonding, social support and breastfeeding difficulties (if applicable), as well as recent stressful life experiences and experiences of discrimination.

Study end Assessments (approximately 30 minutes):

- Participants will be asked to complete a set of self-report assessments 12 weeks after treatment initiation.
- The online self-report assessments that participants will complete at baseline capture information about depression symptoms (including suicidality),

changes in medical or treatment history, pregnancy and delivery status, sleep quality and daily routines, infant bonding, social support and breastfeeding difficulties (if applicable), recent stressful life experiences and experiences of discrimination, and feedback about their experience in the study.

Additional Clinical Assessments (approximately 10 minutes):

- After the first treatment session and at the end of clinical care, participants will also be sent a link to complete an assessment of their clinical care (Care Evaluation and/or Treatment Satisfaction). This survey takes less than 5 minutes to complete.

Treatment Intervention: Participants will be assigned to one of the following STAND for PND treatment conditions depending on their screening depression symptom severity scores. The STAND for PND treatment intervention provides access to a system of care, in which type of treatment is allocated based on presenting depression symptomatology. Any endorsement of suicidality with intent or means, regardless of depression inventory score, is considered appropriate for STAND Clinical Care (Tier 3). Participants will be notified of their treatment assignment at the time of enrollment.

The remote onboarding session, which includes installation of the study app on the participant's iPhone, must occur prior to the initiation of care. An Orientation or Intake session for participants assigned to Tiers 2 and 3, respectively, will occur prior to treatment initiation. As such, at least one week of digital sensing data collection will occur between baseline and initiation of treatment.

Tier 2 - PND Digital Therapy with Coaching: Participants with a recent EPDS score in the moderate range (11-18) and no current suicidality will be given access to a perinatal depression online cognitive-behavioral therapy course, which is called the ParentMood program. Some of the lesson content is presented in the form of illustrated videos. Following each lesson, participants can download a document that summarizes the key information in each lesson, and which includes practical homework exercises that reinforce the content of the lesson. Participants are encouraged to practice their lesson homework for at least one week before starting the next lesson. Lessons will be completed sequentially. The ParentMood program can be accessed through the study app that participants will be guided to install on their iPhone during the onboarding session. Participants additionally have the option of accessing the content through a web-browser. Participants may receive up to 9 coaching sessions with their assigned Coach, in addition to an initial Orientation session, which will occur through secure video conference. While the initial Orientation session is required for study participation, the additional coaching sessions thereafter are optional.

All coaching sessions will be recorded for supervision purposes. Recordings will be stored in a HIPAA compliant cloud-based storage solution, where access is restricted to study team members listed on the IRB. Participants are informed about the requirement to record coaching sessions in the consent form.

Participants have the option of allowing these recordings to be retained and used for future research when providing consent; if a participant does not opt-in to sharing these recordings for research purposes, they will be deleted once their participation in the study has ended.

Tier 3 – Clinical Care: Participants with a recent EPDS score in the severe range (19-30) and/or significant suicidality with intent or means will be given access to a clinical care, which entails weekly psychotherapy sessions. The number and schedule of psychotherapy sessions in the study is determined by the clinical care team.

Treatment appointments will occur through secure video conference. All treatment sessions, including the intake session, will be recorded for supervision purposes. Recordings will be stored in a HIPAA compliant cloud-based storage solution, where access is restricted to study team members listed on the IRB. Participants are informed about the requirement to record treatment sessions in the consent form. Participants have the option of allowing these recordings to be retained and used for future research when providing consent; if a participant does not opt-in to sharing these recordings for research purposes, they will be deleted once their participation in the study has ended.

If the clinical team believes that consultation with a psychiatrist is warranted, a referral will be made to a UCLA Health clinic (e.g., the MOMS Clinic) for a consultation session and possible pharmacotherapy.

Treatment Changes: Treatment changes (between Tiers 2 and 3) will be made according to the following criteria:

- If any participant endorses suicidality with intent or means, treating clinicians will be notified, and the participant will be offered Tier 3 Clinical Care if they are not already actively engaged in Tier 3 care.
- Tier 2 Digital Therapy participants may be offered Tier 3 Clinical Care in the case that their EPDS depression scores are in the severe range for two consecutive assessments.
- Tier 3 Clinical Care participants who have completed their course of therapy may be offered additional therapy sessions within the 12-week study duration in the case that their EPDS depression scores are in the severe range for two consecutive assessments.
- Tier 3 Clinical Care participants who have completed their course of therapy may be offered Coaching and given access to the digital therapy program if their EPDS depression scores are in moderate range (11 or higher) on weekly EPDS assessments after completing therapy.
- Participants who miss over four appointments (not due to clinician/coach cancellation or schedule changes) may be discontinued from treatment.
- If upon completion of all available clinical appointments, a participant requires additional care, they would be referred to appropriate resources in the community.

Both treatment interventions provide evidence-based care. Tier 3 Clinical Care will be provided by a Licensed Clinical Social Worker (Christine Rodriguez or Gayane Grigoryan).

Participants will not be billed for treatment provided in Tier 2, or for psychotherapy provided in Tier 3. If participants are referred to a UCLA Health Clinic for a consultation with psychiatry, the scheduling and billing will be managed by the clinic and is not part of our research workflows. The cost to see a psychiatrist and receive medication will depend on the participant's prescription coverage and co-payment plan.

Study End: Participants will receive information by email about their progress in the study and compensation earned. They will also receive instructions for withdrawing from the study configuration in the study app and instructions to delete the study app from their iPhone, if preferred. For participants who drop from the study early, or who do not provide enough data to meet the threshold to be able to keep the Apple Watch, they will be provided instructions for unpairing and resetting the watch, and will be sent shipping materials to be able to return the Apple Watch if it was provided to them to our research offices.

Time Commitment: The total time expected for study participants is 270 minutes (approximately 4.5 hours). This estimate is based on the time required to complete the following:

- Online screening & enrollment: 20 minutes (not included in compensation)
- Baseline self-report surveys (60 minutes)
- Onboarding session (60 minutes)
- Weekly depression symptom ratings (65 minutes; 5 minutes each for 13 weeks)
- Online surveys at mid-point (30 minutes)
- Online surveys at study end (30 minutes)
- Online clinical assessments at the start and end of clinical care (10 minutes)
- Study end tasks (5 minutes)
- **Total Expected Time:** 260 minutes (4.5 hours over approximately 13 weeks)

In addition, participants spend time in coaching or clinical sessions, engaging with the Digital Therapy lessons or completing associated practice assignments, which varies per participant and based on clinical recommendations. Estimates of time commitment do not include time required to engage in treatment.

Estimates of time commitment do not include the time required to follow a daily charging or device use requirement in the first four weeks, or include the time required to response to reach out attempts by study staff when data are missing or device troubleshooting is required.

If the participant delivers after enrollment in the study and the study schedule is delayed by up to two weeks, the time commitment does not include the period of time after delivery when the treatment and assessment schedule is postponed.

Compensation: Study participants will be compensated for completing study assessments and for using the devices as instructed during the first four-week period. Participants may receive a completion bonus.

Study assessments will be compensated as follows:

- Participants will receive $50 for completing all baseline assessments, including the onboarding session.
- Participants will receive $20 for completing all mid-point assessments.
- Participants will receive $20 for completing all study end assessments.
- Participants will receive compensation according to the amount of recorded watch wear in block 1:
    - For wearing the watch on 4/7 days each week, on average, across block 1, participants will reach Base tier and earn $10 in compensation.
    - For wearing the watch on 5/7 days each week, on average, across block 1, participants will reach Silver tier and earn $15 in compensation.
    - For wearing the watch on 6/7 days each week, on average, across block 1, participants will reach Gold tier and earn $20 in compensation.
- Participants will receive compensation according to the amount of weekly mood surveys completed in each approximately four-week interval. At the end of blocks 1, 2, and 3:
    - Participants who complete at least 2 of the 4 weekly surveys in the previous block will reach Base tier and earn $10 in compensation.
    - Participants who complete at least 3 of the 4 weekly surveys in the previous block will reach Silver tier and earn $15 in compensation.
    - Participants who complete all 4 of the 4 weekly surveys in the previous block will reach Gold tier and earn $20 in compensation.
- In addition, participants who reach Gold tier for watch wear in the first block and Gold tier in each of the three blocks will earn a completion bonus of $30.

As such, participants can earn up to $200 for completing the majority of study assessments. See **Figure 2** for the compensation schedule.

	Compensation Amount		
Baseline assessments & Onboarding session*	$50		
Mid-point assessments*	$20		
Study end assessments*	$20		
	Base Tier*	**Silver Tier**	**Gold Tier**
Watch Wear (block 1)	$10	$15	$20
Weekly Surveys (block 1)	$10	$15	$20
Weekly Surveys (block 2)	$10	$15	$20
Weekly Surveys (block 3)	$10	$15	$20
Gold Tier Bonus			$30

*Must be met in order to keep the Apple Watch at the end of the study

Figure 2: HARMONY Study compensation schedule

If the participant delivers after enrollment in the study and the study schedule is delayed by up to two weeks, those two weeks will not be considered for compensation purposes. Compensation will be based on data collection prior to delivery and the remaining time after the two-week pause, even though participants may be asked to complete weekly mood assessments over this interval.

The study will be conducted remotely, so no transportation reimbursement will be provided.

Participants will not be compensated for completing assessments related to the treatment component of the study.

All participants will receive an unregistered US Bank Focus Blue Program Visa card at the start of the study. For compensation earned after the baseline assessment and onboarding session are completed, study staff will register the card to the participant and issue compensation to the card. Study staff will collect the participant's date of birth in order to register the US Bank Focus Blue Program Visa card to the participant.

All parts of the baseline must be completed before the first payment is issued, including baseline surveys and the remote onboarding session. Subsequent compensation will be provided at the end of each approximately four-week period (i.e., after block 1, 2 and 3), once study assessments are completed and any outstanding data missingness issues have been resolved. Participants who discontinue study participation before the end of a given four-week interval will not receive compensation based on amount of tasks completed in that four-week interval.

Study staff will remind participants to use the funds within 365 days of being added to the card to avoid incurring any fees beyond that time. If a participant does not want to receive compensation through a prepaid Visa debit card, they can ask study staff for eGift Cards instead, which will be ordered and mailed at these same intervals. Participants will be notified of the estimated time to receive alternative eGift Cards.

Risk Protocol:

As this study is minimal risk, no independent Data Safety Monitoring Board or Committee is instituted for this study. If it is determined in the future that such a committee or board is necessary, we will implement one.

Below, we share information regarding our Risk Protocol, which is developed by the study team and overseen by study PIs, Drs. Nelson Freimer and Michelle Craske. Our Risk Protocol Supervisors are our staff social workers, Christine Rodgriguez and Gayane Grigoryan. Staff members who have direct contact with participants and may conduct a follow-up assessment following endorsement of suicidality or harm to infant are trained and supervised by these Risk Protocol Supervisors. We contract a crisis call center to

make initial outreach following endorsements of suicidality in remote surveys. All documentation is maintained in our REDCap database.

A Risk Protocol is necessary for this study, as women experiencing moderate-to-severe depression will be asked to frequently report on their symptoms of depression, including suicidality, over the course of the study. The following protocol will be implemented in response to reports of suicidal ideation or worsening depression.

In response to an endorsement of suicidal thoughts, an automated alert system built into REDCap will notify the study team, including Risk Supervisors. Alerts of suicidality triggered by assessments collected through REDCap will automatically send a notification to ProtoCall Services, a 24/7 triage and crisis intervention service provided through contract. ProtoCall Services will initiate outreach with the participant to assess suicidality and provide urgent intervention if needed. Simultaneously, an automated alert will be sent to the DGC risk monitoring team. DGC's risk monitoring team will review the report provided by ProtoCall services and either conduct a follow-up with the participant if ProtoCall was unable to make contact in the first 24-72 hours, conduct a follow-up with the participant if the ProtoCall report indicates that a follow-up is expected, or sign off on the participant's record in the database that the report was reviewed and no follow-up was needed. Follow-up by a member of the DGC risk monitoring team will occur within one business day (Monday-Friday, 8am-5pm) if needed based on information provided by ProtoCall Services (e.g., in case of no contact). If information about the participant's current provider (e.g., OB/GYN) is on file, they may be additionally notified, if recommended by the Risk Supervisors.

In response to an endorsement of symptom worsening, this will be reviewed by the DGC risk monitoring team. See *Treatment changes* section related to response to elevated depression for participants.

In response to an endorsement of aggressive thoughts towards their infant when completing self-report assessments about mother-infant bonding, the DGC risk monitoring team will be notified. A member of the risk monitoring team will contact the participant to assess any risk. This will be reviewed by the Risk Supervisor.

The above events must be reviewed and verified by DGC Risk Supervisors. All actionable alerts will be fully documented, along with follow-up and outcome reporting. Any mandated reporting is conducted or supervised by DGC Risk Supervisors. If a response is not received from the clinical team, the clinical supervisor will be automatically notified.

Response to these alerts might be escalated (e.g., calling emergency contact or wellness check) as clinically indicated. The response provided by our risk monitoring team and/or the treating clinician will include a list of local resources, including information about crisis hotlines.

If a participant is determined to be not eligible because they need a higher level of care, either at screening or over the course of the study, resources will be provided to the

individual, including a list of treatment resources in the area. If a participant is determined to need continued care after the end of the 12-week treatment intervention, a list of treatment resources will be shared with the participant.

The consent form will advise participants that staff will monitor any alerts triggered by responses to symptom surveys. We include the following in the consent form: *"We will ask you questions about potentially sensitive topics. If your responses to study surveys at any point indicate that you are feeling suicidal and with a plan to harm yourself or you endorse thoughts of harming your infant or having harmed your infant, our clinical team will be notified and will review this information, confidentially. The clinical team will contact you to determine if there are safety concerns that require immediate help, may follow-up on potentially concerning responses to the symptom surveys, and may provide referrals to clinical services that may be available to you. If we are concerned that you are going to seriously harm or kill yourself or someone else imminently, we may need to share that information with someone outside of our research team to ensure your safety or the safety of others. We may additionally need to share information with your current provider."*

The consent form also includes the following section on mandated reporting: *"Identifying information may be released in some circumstances. Specifically, the study staff are legally required to report known or reasonable suspicion of abuse to a child, elder, or dependent adult and serious threats against a reasonable identifiable victim or victims. Information will be released only to responsible agencies and others that the study staff are mandated to report to by law or University policy, including relevant authorities such as law enforcement We also might need to release information about you if you are in danger and need emergency care (for example if we believe there is an imminent threat of suicide or serious self-harm or that you may harm others). Any relevant information obtained during the course of the study can be used in mandated reporting if indicated (e.g., emergency contact). This information obtained may be shared with your treating OBGYN provider and your clinical team. You have the right to privacy, and it is your choice whether or not you answer a question or provide information."*

APPENDIX

Study Assessment Table

Domain	Description	Administered by	System/ Method of Data Collection
Consent	Participant-signed consent form, including name and date	Self-report	REDCap eConsent
	HIPAA Authorization for Research	Self-report	REDCap eConsent
Health History	Previous and current prescribed medication use	Assessor administered	REDCap
	Standard measure of demographics (age, sex, ethnicity, education, etc.)	Self-report	Web-based (REDCap)
	Medical comorbidities	Self-report	Web-based (REDCap)
	Medication and treatment history	Self-report	Web-based (REDCap)
Maternal Health	Pregnancy & birth control history	Self-report	Web-based (REDCap)
	Breastfeeding difficulties	Self-report	Web-based (REDCap)
	Maternal Social Support Scale	Self-report	Web-based (REDCap)
	Postpartum Bonding Questionnaire	Self-report	Web-based (REDCap)
Symptom & Mood Scales	Self-report measure of depression (Edinburgh Postnatal Depression Scale or Patient Health Questionnaire, with suicidality follow-up items)	Self-report	Web-based (REDCap)
Life History & Behaviors	Stressful life events inventory	Self-report	Web-based (REDCap)
	Experiences of discrimination	Self-report	Web-based (REDCap)

	Sleep quality (Pittsburgh Sleep Quality Index)	Self-report	Web-based (REDCap)
	Routine behaviors, including phone usage	Self-report	Web-based (REDCap)
Treatment Satisfaction	Care Evaluation & Treatment Satisfaction	Self-report	Web-based (REDCap)
	Program feedback	Self-report	Web-based (REDCap)

Health app Data

Health data are collected from the Health app, which is a default app installed on the participant's iPhone. Data can be collected from the participant's iPhone or Apple Watch, stored in the Health app, and then shared with the study team via the study app installed on the participant's iPhone.

These include data such as exercise time, stand minutes/hours, steps, flights climbed, walking and wheelchair related data, resting energy, active energy, VO_2 max, heart rate related data (including irregular rhythm notifications), sleep related data, awake time, respiration rate, environmental sound levels, blood oxygen (including pulse strength), weather and time zone. Some data may only be collected if the participant makes an entry or complete an applicable activity. Examples include respiratory rate, workouts, ECG results, daily mood, emotions, mindful minutes, height, weight, body mass index, blood pressure, sleep apnea event, body temperature, oxygen saturation, respiratory rate, symptoms (including those related to menstrual cycle), information related to menstruation, pregnancy, ovulation and related tests, lactation, contraceptives, sexual activity, the results of a test to detect the softest sounds that can be heard, audio exposure, nutrition information such as macronutrients, minerals, hydration, caffeine, and vitamins, and information on whether the data was entered by the participant will be collected. This collection may include data from the past 24 months before the participant enrolled in this study if any such data were stored in the Health app.

Digital Sensing Data

Data captured from sensors embedded in the participant's iPhone and Apple Watch will be obtained via the MyDataHelps app that is installed on the participant's iPhone. The participant must opt-in to sharing these data during study onboarding, when enrolling in the study bundle in the app.

- Accelerometer data as collected by the iPhone or Apple Watch provides information about physical activity, which is relevant for studying depression, and provide more precise information about circadian rhythms.

- Ambient light as collected by the iPhone or Apple Watch provides information relevant about time spent in daylight, with time spent in daylight related to circadian rhythm, sleep activity, and mood.
- Device usage captures the frequency and duration that a participant uses their device or particular Apple apps or websites. This information supports investigation into the relationship between screen time, or the nature of screen time, and symptoms of depression.
- Face metrics provide metrics about the participant's face; tonic facial expressivity and changes in facial expression in response to socially relevant stimuli have been shown to be associated with symptoms of depression.
- Gyroscopic data as collected by the iPhone or Apple Watch provides information about movement, which is relevant for studying depression, and provide more precise information about circadian rhythms.
- Heart rate measures obtained from the Apple Watch is reflective of several physiological processes, and can be used to infer physical activity, which has been associated with symptoms of depression.
- Keyboard metrics as collected by the iPhone or Apple Watch provides information about keyboard usage patterns. This information is relevant to neurocognitive function in relation to depression symptom severity, as well as texting sentiment analyses.
- Message usage as collected by the iPhone or Apple Watch provides information about a participant's Messages app activity, which is a key indicator of social activity, and relevant to depression.
- On wrist state provides information about the configuration of the Apple Watch on the participant's wrist, as well as information about protocol compliance, which is used in the analysis of Health app and digital sensing data.
- Pedometer data as collected by the iPhone or Apple Watch provides information about the distance traveled by a user on foot, and is a key indicator of physical activity, relevant to depression.
- Phone usage as collected by the iPhone or Apple Watch provides information about a participant's phone activity, which is a key indicator of social activity, and relevant to depression.
- Rotation rate as collected by the iPhone or Apple Watch provides information about movement, which is relevant for studying depression, and provide more precise information about circadian rhythms.
- Speech metrics as measured by the iPhone or Apple Watch provides information about speech characteristics. Alterations in speech patterns and characteristics have been associated with symptoms of depression.
- Visits captures information about a participant's daily travel routine. This metric allows us to determine total time spent at home. Location entropy is one of the most consistent digital sensing features associated with depression.
- Wrist Temperature as measured during sleep by the Apple Watch is associated with several aspects of depression, menstrual cycle status, illness, and mood.
- Media events capture information about a participant's interaction with a media object, such as an image or a video. This information supports investigation into

the relationship between screen time, or the nature of screen time, and symptoms of depression.

Electronic medical record

Study staff will obtain HIPAA Authorization for research from participants that are UCLA Health system patients using the External REDCap eConsent framework before the baseline assessment to access relevant clinical information in CareConnect. Study staff will conduct chart review in order to extract the minimum information necessary related to previous diagnoses, hospitalizations, and medication, which will be transcribed into our REDCap research database, or will request data extraction through CTSI. Relevant information will be extracted at study enrollment and again at the end of the study.