The Mindful Kidney: A Digital Mindfulness Intervention for Adults with Chronic Kidney Disease

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2000042104

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Clinical Trials Registration Number: Trial to be registered on ClinicalTrials.gov before first participant enrolled.

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Confidentiality Statement:

Participant confidentiality and privacy is strictly held in confidence by the participating investigators, their staff, and sponsors. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence, except where required by U.S. law (e.g., knowledge of abuse of a child or elderly person). The study will not obtain a certificate of confidentiality since none of the collected data will be sensitive enough to warrant one.

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Synopsis

Purpose	Mindfulness is a cognitive skill focused on maintaining moment-to-moment awareness of one's internal state and surroundings. Limited evidence exists on digital mindfulness interventions for adults with chronic kidney disease (CKD). This pilot study will evaluate the feasibility, acceptability, and preliminary efficacy of Calm Health, a commercial mindfulness mobile application, among adults with CKD.
Objectives	Objective #1: Determine whether it is feasible and acceptable to use Calm Health among adults with CKD. Objective #2: Determine whether using Calm Health has favorable effects upon perceived stress, quality of life, well-being, mental health, and blood pressure. Objective #3: Develop visualizations of biometric data and mindfulness app usage timestamps, to help adults with CKD review and understand their health data and refine reports by a user-centered design.
Study Population	Adults aged 18 years and older diagnosed with CKD for at least 6 months with at least two consecutive nephrology visits within a 1 year window, the last occurring within the past year. They will be patients of Yale Medicine Nephrology or Yale New Haven Hospital.
Number of Participants	26
Study Design	This is a prospective, non-randomized, single-arm pilot clinical trial to evaluate the feasibility, acceptability, and efficacy signal of the Calm Health app among adults with CKD.
Study Duration	Individual participant duration: recruitment to baseline visit will take 1–30 days, and baseline visit to end of follow-up will take 6 weeks, for a total duration of approximately 2.5 months. The cutoff date for enrollment will be October 15, 2026 so that each participant can complete the 6 weeks of app access before the accounts expire on November 30, 2026. The period from December 2026 – March 2027 has been allocated for data analysis and dissemination. Total study duration: 1 year (April 15, 2026 – March 31, 2027).
Outcome Variables	Primary: Mindfulness app usage minutes, implementation outcome measures (acceptability, appropriateness, feasibility), net promoter score, semi-structured interviews. Secondary: Five Facet Mindfulness Questionnaire, Self-Compassion Scale, Chronic Disease Self-Efficacy Scale, Brief Resilience Scale, Perceived Stress Scale (PSS-10), Kidney Disease Quality of Life (KDQOL-36), Short Warwick-Edinburgh Mental Well-Being Scale, Generalized Anxiety Disorder 7 (GAD-7), Patient Health Questionnaire 8 (PHQ-8), blood pressure.
Locations/Facilities	Yale School of Medicine, New Haven, CT (data collection) Yale New Haven Hospital, New Haven, CT (recruitment) Yale Medicine Nephrology, Stamford, CT (recruitment)

Abbreviations

Abbreviation	Explanation
AE	Adverse event
BRS	Brief Resilience Scale
CDSES	Chronic Disease Self-Efficacy Scale
CKD	Chronic kidney disease
CSV	Comma-separated values (format of export file)
eGFR	Estimated glomerular filtration rate
FFMQ	Five Facet Mindfulness Questionnaire
GAD-7	Generalized Anxiety Disorder 7-Question Assessment
IRES	Integrated Research Enterprise Solution (hosts IRB protocols)
KDQOL-36	Kidney Disease Quality of Life 36-Item Short Form
MBSR	Mindfulness-Based Stress Reduction
PHQ-8	Patient Health Questionnaire 8-Question Assessment for Depression
PSS-10	Perceived Stress Scale (10-item)
SCS	Self-Compassion Scale
SWEMWBS	Short Warwick-Edinburgh Mental Well-Being Scale

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Glossary of Terms

Term	Explanation
Mindfulness	A cognitive skill focused on maintaining moment-to-moment awareness of one's internal state and surroundings.
Chronic Kidney Disease	A condition characterized by gradual loss of kidney function over time, classified by stages based on estimated glomerular filtration rate (eGFR).

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Protocol Revision History

Version Date	Summary of Substantial Changes
March 8, 2026	Original version

1 Background

1.1 Background

Chronic kidney disease (CKD) and mental health. CKD is a progressive condition affecting an estimated 37 million adults in the United States. A global systematic review and meta-analysis of 65 studies (80,932 individuals with CKD) found an overall pooled depression prevalence of 26.5% (95% CI 23.1–30.1%), with higher rates among those on chronic hemodialysis compared to pre-dialysis patients (29.9% vs. 18.5%; p=0.01)[1]. Anxiety rates are similarly elevated, with one study finding clinically significant anxiety in 50.7% and depression in 35.4% of participants across CKD stages, using the Hospital Anxiety and Depression Scale[2]. Notably, 26.4% of CKD patients in that study had experienced suicidal ideation and 9.3% had attempted suicide[2]. Depression and anxiety in CKD are associated with lower health-related quality of life, poorer treatment adherence, increased hospitalizations, and higher mortality[1,2]. Despite these risks, mental health treatment engagement remains low among adults with CKD due to barriers such as time demands of medical management (including dialysis schedules), transportation constraints, stigma, and limited access to specialists with nephrology-specific expertise[2,3].

Mindfulness interventions for CKD. Mindfulness, a cognitive skill focused on maintaining moment-to-moment awareness of one's internal state and surroundings, is typically acquired through meditation practice. A systematic review of mind-body interventions in pre-dialysis CKD analyzed 32 RCTs and found anxiety reductions of 8–44% with various modalities (music therapy, relaxation therapy, spiritual therapy), with no adverse effects reported[4]. Among patients on dialysis, systematic reviews of mindfulness-based interventions have found promising improvements in depression, anxiety, stress, sleep, and quality of life[5–8]. A recent systematic review of psycho-behavioural interventions in CKD patients not yet on dialysis (5 RCTs, N=631) found moderate-certainty evidence of consistent improvements in self-efficacy and physical function, with emerging evidence for mental health benefits[9].

A landmark RCT by Jeong et al. (2025) randomized 29 patients with CKD stages III–IV to an 8-week Mindfulness-Based Stress Reduction (MBSR) program versus a Health Enhancement Program. Using direct intraneural recordings of muscle sympathetic nerve activity (MSNA), the study found a significant reduction in sympathetic reactivity during mental stress (p=0.029) with a large effect size (Hedges' $g = -0.858$)[10]. An earlier acute study in 15 hypertensive African-American males with CKD demonstrated that a single 14-minute guided mindfulness session lowered both sympathetic nerve activity and blood pressure compared to a control condition[11]. These findings establish unique sympathoinhibitory effects of mindfulness beyond simple breathing modifications, with direct relevance to the cardiovascular complications of CKD.

Digital delivery of mindfulness. Digital mindfulness interventions offer several advantages for CKD populations, including increased accessibility, scalability, cost-effectiveness, and sustained contact over an extended period of time. Calm Health is an evidence-based and affordable

($6/month) commercial mobile health application rooted in mindfulness. Four fully powered randomized controlled trials support the effectiveness of the Calm app in reducing mental health symptoms across different populations[12–15] and improving clinical benefits for other underlying conditions[13,14]. We recently partnered with Calm Health to create a CKD-specific module of mindfulness exercises as an unpaid consultant (Co-I Dr. Griffith). This module, combined with their other modules for general mindfulness and mental health, could be an effective and implementable tool for CKD distress.

1.2 Prior Experience

Calm Health App. Table 1 summarizes five non-Yale clinical trials of the Calm app. Participants used the app on an on-demand schedule averaging 38–105 minutes per week across studies. Four RCTs and one pilot trial demonstrated favorable effects on mental health symptoms, with high satisfaction ratings (81–93% satisfied) and willingness to recommend (76–79%). Unintended responses were reported with 0% prevalence in the two studies that evaluated them.

Table 1. Randomized controlled trials of Calm Health

Trial	Population	Intervention	Control	Outcomes	Treatment Evaluation	Unintended Effects
NCT03891810 Ref: [12]	College students, mean age 21yr (n=41 intervention, n=47 control)	Introductory module on mindfulness ("7 Days of Calm") followed by exercises of choice. Averaged 38 min/wk. 8 weeks.	Wait list to receive Calm after study.	Favorable (perceived stress, mindfulness, self-compassion). Neutral (sleep, drinking, physical activity, diet). Excluded non-completers (17%) and non-users (3%).	68% likely to use in future. 76% likely to recommend.	0%
NCT04045275 Refs: [13]	Adults with sleep disturbance, mean age 45yr (n=124 intervention, n=139 control)	Introductory module then exercises of choice. Averaged 105 min/wk. 8 weeks.	Wait list to receive Calm after study.	Favorable (daytime fatigue, sleepiness, pre-sleep arousal, depression, anxiety). Neutral (sleep quality). Intention-to-treat.	Not evaluated.	0%
NCT05120310 Ref: [14]	Employees of large retailer, mean age not reported (n=585 intervention, n=444 control)	Self-select exercises. Averaged 102 min/wk. 8 weeks.	Wait list to receive Calm after study.	Favorable (depression, anxiety, insomnia, sleepiness, nonwork impairment, medical visit frequency). Neutral (stress, resilience, absenteeism, presenteeism). Intention-to-treat.	Not evaluated.	Not evaluated.
NCT04329533 Ref: [15]	Pregnant women or women with delayed/cancelled gynecology surgeries during COVID-19, mean age 36yr (n=51 intervention, n=50 control)	Self-select exercises. 37% used 5+/wk, 37% used 3-4/wk, 26% used ≤2/wk. 30 days.	Wait list to receive Calm after study.	Favorable (stress, depression, anxiety, sleep disturbance). Intention-to-treat.	81% satisfied. 86% said easy to use.	0%
NCT04272138 Ref: [23]	Middle-aged adults with elevated stress, mean age 52yr	Self-select exercises. 33 completed follow-up; averaged 103 min/wk,	App with health/wellbeing podcasts but no mindfulness. 27	No statistically significant changes (pilot not powered to detect significance).	93% said useful. 79% likely to recommend.	0%

	(n=39 intervention, n=35 control)	71% used ≥49 min/wk. 4 weeks.	of 35 completed follow-up; 62% used ≥49 min/wk.		64% would continue.	

**Ref 23 = Laird et al. 2022, a pilot feasibility study (not a fully powered RCT).*

Calm Health is also being used for clinical trials in preparation or ongoing in Yale Oncology (NCT06923501, HIC 2000037763) and Yale Pediatrics (NCT07062887**,** HIC 2000039191). Dr. Ash was an investigator on stakeholder interviews in preparation for the pediatrics trial (HIC 2000038023)[24].

Team experience with related digital interventions. The investigative team has extensive experience delivering digital lifestyle interventions for related populations including exercise support for middle-aged adults with type 1 diabetes (Yale HIC #2000025992, #2000035846; PI: Ash)[16] and sleep and alcohol support for young adults with heavy drinking habits (Yale HIC #2000021048, #2000030417; Co-I's: Ash, Griffith)[17–20]. These past studies included both lifestyle support guidance and biometric feedback.

2 Rationale/Significance

2.1 Rationale and Study Significance

Adults with CKD experience numerous psychosocial and behavioral challenges. Depression affects approximately 26.5% of adults with CKD globally[1], and clinically significant anxiety affects up to half of all CKD patients[2]. These mental health conditions impair treatment adherence, reduce quality of life, and increase mortality risk. Despite this burden, barriers to mental health care are substantial, including the time demands of CKD management, transportation constraints, and limited availability of nephrology-informed mental health providers.

Mindfulness meditation interventions have shown efficacy in CKD populations, with evidence from pre-dialysis through dialysis stages demonstrating improvements in sympathetic nervous system function, perceived stress, sleep quality, and inflammatory biomarkers. However, most evidence comes from in-person programs during dialysis sessions, and digital mindfulness delivery for CKD has not been tested. There is a critical need for scalable, accessible mental health tools for this population.

The main purpose of the present study is to pilot test the Calm Health app among adults with CKD to determine what refinements are needed before conducting a fully powered randomized controlled trial. If that future trial shows a positive signal, it would support the implementation of Calm Health for prevention and treatment of mental health conditions among adults with CKD.

Additionally, the app might drive behavior change more strongly if augmented with a biometric dashboard enabling adults with CKD to understand connections among mindfulness practice, physiological manifestations of distress (sympathetic overdrive, sleep disturbance), and blood pressure patterns. In our prior studies, multimodal biometric feedback was enthusiastically

received and mitigated health risk scores[19,20]. Among people with CKD, while routine care often involves home blood pressure monitoring, integration of multiple behavioral and cardiovascular biometrics for mental health is in nascent stages.

2.2 Risks

#1. Confidentiality: Due to the collection of private identifiable information, there is a possibility of a security breach compromising subject confidentiality. Such breaches are extremely uncommon when proper IRB-approved precautions are taken.

#2. Unintended psychological changes during intervention: Among the 5 prior clinical trials of Calm (Table 1), unintended responses were reported to occur with 0% prevalence in 4 studies (255 participants using Calm) and not evaluated in 1 study. Nonetheless, any psychological intervention carries risk of unintended changes. A systematic review of meditation practice studies assessed 6,703 total participants for adverse events; the overall weighted prevalence was 8% (95% CI 5%–12%). By comparison, adverse event prevalence in psychotherapy reviews exceeded 30%, and in one trial comparing mindfulness to escitalopram for anxiety disorders, adverse events occurred for 79% on medication versus 16% receiving mindfulness[21].

The GAD-7 and PHQ-8 will be administered every 4 weeks. The PHQ-8 does not include a suicidal ideation question; however, any spontaneous disclosure of suicidal ideation during check-in calls triggers an immediate safety assessment and crisis response protocol. Response thresholds to GAD-7 and PHQ-8 scores focus on change from baseline rather than absolute scores, as chronic illness burden may elevate baseline anxiety and depression. Mild/moderate scores (PHQ-8 <15, GAD-7 <15) require no immediate follow-up. Severe scores (PHQ-8 ≥15, GAD-7 ≥15) or notable worsening (≥5 point increase from baseline on either scale, or movement from the moderate to the severe category) trigger follow-up within 48 hours by a trained study investigator. Follow-up actions include: (1) providing resources both verbally and in writing (Appendix 3: 211 for local social services; 988 National Suicide and Crisis Lifeline, which has a Spanish-speaking option; 741741 Crisis Text Line for text-based support; 911 for emergencies); (2) offering clinical referral to a mental health provider (psychologist, psychiatrist, counselor) with facilitated warm handoff when possible and provision of institutional resources such as Yale mental health services; and (3) noting that the participant is concurrently receiving app-based suggestions from Calm Health. Participants with active suicidal or homicidal ideation will be withdrawn and staff will call 988 and inform their primary provider. Note that uremic symptoms, fatigue, and chronic illness burden in CKD may contribute to elevated PHQ-8/GAD-7 scores; therefore medical events (hospitalizations, significant lab changes, symptom exacerbations) that coincide with mental health changes will be documented.

Monthly health coaching calls will include a verbal check-in: “Since your last connection with our team, have you noticed any changes in your mood or mental health?” These encounters will be documented on an excel database stored on OneDrive. A one-week check-in call will be made if the patient has not logged into the Calm App, also documented on OneDrive. The research

coordinator will review all completed assessments and app check-ins weekly, with Dr. Ash performing a second check on a monthly basis.

To facilitate timely responses, surveys and interviews will be administered during in-person or remote study visits while on a live Zoom call with research staff.

#3. Study questionnaires and interviews: Participants may experience some distress when discussing factors related to CKD, CKD management, and psychosocial stressors. The probability of such responses is uncommon and the typical magnitude is mild.

#4. Wrist Actigraphy: In a small number of participants, wearing an actigraphy watch may contribute to skin irritation or allergies (reported in 3% of wearers in a prior clinical trial). We minimize risk by providing the watch with a hypoallergenic band, training participants in manufacturer guidelines, and referring for skin care if irritation occurs.

There are no potential social, cultural, financial, or legal risks.

2.3 Anticipated Benefits

All participants will receive guidance and support for mindfulness from an evidence-based app. It is possible they will continue mindfulness practice after the study. The benefits to science may include a better understanding of how to engage adults with CKD in mindfulness and improved design of future interventions. There is a need to equip adults with CKD with more accessible tools for mental health support.

3 Study Purpose and Objectives

3.1 Purpose

The purpose of this study is to pilot test the feasibility, acceptability, and preliminary efficacy of a digital mindfulness intervention (Calm Health) among adults with chronic kidney disease, and to develop user-informed biometric data visualizations to augment the intervention.

3.2 Hypotheses

Objective #1, Hypothesis: Adults with CKD will rate Calm Health to be satisfying (≥4 out of 5 on surveys), citing accessibility and asynchronous availability as strengths.

Objective #2, Hypothesis: Outcome metrics related to perceived stress, quality of life, well-being, and mental health will show favorable effects after engaging in the mindfulness-based app intervention. These variables will be measured at baseline and at 6-week follow-up.

Objective #3, Expected Outcome: Participants seeing a biometric display of their health data will have meaningful and actionable reactions, while offering suggestions to improve the way it is presented.

3.3 Objectives

Primary Objective

Objective #1: Determine whether it is feasible and acceptable to use Calm Health, a mobile app guiding mindfulness practice, among adults with CKD.

Secondary Objective(s)

Objective #2: Determine whether using Calm Health has favorable effects upon perceived stress, quality of life, well-being, mental health, and blood pressure.

Objective #3: Develop visualizations of biometric data and mindfulness app usage timestamps, to help adults with CKD review and understand their health data and refine reports by a user-centered design.

4 Study Design

This will be a single-group, nonrandomized, unblinded, behavioral clinical trial (Figure 1). Adults with CKD will use Calm Health for 6 weeks. They will complete pre-post surveys and wear an actigraphy watch. We will capture and measure efficacy signal for psychosocial and biometric outcomes. At the 6-week visit they will complete an exit survey and interview to assess feasibility and acceptability, as well as provide user-centered design input for a biometric coaching dashboard.

Calm Health is classified by the FDA as a "general wellness item" (i.e., a product intended to improve general health and wellness), which is not within the FDA's current scope of oversight. It is currently commercially available to the general population including adults with CKD. We will not modify it from its usual commercial state. Another Yale IRB protocol is testing Calm Health for another population (young adults with type 1 diabetes) as a non-medical device, social & behavioral research trial (IRES IRB# 2000039191).

Participants can use the app on an on-demand schedule. We will recommend they use it for an average of 45 minutes per week, which is approximately one mindfulness session per day. The exposure length will be 6 weeks to test retention after initial novelty. Participants will also have complementary app access after the study, until November 30, 2026. Calm Health is not currently considered standard of care, so all participants will be using it for research purposes. Health coaching check-ins will be conducted at Week 1 (troubleshooting for non-users) and Week 4 (motivational interviewing session to trial human-delivered coaching in concert with the app) by an Allied Health Professional (clinical psychologist, exercise physiologist, dietician, or certified health coach).

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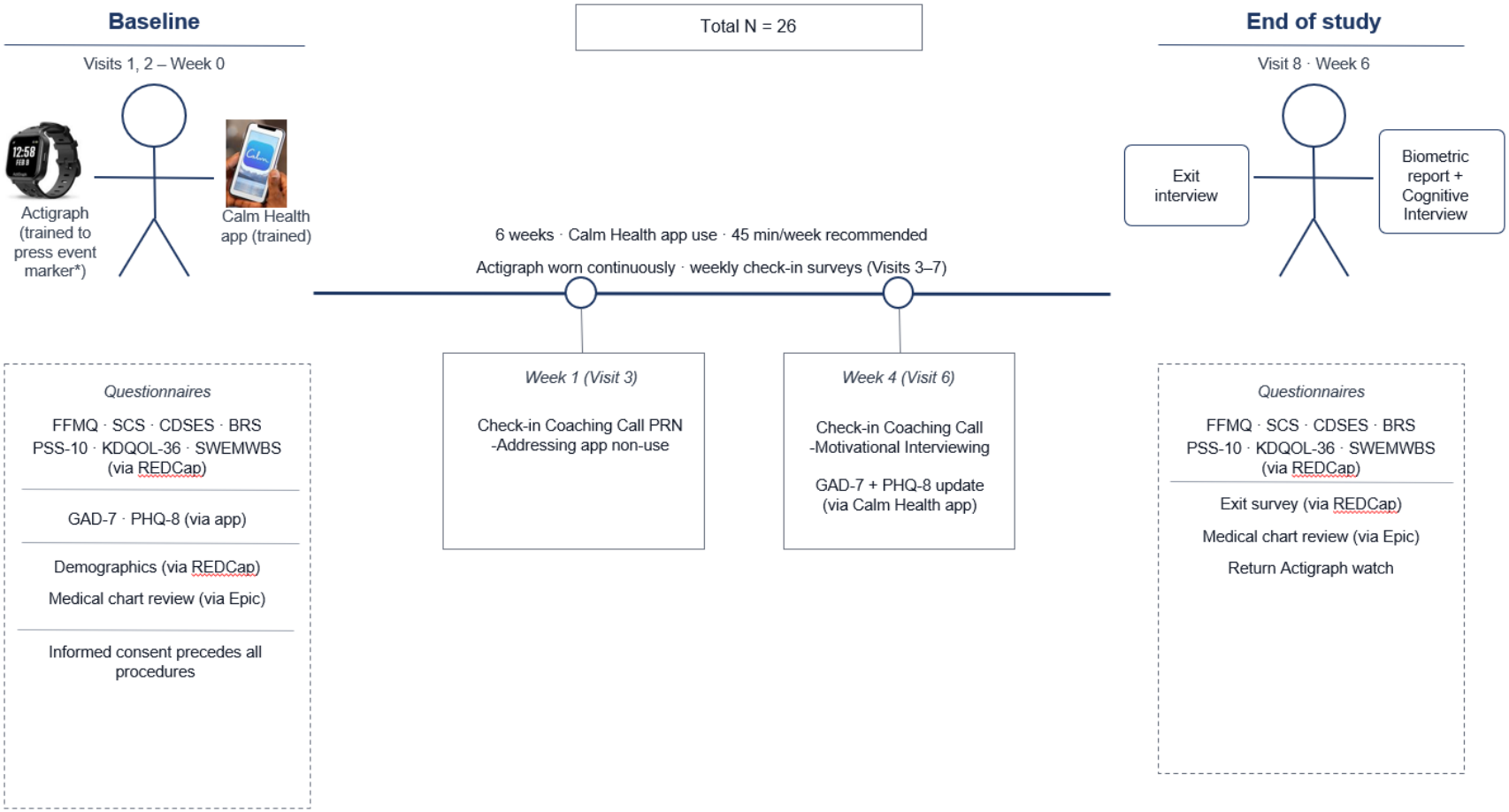

Figure 1. Study design. An unscheduled visit 9 may occur for adverse event follow-up. *Event markers capture self-directed mindfulness not involving the app, as well as sleep onset/wake.

Planned Protocol Modification Informed by Stakeholder Input. A concurrent IRB-exempt formative study (Yale HIC #2000042303) will interview at least 3-5 adults with CKD as stakeholder input on the study design. The Calm Health app intervention is fixed and will not be modified, as it is controlled by the manufacturer. However, elements of the study procedures that are delivered by the research team—particularly the health coaching check-in content, format, and frequency, as well as survey burden—may be refined based on stakeholder feedback. Any such modifications will be submitted as a protocol amendment for IRB approval before implementation. Participants enrolled prior to the amendment will continue under the original protocol unless the amendment is deemed applicable and beneficial, in which case they will be notified.

4.1 Study Duration

Individual participant duration: recruitment to baseline visit will take 1–30 days, and baseline visit to end of follow-up will take 6 weeks, for a total duration of approximately 2.5 months. The cutoff date for enrollment will be October 15, 2026 so that each participant can complete the 6 weeks of app access before the accounts expire on November 30, 2026. The period from December 2026 – March 2027 has been allocated for data analysis and dissemination. Total study duration: 1 year (April 15, 2026 – March 31, 2027).

4.2 Outcome Variables/Endpoints

4.2.1 Primary Outcome Variables/Endpoints

Objective #1

Metrics of Feasibility. Minutes per week of mindfulness app use, including mindfulness exercises, sleep mindfulness exercises, and other general content (music, daily wisdom, etc.) will be recorded using the Calm Health app backend dashboard.

Metrics of Acceptability. Quantitative methods: Participants will complete an exit survey including implementation outcome measures (acceptability, appropriateness, feasibility; α=.85–.91), net promoter score, and Likert-style satisfaction items. Qualitative methods: Semi-structured interviews will elicit perspectives about acceptability of the app, how app use affected attitudes toward CKD management, barriers and facilitators to using the app (including cultural influences), and overall satisfaction.

4.2.2 Secondary and Exploratory Outcome Variables/Endpoints

Objective #2

Table 2. Efficacy outcome assessments

Psychometric Assessment	Role in Study	Description	No. Items	Time	Timing

Five Facet Mindfulness Questionnaire (FFMQ)	Verification of intervention delivery	Validated self-report measuring 5 domains: observing, describing, acting with awareness, nonjudging, nonreacting.	39	10–15 min	Baseline & 6-wk follow-up
Self-Compassion Scale (SCS)	Mechanism targeted by intervention	Validated measure of self-kindness, self-judgment, common humanity, isolation, mindfulness, and over-identification.	26	7 min	Baseline & 6-wk follow-up
Chronic Disease Self-Efficacy Scale from Stanford (CDSES)	Mechanism targeted by intervention	Validated self-report assessing confidence in managing chronic illness across domains.	33	10 min	Baseline & 6-wk follow-up
Brief Resilience Scale (BRS)	Mechanism targeted by intervention	Validated 6-item measure of ability to bounce back from stress.	6	2 min	Baseline & 6-wk follow-up
Perceived Stress Scale (PSS-10)	Mental health mechanism reachable by intervention	Validated 10-item measure of perceived stress over the past month; widely used in CKD research.	10	5 min	Baseline & 6-wk follow-up
Kidney Disease Quality of Life (KDQOL-36)	Downstream life impact	CKD-specific quality of life measure including burden of kidney disease, symptoms/problems, and effects of kidney disease subscales, plus SF-12.	36	10 min	Baseline & 6-wk follow-up
Short Warwick-Edinburgh Mental Well-Being Scale (SWEMWBS)	Downstream life impact	Validated 7-item measure of positive mental well-being.	7	2 min	Baseline & 6-wk follow-up
Generalized Anxiety Disorder 7 (GAD-7)	Calm Health App Calibration	Validated screener for anxiety.	7	5 min	Baseline & 4-wk follow-up
Patient Health Questionnaire 8 (PHQ-8)	Calm Health App Calibration	Validated 8-item screener for depression (does not include suicidal ideation question).	8	5 min	Baseline & 4-wk follow-up

Objective #3: Participants will review a biometric report over televideo screenshare and complete cognitive interviewing (think aloud) during the presentation, followed by questions about perceptions of their health data, strengths and limitations of the format, and proposed refinements.

The biometric report is a personalized, multi-modal visualization of data collected during all weeks of the 6-week intervention period. It will display participant-level trends across: (1) Calm Health app usage, including session timestamps and cumulative minutes; and (2) actigraphy-

derived metrics including physical activity, sleep duration, heart rate, heart rate variability, blood pressure, respiratory rate, and skin temperature. Data streams will be aligned on a common timeline to allow participants to observe potential relationships between mindfulness practice patterns and physiological indicators (Appendix 7a). Actigraph data are not for clinical use and will not be reviewed by a physician.

The report will be presented to participants via televideo screenshare at Visit 8, during which they will complete a cognitive interviewing (think-aloud) protocol followed by structured questions about data comprehension, report format, and proposed refinements (see Appendix 7b: Cognitive Interview Guide).

The Actigraph Leap 2 watch does not directly measure blood pressure or display blood pressure readings. It collects a photoplethysmography (PPG) signal - the same physiological input used by dedicated blood pressure wearables - but delivers the raw waveform data rather than a pre-processed blood pressure value. The study team will process this raw PPG signal into blood pressure estimates using the algorithm described by Radha et al.[26], which applies heart rate variability and pulse morphology features extracted from wrist PPG to a Long Short-Term Memory (LSTM) neural network to estimate within-person blood pressure trends. This approach is validated for free-living ambulatory use and is appropriate for the study's goal of tracking relative patterns (e.g., higher versus lower BP periods) rather than absolute clinical-grade readings. Participants will be informed that these estimates are not for clinical use. This data workup will be completed by the study team prior to Visit 8 so that blood pressure trend data are available in the participant's personalized biometric report at that visit.

5 Study Participants

5.1 Study Population

Participants aged 18 years and older diagnosed with CKD for at least 6 months with at least two consecutive nephrology visits within a 1 year window, the last occurring within the past year. They will be patients of Yale Medicine Nephrology or Yale New Haven Hospital. These institutions serve a diverse sample of adults with CKD. This population was selected because they face many barriers to accessing healthcare for the mental health sequelae of CKD, and could benefit from a mobile mindfulness solution.

5.2 Number of Participants

We will enroll 26 participants. We may need to screen up to 52 participants.

5.3 Eligibility Criteria

In order to be eligible for inclusion in the study, an individual must meet all of the following criteria:

1. Provision of signed and dated informed consent form.
2. Stated willingness to comply with all study procedures and availability for the duration of the study.
3. Aged 18-80 years inclusive.
4. Diagnosed with CKD for at least 6 months with at least two consecutive nephrology visits within a 1 year window, the last occurring within the past year.
5. Receiving CKD care at Yale Medicine Nephrology or Yale New Haven Hospital.
6. Able to use a smartphone. The study team will provide a smartphone if the individual does not own one.
7. Able to read and write English.

Any individual who meets any of the following criteria will be excluded from participation in this study:

1. Current meditation or mindfulness practice meeting or exceeding the a typical recommended schedule (70 minutes per week)[25] over the past 1 month.
2. New or unstable psychopharmaceutical treatment in past 2 months. Note: Stable maintenance therapy (no dose/medication changes for ≥8 weeks) is acceptable.
3. Current intensive psychiatric treatment (psychiatric hospitalization in past 6 months, intensive outpatient program, inpatient rehabilitation).
4. Current or planned pregnancy in the next 6 months, based on self-report and confirmed by medical record review.
5. Average resting blood pressure exceeding 160/100 mmHg based on readings available in the medical record, with reconfirmation by additional readings prior to exclusion if only an isolated reading in this range is available.

5.4 Recruitment Procedures

Clinic attendings will identify study candidates from the daily clinic schedules. They or research staff will contact these patients by phone, text message, email, mail, MyChart message, or in-person at regular clinic visits. Calls and text messages will be sent during hours of 10am–8pm. The HRPP's guidance on recruitment of patients will be followed. If the potential participant was not first identified during a clinic visit, their primary nephrology provider will make the initial contact and obtain their verbal permission for non-clinical research team members to make contact.

The study will also be publicly announced via research flyers at Yale Medicine Nephrology and Yale-New Haven Hospital. The study will be posted on clinicaltrials.gov and the YCCI website. In the event of recruitment shortfall, we may elect to amplify these postings through social media and 3rd-party sites such as ResearchMatch.

Interested individuals will be invited to inquire about the study by contacting investigators by telephone or email, or by providing eligibility information on a secure HIPAA-compliant Qualtrics webform (Appendix 8). Participants passing both the first and second tiers of the eligibility interview (Appendix 8) will be invited to schedule a consenting televideo visit on Zoom.

5.5 Consent/Assent Procedures/HIPAA Authorization

- Consent will use the standard IRB-approved compound consent / HIPAA research authorization form.
- A PDF of each IRB-approved form will be converted to an electronic survey on YCCI's approved REDCap e-consent framework, which includes a final certification screen, PDF storage, and fields for wet signatures.
- The forms describe in detail the study intervention, study procedures, and risks. Written electronic documentation of informed consent is required prior to starting study assessments.
- A principal investigator, co-investigator, or research assistant will explain the research study to the participant and answer any questions. This conversation will take place over a Zoom televideo call from as private a physical setting as possible.
- Participants will have the opportunity to carefully review the electronic written forms and ask questions prior to signing. A quiz will be used to ensure understanding (Appendix 14). Participants may discuss the study with family before agreeing.
- Participants must be informed that participation is voluntary and that they may withdraw at any time, without prejudice. A PDF of the signed consent document will be sent by encrypted email.

This study does not involve children. Assent will not be obtained.

6 Study Methods/Procedures

6.1 Study Procedures

Table 3. Visit Schedule

Procedure	Pre-screen	Consent	Enroll	Wkly Check-In	Health Coaching and Recalibration	Wkly Check-In	Follow-Up	Unscheduled
Visit Number	0	1	2	3-5	6	7	8	9
Week Number	-2	-1	0	1-3	4	5	6	N/A

Screening Phone Call	X							
Informed Consent		X						
Demographics		X						
Clinical history		X					X	X
REDCap surveys (FFMQ, CDSES, CDSES, BRS, PSS, KDQOL, SWEMWBS; Table 2)		X					X	
Actigraph watch			Continuous → → →→→→→→→→→→→→→→→→→→					
Train to use Calm Health app			X					
Calm Health in-app calibration surveys (GAD-7, PHQ-8; Table 2)			X		X			
Use Calm Health App			Continuous → → →→→→→→→→→→→→→→→→→→					
Check-in: app usage, barriers, other mindfulness, other digital interventions, mental health services,				X	X	X	X	
Health coaching				X (visit 3, only if not using Calm Health)	X			

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Exit survey & interview							X	
Biometric report interview							X	
Adverse events check-in				X	X	X	X	X
Time of procedures (min)	15	60	90	15	15	15	90	60
*Depicted in this chart are extra readings taken for study purposes. Participants will also take all readings ordered by their physician as standard of care.								

All procedures in this chart are taken for research purposes. Total research procedure time is approximately 5 hours. In addition, participants are asked to use the app 45 minutes per week for 6 weeks, for an expected total time commitment of approximately 10 hours.

Health Coaching Check-Ins. In addition to the monitoring schedule above, two structured health coaching check-ins will be conducted by an Allied Health Professional (clinical psychologist, exercise physiologist, dietician, or certified health coach). At Week 1, participants who have not logged into the app will receive a coaching call to troubleshoot barriers to engagement. These barriers may be technical (app navigation, device compatibility) or logistical (adjusting daily routine to make time for using the app). At Week 4, a health coaching session will trial approaches for how human-delivered coaching can work in concert with the app-based intervention. This session will use a motivational interviewing approach, with fidelity assessed using the Motivational Interviewing Treatment Integrity (MITI) evaluation framework (motivationalinterviewing.org). The Week 4 coaching session will explore the participant's experience with the app, reinforce intrinsic motivation for mindfulness practice, and collaboratively problem-solve any ongoing barriers. The health coaching curriculum (Appendix 13c) may undergo refinement based on stakeholder interviews that are occurring on a separate protocol currently in review for IRB exemption (HIC #2000042303), upon which a modification to the current trial would be submitted.

6.1.1 Data Collection

Survey data will be collected via REDCap (Visits 1, 2, 8) and Qualtrics SMS surveys (Visits 3–7). Calm Health usage data and responses to the calibration surveys (GAD-7, PHQ-8) will be captured through the app backend dashboard. Actigraph watch will be shipped back in a prepaid package and data will be downloaded from the device before Visit 8. Participants will not be penalized for lost Actigraph watches since they do not have resale value. Interviews will be audio-recorded on Zoom – for participants who consent to recording - and transcribed. See Section 8 (Table 4) for full data collection workflows.

Medical Chart Review. At enrollment and follow-up visits, research staff will review the participant's medical chart (Epic) to capture: demographics and vital signs such as height and weight; diagnoses and medications; metabolic panel; cystatin C). Chart review data will be compared against participant self-report and used to characterize the clinical profile of the sample.

Actigraph Event Markers. The Actigraph Leap 2 watch includes an event marker button. Participants will be trained to press the event marker button at two times: (1) when they begin and end a mindfulness practice that is not guided by the Calm Health app (e.g., informal mindfulness during a walk), and (2) at sleep onset and wake time, to supplement the actigraphy sleep algorithms which can sometimes misidentify sleep start and stop times.

Weekly Surveys. On a weekly basis (Visits 3–7), participants will complete a brief SMS survey covering: facilitators and barriers to engaging with Calm Health; barriers or challenges to study participation more broadly; windows of Actigraph removal (if any); mental health services utilization (e.g., therapy appointments, psychiatric visits, crisis contacts); other digital health interventions used (devices and modules outside the study); other mindfulness practices outside of Calm Health; and any clinical events or adverse events. Research staff will follow up on any reported barriers or adverse events by telephone.

Biometric Report Preparation and Delivery. Prior to Visit 8, research staff will compile a personalized biometric report integrating data collected across the 6-week intervention period. The report will display participant-level trends across: Calm Health app usage, including session timestamps and cumulative minutes; self-directed mindfulness practice captured via Actigraph event marker presses; and actigraphy-derived metrics including physical activity, sleep duration, heart rate, heart rate variability, blood pressure, and skin temperature. Data streams will be aligned on a common timeline to allow participants to observe potential relationships between mindfulness practice patterns and physiological indicators. The report will be presented to participants via televideo screenshare during Visit 8 (see Appendix 7a for a sample report).

Cognitive Interview. The biometric report will be presented using a think-aloud cognitive interviewing protocol (Appendix 7b), in which participants verbalize their thoughts and reactions in real time as they view each section of the report. This procedure is distinct from the exit interview (Appendix 2), which addresses overall app acceptability and experience; the cognitive interview focuses specifically on participants' comprehension of and reactions to their health data as presented in the biometric report. Following the think-aloud portion, structured questions will address perceived strengths and limitations of the report format and proposed refinements. Responses will inform iterative, user-centered development of the biometric report for future trials. The session will be audio-recorded on Zoom and transcribed per the procedures described in Table 4.

6.2 Method of Assignment/Randomization

Not applicable. This is a single-arm study with no randomization.

6.3 Adverse Events Definition and Reporting

An adverse event is any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related. An adverse event or suspected adverse reaction is considered serious if, in the view of either the investigator or study physician, it results in any of the following outcomes: death; a life-threatening adverse event; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or a congenital anomaly or birth defect.

Adverse event monitoring will follow a structured schedule. The GAD-7 and PHQ-8 will be administered every 4 weeks. Results will be stored on the Calm Health portal and exported weekly by the program coordinator. The research coordinator will conduct weekly data reviews of all completed assessments and app check-ins. Monthly check-in calls will include a verbal check-in asking whether participants have noticed changes in mood or mental health; these encounters will be documented on an excel database stored on OneDrive. A one-week check-in call will be made only if the patient has not logged into the Calm App, also documented on OneDrive. Dr. Ash will perform a second check on a monthly basis. Adverse event information will also be recorded from the medical record at the unscheduled follow-up visit.

An adverse event report will be generated for each event including: description of the event; when and how it was reported; official chart records; and principal investigator assessment of likelihood of being related to the study (not, unlikely, possibly, probably, definitely), severity (mild, moderate, severe), whether the severity was anticipated, and whether the frequency was anticipated.

Timeline for reporting: Events that may require interruption of study activities will be verbally reported immediately with a written report within 5 business days. Reportable Events (serious or life-threatening, unanticipated, and possibly related) will be filed within 5 business days. Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) will be filed within 5 business days with a management plan.

6.4 Reaction Management

Response thresholds focus on change from baseline rather than absolute scores, as chronic illness burden (uremic symptoms, fatigue) may elevate baseline anxiety and depression in CKD. Medical events that coincide with mental health changes (hospitalizations, significant lab changes, symptom exacerbations) will be documented. Suicidality Monitoring: The PHQ-8 does not include a suicidal ideation question. Any spontaneous disclosure of suicidal ideation during check-in calls triggers an immediate safety assessment and crisis response protocol. Score Interpretation: Mild/Moderate scores (PHQ-8 <15, GAD-7 <15) require no immediate follow-up. Severe scores (PHQ-8 ≥15, GAD-7 ≥15) or notable worsening (defined as ≥5 point increase from baseline on either scale, or movement from the moderate to the severe category) trigger follow-up actions within 48 hours by a trained study investigator. Follow-up actions for severe or

worsening scores include: (1) Initiate follow-up within 48 hours by a trained study investigator. (2) Provide resources both verbally and in writing: 211 for local social services; 988 National Suicide and Crisis Lifeline (988lifeline.org, has Spanish-speaking option via press 2); 741741 Crisis Text Line (complements 988 by providing text option; text HOME for English or AYUDA for Spanish); 911 for emergency services. Document that resources were provided. (3) Offer clinical referral by connecting the participant to a mental health provider (psychologist, psychiatrist, counselor), facilitating a warm handoff when possible, and providing institutional resources (e.g., Yale mental health services). (4) Note that concurrently, the user is getting suggestions from the Calm Health app. Participants with active suicidal or homicidal ideation will be withdrawn and staff will call 988 and inform their primary provider.

6.5 Withdrawal Procedures

Participants may withdraw voluntarily at any time for any reason. Participants having active suicidal or homicidal ideation will be withdrawn early from the study. Participants withdrawing early due to lack of interest in mindfulness exercises will be invited to still complete the 6-week follow-up assessments (visit 8), but will stop receiving weekly check-in surveys.

6.6 Locations/Facilities

1 site for data collection: Yale School of Medicine, New Haven, CT.

2 sites for recruitment: Yale New Haven Hospital, New Haven, CT; Yale Medicine Nephrology, Stamford, CT.

7 Statistical Design

7.1 Sample Size Considerations

We will enroll 26 participants, which gives 80% statistical power to detect any feasibility problems having ≥6% incidence[22]. We will submit a modification to enroll additional participants if needed to have interviews reach thematic saturation, which typically occurs within 10–20 participants.

7.2 Planned Analyses

Aim 1 – Quantitative Analysis: Metrics of mindfulness app usage and satisfaction survey scores will be summarized by descriptive statistics. We will compare results with a priori standards: 1) engagement compared to 45 minutes per week; 2) general satisfaction scores of 4–5 out of 5.

Aim 1 – Qualitative Analysis: Interviews will be audio-recorded for participants who consent to it, transcribed verbatim, and imported into NVivo. Interviewers will also add summaries of interviews where participants do not consent to recording. The investigative team will collaboratively identify general coding categories from nephrology and implementation science

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perspectives, followed by identification of subthemes and coding of excerpts using inductive, directed qualitative content analysis.

7.2.1 Secondary Objective Analyses

Aim 2: Our focus is calculating pre-post effect sizes for each variable. We will consider data distributions and choose an appropriate effect size formula (Hedge's g for a small but normally distributed sample, or biserial r for a non-normally distributed sample). We will use Fritz's formulas to convert to Cohen's d and evaluate size ($d \geq 0.20$ small, ≥ 0.50 moderate, ≥ 0.80 large), while also considering the raw metric in relation to clinically meaningful change.

Aim 3: Qualitative analysis will employ similar core methods as Aim 1. The outcome will identify common themes to guide refinement of personalized biometric reports.

Safety: Safety will be quantified as the frequency of adverse events overall and by type, expressed as proportions with 95% confidence intervals. It will be compared numerically to the literature finding of 8% adverse events from meditation.

7.2.2 Analysis of Subject Characteristics

Demographics (age, sex, gender, race, ethnicity, household income, education level, public vs. private insurance, duration of CKD, CKD stage), descriptive clinical characteristics from chart review (eGFR, metabolic panel, lipid panel, glucose measures, diagnoses, medications, height, weight), and derived indices (body mass index) will be tabulated. Categorical variables will be reported as proportions; continuous variables will be reported as mean±standard deviation if normally distributed or median (25th, 75th percentile) if non-normally distributed.

7.2.3 Interim Analysis

The sole stopping rule will be clear evidence of harm. There is no possibility of futility of treatment or overwhelming evidence of benefit, as this study evaluates feasibility and psychological mechanisms. No interim analyses are planned.

7.3 Data Relevance

All data collected are directly relevant to the study objectives. The survey instruments were selected to capture mechanisms targeted by mindfulness (self-compassion, self-efficacy, resilience), mental health outcomes reachable by the intervention (perceived stress, anxiety, depression), and downstream quality of life and well-being impacts specific to CKD (KDQOL-36, MWBS).

7.4 Data Coding

Quantitative data will be coded by anonymous study ID number. Qualitative interview data will be de-identified during transcription and coded using NVivo.

7.5 Data Analysis Tools

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Quantitative analyses will be performed using R or Stata. Qualitative analyses will use NVivo. Biometric data processing will use ActiLife software (Actigraph) and manufacturer dashboards.

7.6 Data Monitoring

Calm Health usage will be monitored weekly through the backend dashboard.

Weekly SMS surveys will be monitored through Qualtrics.

Actigraph data will be audited at device download for completeness. Actigraph data are not for clinical use.

Dr. Ash will perform data audits after the first month and at least twice per year.

7.7 Handling of Missing Data

We will run an intention-to-treat analysis with last observation carried forward and a per-protocol (completers only) analysis. To avoid missing data, we will make efforts to contact individuals who stop using the app to nonetheless complete the 6-week assessment, though they will not receive the weekly surveys since those mostly pertain to app usage and barriers.

We will analyze both the full sample and individuals completing the recommended dose of 45 minutes per week. We acknowledge possible confounders (life events, changes in lifestyle habits) and moderator variables (gender, race, ethnicity, education level), but this pilot study is not powered for these analyses.

8 Data/Specimen Handling and Record Keeping

Table 4 details the data sources, timing, HIPAA identifiers, collection workflows, and protocols for exporting and deidentifying data during the study. Data can be accessed by members of the research team. The master key of participant IDs will be destroyed 1 year after the completion of data collection, thus kept for a total of 2 years for the earliest participants and 1 year for the latest participants. De-identified data will be stored indefinitely.

Table 4. Data sources and collection workflows

Data Source	Timing	HIPAA Identifiers	Data Collection Workflow	Data Export to Yale Server and Deidentification
Actigraph Leap 2 Watch	Visit 2 through Visit 8	None	Researchers connect watch by physical cord to computer with ActiLife software.	Researchers export from ActiLife Software.
Calm Health	Visit 2 through Visit 9	IP address and phone number used by manufacturer to deliver content, not shared with research team. Participant is asked to enter DOB to help app make content recommendations. Participant has	Researchers view backend dashboard displaying usage from user accounts (does not display location) which are identified by anonymous email address created by research team.	Researchers export from backend dashboard, remove names, and align anonymous email address with study ID number.

		option to enter first and/or last name so app can personalize greetings.†		
Yale REDCap	Visits 1, 2, 8	Identifying information on contact details form. Separate from other data.	Researchers and participants enter information into survey forms and source documents.	Researchers export data except identifying information.
Yale Qualtrics	Visits 3–7	Participant phone number entered to transmit SMS survey. Separate from other data.	Participants enter information into survey forms.	Researchers export data except identifying information.
Yale Zoom recordings of interviews	Visit 8	Voice, names, places, others that participants may mention.	Zoom saves recording and transcript on its Yale cloud.	Researchers download from cloud, remove identifying information (names, places, other) from transcript, and check transcript for accuracy against recording. Recording will then be promptly destroyed.
Yale clinic medical charts	Visits 1, 8, 9	Medical records include patient identifiers required by Yale health system.	Researchers view records to verify information reported by participant during study visits.	Corrections to participant reports are manually logged by researchers in REDCap. No data are directly exported.

†Calm Health has completed a security planning assessment with Yale ITS for the handling of high-risk data. Documentation is attached.

8.1 Subject Data Confidentiality

Participant confidentiality and privacy is strictly held in confidence by the participating investigators, their staff, and the sponsor(s)/funding agency. All research activities will be conducted in as private a setting as possible. Representatives of the IRB, regulatory agencies, or study funding agencies may inspect all documents required to be maintained by the investigator.

Study participant research data will be transmitted to and stored at Yale University servers. Individual participants will be identified by a unique study identification number (MK01, MK02, etc., assigned in order of consenting). The study data entry and management systems will be secured and password protected. A master list linking study number to participants is only accessible to authorized study personnel via REDCap report view.

8.2 Data Quality Assurance

Staff will attend training sessions with Dr. Ash on database monitoring. Actigraph data will be audited at device download. Calm Health usage will be monitored weekly. Audio-recorded interviews – for participants consenting to audio recording - will be checked for accuracy before recordings are destroyed. REDCap survey and source documents will be checked after each visit. Dr. Ash will perform data audits after the first month and at least twice per year. Health coaching fidelity will be assessed through periodic peer review by Dr. Ash or another qualified health coach (Appendix 13a) and coach self-reflection (Appendix 13b) at least once during the study, with additional reviews conducted if quality concerns are identified.

8.3 Data or Specimen Storage/Security

REDCap and Yale OneDrive are password-protected with authorized access only. All research team members will complete standard IRB trainings before protocol access. All data are coded by anonymous study ID number linked in one section of REDCap to identifiers. Calm Health has completed a security planning assessment with Yale ITS for the handling of high-risk data; documentation is attached.

8.4 Study Records

Study records will be maintained by Dr. Ash on Yale OneDrive. These include IRB documents on Yale OneDrive and IRES, an internal standard operating procedure manual, adverse event forms, and confidential data sources. E-Consent forms are stored on REDCap.

8.5 Access to Source

Source documents include exports from Yale clinic dashboards, Actigraph ActiLife software, Calm Health, REDCap, and Qualtrics. They will be aligned into a master database with person-level demographics, health outcomes, and continuous biometrics (blood pressure, physical activity, sleep, heart rate, heart rate variability, skin temperature).

8.6 Retention of Records

The code key linking participant identifying information to data will be destroyed 1 year after the end of the study. De-identified data will be kept indefinitely. Participant contact information will be retained if they express interest in future studies, until they ask to no longer be contacted.

8.7 Data and Safety Monitoring Plan

As the contact Principal Investigator, Dr. Ash will monitor the data, assure protocol compliance, and conduct safety reviews at least annually. He will evaluate whether the study should continue unchanged, require modifications, or close to enrollment.

Dr. Ash will promptly report any Reportable Events and Unanticipated Problems Involving Risks to Subjects or Others to the IRB and any appropriate funding and regulatory agencies within 5 business days. He will apprise fellow investigators of all UPIRSOs and adverse events and submit annual renewal progress reports per IRB standard procedures.

Dr. Ash will immediately report any Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities (if possible), followed by a written report within 5 business days of Dr. Ash becoming aware of the event to the IRB and any appropriate funding and regulatory agencies.

Dr. Ash will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project.

Dr. Ash’s assessment is that the study activities pose minimal risk. The risks stated in section 2.2 are either standard research risks (confidentiality, adverse response to questionnaires), inherent

to mindfulness which is a widely recommended wellness practice, or tantamount to wearing commercially available fitness watches.

9 Study Considerations

9.1 Institutional Review Board (IRB) Review

The protocol will be submitted to the IRB for review and approval. Approval must be obtained before initiating any research activity. Any change to the protocol will require an approved IRB amendment before implementation. The IRB will have final determination whether informed consent and HIPAA authorization are required. Study closure will be submitted to the IRB after all research activities have been completed. Other study events (e.g., data breaches, protocol deviations) will be submitted per Yale policies.

9.2 Research Personnel Training

All research team members will complete standard IRB trainings in protection of human subjects before being added to the protocol. Staff will attend training sessions with Dr. Ash on study procedures, database monitoring, and adverse event detection and management.

9.3 Study Monitoring

Safety monitoring will be handled by the contact PI and study physician according to the protocol specified in Section 8.7. Data quality monitoring will be handled by the contact PI according to Section 8.2.

9.4 Unanticipated Problems and Protocol Deviations

Unanticipated problems involving risks to participants or others include, in general, any incident, experience, or outcome that meets all of the following criteria: (1) unexpected in terms of nature, severity, or frequency given the research procedures described in the IRB-approved protocol and informed consent document, and the characteristics of the participant population being studied; (2) related or possibly related to participation in the research, where "possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and (3) suggests that the research places participants or others at a greater risk of harm — including physical, psychological, economic, or social harm — than was previously known or recognized.

A protocol deviation is any noncompliance with the protocol. Corrective actions are to be developed and implemented promptly. Deviations will be detected through data audits and source document checklists. The principal investigators will review deviations to determine whether they involve risks to participants and/or are likely to recur.

Unanticipated problems involving risks to participants or others will be reported to the IRB within 5 business days of the investigator becoming aware of the event. Reports will include:

protocol identifying information; a detailed description of the event; the basis for determining it represents an unanticipated problem; and corrective actions taken or proposed. Protocol deviations that do not meet the threshold for an unanticipated problem will be reported to the IRB per Yale IRB policies and will be documented in study source documents. All deviations - whether or not they constitute unanticipated problems - will be reviewed by the principal investigators to determine whether they involve risks to participants and whether they are likely to recur, and corrective actions will be implemented promptly.

9.5 Study Discontinuation

Either principal investigator, the study physician, or the Yale IRB has authority to discontinue the study as a corrective action to UPIRSOs defined in Section 6.3.

9.6 Study Completion

Estimated study completion: March 31, 2027. The IRB will be notified by submission of a closure.

9.7 Conflict of Interest Management Plan

The independence of this study from any actual or perceived influence is critical, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial. The study leadership in conjunction with the appropriate conflict of interest review committee has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

All investigators will follow applicable conflict of interest policies. Any actual or perceived conflict of interest will be disclosed and managed.

Calm Health has formed a professional services agreement with Yale University to provide app access, backend dashboard access, and configure the app according to the study protocol. They will have no involvement with any aspect of the research including conduct, analysis, or publication.

Co-Investigator Dr. Griffith is an unpaid consultant for Calm Health and clinical author of their CKD module of mindfulness exercises that is under construction. Dr. Frances Griffith will not determine subject eligibility, be involved in the consent process, or perform analysis of identifiable or non-identifiable data.

Dr. Garrett Ash, principal investigator for this study, is a scientific advisor to Behavioral Health Tech Innovations LLC and has a provisional patent filed for a digital system for lifestyle medicine (047162–5346-P1US). A management plan for these conflicts is in place with Yale

University and generally involves Dr. Ash's recusal from purchasing decisions involving these entities. Behavioral Health Tech Innovations LLC is unrelated to this study and not involved in this research. Dr. Garrett Ash has no direct conflict of interest with Calm Health that requires management.

9.8 Funding Source

Gift funds in the Section of Nephrology (Hollis Family).

9.9 Publication Plan

The principal investigators are responsible for presenting and publishing the study results. We plan to present results at the American Society of Nephrology Scientific Sessions or the Society of Behavioral Medicine, and intramurally at Nephrology and General Internal Medicine Research in Progress meetings. We plan to publish at least 1 manuscript in journals such as the Journal of Medical Internet Research or the Journal of the American Society of Nephrology.

10 Appendices

Appendix #	Title	Section	Topic
1	Exit (treatment evaluation) Survey	4.2.1 Primary Outcomes	Treatment Evaluation
2	Exit (treatment evaluation) Interview	4.2.1 Primary Outcomes	Treatment Evaluation
3	Crisis Resources	2.2 Primary Outcomes	Adverse Reaction Management
4	FFMQ, SCS, CDSES, BRS, PSS-10	4.2.2 Secondary Outcomes	Efficacy outcome measures
5	KDQOL-36, SWEMWBS	4.2.2 Secondary Outcomes	Efficacy outcome measures
6	Generalized Anxiety Disorder (GAD-7) Scale, Patient Health Questionnaire (PHQ-8) Scale	4.2.2 Secondary Outcomes	Efficacy + safety monitoring
7a	Biometric Report Sample	4.2.2 Secondary Outcomes	User-centered design
7b	Cognitive Interview Guide	4.2.2 Secondary Outcomes	User-centered design
8	Eligibility Interview	5.4 Recruitment	Recruitment & Screening
9	Advertisements	5.4 Recruitment	Recruitment
10	Research Intake Source Document	6.1 Study Procedures	Source Document
11	Calm Health User Experience	6.1 Study Procedures	Mobile App Information
12	Weekly Check-In Survey	6.1 Study Procedures	Source Document
13a	Health Coaching Fidelity Review Form	8.2 Data Quality Assurance	Quality Monitoring

13b	Health Coach Self-Reflection Form	8.2 Data Quality Assurance	Quality Monitoring
13c	Health Coaching Curriculum	6.1 Study Procedures	Staff Materials
14	Consent Quiz	5.5 Consent & Authorization Procedures	Consent Materials

11 List of Tables

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COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY
YALE MEDICINE
YALE-NEW HAVEN HEALTH

Study Title: The Mindful Kidney: A Digital Mindfulness Intervention for Adults with Chronic Kidney Disease

Principal Investigator (the person who is responsible for this research):
Garrett Ash, PhD (Principal Investigator), Assistant Professor of Medicine, Yale School of Medicine, Section of General Internal Medicine
100 Church Street South, Room F201c, New Haven, CT, 06519. Phone: 203-444-3079. Email: Garrett.Ash@yale.edu

Menaka Sarav, MD (co-Investigator), Assistant Professor of Medicine, Internal Medicine, Section of Nephrology.

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to test a mindfulness app called Calm Health among adults with chronic kidney disease (CKD).
- Study activities will include: using the mindfulness app for 6 weeks, wearing an actigraphy watch, answering surveys and interviews about the app, and receiving two health coaching check-ins.
- Your involvement will require approximately 10 hours over 6 weeks (including app use of 45 minutes per week).
- There may be some risks from participating in this study. There is a chance that some people may find the survey questions a little upsetting. Mindfulness can uncommonly have negative mental health effects. A watch can rarely irritate some people's skin. Finally, we take multiple steps to protect your confidentiality, but no study can guarantee that your information will remain confidential.
- The study may have no benefits to you. The study will provide you with a free subscription to a mindfulness app until November 30, 2026, and mindfulness can have mental health benefits. However, the app and study may have no benefits to you. This study may help to improve mindfulness-based care for other adults with CKD in the future.
- There are other choices available to you outside of this research. For example, you can purchase other mindfulness apps, go to a mindfulness class taught by a professional instructor, or read about mindfulness on the Centers for Disease Control and Prevention website.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits and will not have any effect on your relationship with Yale University, Yale Medicine Nephrology, or the Yale New Haven Health system.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Ask the study staff questions about

anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?
We are asking you to take part in a research study because you are an adult with chronic kidney disease who uses a home blood pressure monitor. We are looking for 26 participants to be part of this research study.

Who is paying for the study?
This study is funded by gift funds in the Section of Nephrology (Hollis Family). Calm Health is providing the study with app access for a much lower fee than regular customers.

What is the study about?
The purpose of this study is to test a mindfulness app called Calm Health among adults with chronic kidney disease (CKD) for how well people like it and its influence on mental and physical health. In addition, we want to get your feedback on a new dashboard for the app that will help you track the relationship between mindfulness and your blood pressure, stress, and sleep.

What are you asking me to do and how long will it take?
If you agree to take part, your participation in this study will involve:

Consenting Visit: Consent to the study. Survey of basic medical and demographic information like age, race, ethnicity, type of kidney disease, eGFR, height, and weight. We will access your medical record to verify this information.

Week #0 Visit: Surveys about feelings, anxiety, stress, quality of life, and well-being. Learn to use the mindfulness app and start using it for 45 minutes per week. Learn how to place and charge study wristwatch (mailed in advance). The watch face is about 2 inches measured diagonally. It contains a silicon chip that senses movement and a green light on the back that senses blood flow. It will record physical activity, sleep duration, heart rate, heart rate variability, respiratory rate, skin temperature, and a signal used to estimate blood pressure trends. The watch does not display blood pressure readings; the research team will process the signal into estimates of your blood pressure patterns for your biometric report at the end of the study.
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Weeks #1, #2, #3, #4, #5 Surveys: Complete a short phone text survey about how the study is going and any problems or concerns. At Week #1 you will also receive a health coaching check-in to help troubleshoot any barriers to using the app. At Week #4 you will receive a health coaching session using a motivational interviewing approach.

Week #6 Visit: Mail back watch in prepaid box. Update medical and demographic information. Repeat surveys from Week #0. Complete survey and interview about how you liked the app. See a report of your mindfulness, blood pressure, stress, and sleep data. Complete think-aloud interview about how you liked the report.

We think that the study will take approximately 10 hours over 6 weeks of your time.

Audio Recording
We request consent to audio record the interviews over Zoom at week #8 so that your answers can be transcribed for better analysis. No other parts of the study will be audio recorded. The

recordings will be converted to a written transcript as soon as a research team member is available to do so, and then the recording will be immediately destroyed. The transcript will be stripped of all information that could identify you such as your name and places you mention.

__Yes, I agree to have my interviews recorded

__No, I decline to have my interviews recorded

Are there any risks from participating in this research?

If you decide to take part in this study, you may experience the possible risk of loss of confidentiality. Such loss is extremely rare when our standard steps to protect confidentiality are taken.

There is a low risk that the wristwatch will contribute to skin irritation or allergies. We will show you how to keep the device dry, not wear it too tight, and remove it for an hour every couple of days.

You may experience distress over the nature of the questions. Also, uncommonly, mindfulness can have negative mental health effects. Please inform us right away if you experience any emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. We will provide you with appropriate resources including 988 (crisis line), 741741 (crisis text line), 211 (local social services), or 911 if you are in immediate physical danger, and connect you with a mental health provider. If you share that you have active thoughts, plans, or intentions to harm yourself or another person, we must take action for your safety. We will call 988, inform your primary provider, and you will be asked to stop participating in the study. The mindfulness app is a mental health wellness product. It is not intended to diagnose or treat depression, anxiety, or any other mental or physical condition. It is not a substitute for a healthcare provider. Any questions about the diagnosis, care, or treatment of a medical condition should be directed to a healthcare provider. The Calm app has been used in previous studies with other participant populations and no adverse events were reported, but there may be risks related to use of the Calm Health app that are currently unknown. There may be additional risks that are currently unforeseeable.

How will I know about new risks or important information about the study?

We will tell you if we learn any new information that could change your mind about taking part in this study.

The mindfulness app and watch that gather information for the report are not medical devices. The report will tell you about your health behaviors. It is not intended to diagnose, treat, or prevent any medical condition. Therefore, the study team will not notify you of any possible health issues indicated by device data.

How can the study possibly benefit me or others?

You may benefit from taking part in this study. The study will provide you with a free subscription to the Calm Health mindfulness app until November 30, 2026, and mindfulness practice may improve stress, anxiety, depression, sleep, and overall well-being. You will also receive two health coaching sessions and a personalized biometric report showing how your mindfulness practice relates to your blood pressure, sleep, and stress. However, the app and study may have no direct benefits to you.

We hope that our results may add to the knowledge about how to engage more adults with chronic kidney disease into mindfulness and improve accessible mental health tools for this population.

Are there any costs to participation?

You will not have to pay for taking part in this study. You will not be responsible for costs related to watch damage or loss. The only costs may include your time coming to the study visits and data charges by your cell phone carrier.

If you do not own a smartphone, the study team will lend you one for the duration of the study. You will not be responsible for any costs if it is lost or damaged.

Will I be paid for participation?

You will be paid for taking part in this study. You will receive $25 for completing the intake visit and $50 for completing the follow-up visit. You will also be paid $10 each week you complete the weekly survey and wear the watch at least 90% of the time. If you wear the watch 70%-89% of the time, you get $5 for that week. In summary, the maximum possible compensation is $135.

We will use a pre-paid debit card to provide payment for taking part in the study. We will have to share your name, address, and telephone number with the banking institution issuing the debit card for ePayments. You may receive a card in the mail with the first payment following completion of the first visit. You will need to activate the card over the phone. Payments for additional visits will be automatically added to your card after completion of each following visit. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

What are my choices if I decide not to take part in this study?

Instead of participating in this study, you have some other choices. You could:

- Purchase other mindfulness apps.
- Go to a mindfulness class taught by a professional instructor
- Read about mindfulness on the Centers for Disease Control and Prevention website.
- Take part in another study.
- Choose not to participate in research.

How will you keep my data safe and private?

All of your responses will be held in confidence. Only the researchers involved in this study and those responsible for research oversight (such as representatives of the Yale University Human Research Protection Program, the Yale University Institutional Review Boards, and others) will have access to any information that could identify you that you provide. All research materials are stored on secure, password-protected servers. Also, your data will be coded with an anonymous study number. Things that could identify you like your name, address, or phone number will be stored separately and only one code key will link these identifiers to your data. That code key will be destroyed 1-2 years from now. The non-identifying data will be kept indefinitely. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if we learn that you are hurting a child or an older person.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission. Identifiers will be removed from the identifiable private information and after such removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

Calm Health will collect data about your phone number and IP address, your name if you choose to enter it, date of birth, and how you use the app. This data will be shared with the Yale research team. Calm Health's use of this data is governed by their privacy policy and a Data Use Agreement with Yale University; they will not use it to identify you personally in connection with this research or put you on a contact list that is sold to third parties. Calm Health may use your aggregated, de-identified data for product improvement and other purposes that lead to commercial profit, which may include selling the data to third parties. You will not share in this profit. Once de-identified, the data cannot be linked back to you.

The Yale research team will not provide Calm Health with research results beyond what we provide the public.

If you are open to being contacted about our future studies in which you could participate, we can keep your contact details for this purpose in a separate location from your data. Please indicate here whether we have your permission to recontact you for future studies. If you give this permission, we will retain you on the list indefinitely by default but you can ask to be removed at any time.

Yes_____
No_____

Investigator Interest

Dr. Garrett Ash, principal investigator for this study, is a scientific advisor to Behavioral Health Tech Innovations LLC and has a provisional patent filed for a digital system for lifestyle medicine (047162–5346-P1US).

Dr. Frances Griffith, co-investigator for this study, is a consultant for Calm Health and clinical author of their chronic kidney disease module of mindfulness exercises.

You may contact research staff at any time and make an appointment to speak with Dr. Ash or Dr. Griffith should you have questions regarding these investigator interests.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- The entire research record and any medical records held by *Yale New Haven Health* created from your first encounter with them to the end of your participation in this study.

- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - Questionnaires and interviews
    - The diagnosis and treatment of a mental health condition
    - Records about your use of the study app
    - Data about your physical activity, sleep, heart rate, and nervous system stress recorded by the watch
    - Blood pressure data from your home monitor
    - Laboratory results (eGFR, metabolic panel, lipid panel, glucose measures, cystatin C) and vital signs (blood pressure, height, weight) from your medical chart
    - Diagnoses and medications from your medical chart
    - Calm Health will access information that could identify you including your phone number and IP address to connect to your phone, your date of birth, and your first and last name if you choose to enter them into your profile

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Health care providers who provide services to you in connection with this study.
- The Calm Health app you use in this study.
- Other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Principal Investigator of the study
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to *Garrett Ash, PhD, Yale School of Medicine, Section of General Internal Medicine, 100 Church Street South, Room F201c, New Haven, CT, 06519.*

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able. Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this form.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits. Not participating or withdrawing later will not have any effect on your relationship with Yale University, Yale Medicine Nephrology, or the Yale New Haven Health system.

Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. This may happen if you do not follow study procedures or if the researchers determine it is unsafe or against your best interests to continue. If you stop completing the mindfulness exercises, it is still important that you make every effort to attend the week #6 study visit.

What will happen with my data if I stop participating?

You will cease to provide data, but cannot withdraw data you have already provided. If you continue using Calm Health, those data will continue to be captured.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at 203-444-3079.

If you have questions about your rights as a research participant, or you would like to speak with someone other than the Principal Investigator or study team to discuss problems, concerns, or questions, or to obtain information or offer suggestions, you can call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Yale University is committed to accessibility (https://usability.yale.edu/web-accessibility/accessibility-yale). Please contact the study team at 203-444-3079 if you have trouble accessing content of the Calm app.

Authorization and Documentation of Consent

Your signature below indicates that you read and understand this consent form and the information presented and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date