# A RANDOMIZED TRIAL OF THE SYNC APP

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## PROTOCOL SYNOPSIS

## A RANDOMIZED TRIAL OF THE SYNC APP

**Principal Investigator:** **Sung Won Choi**

**Study Design:** This is a study to assess whether individually tailored lighting and behavioral interventions delivered through an app are able to reduce symptoms of fatigue and improve quality of life across three populations of cancer patients. We will recruit 138 patients (69 control, 69 interventional) across three cancer populations: breast cancer and prostate cancer, and patients who have undergone hematopoietic stem cell transplant (HSCT). Participants will be randomized 1:1 to either the interventional SYNC app or to a control app.

**Primary Objective:** The primary objective is to test the statistical significance or difference between the intervention arm and the control arm in the measured outcome of fatigue, as quantified by daily fatigue surveys and weekly PROMIS Short Form v. 1.0 Fatigue 4a surveys.

**Secondary Objective:** The secondary objective will be to assess user sleep disturbances, anxiety, depression, physical function, and global health via a suite of PROMIS questionnaires.

**Exploratory Objectives:** Exploratory objectives will be to assess: i) physical activity through physiological data capture using the wearable sensor; ii) health care utilization (i.e., total count of hospital days, ED visits, readmissions, and ambulatory care clinic visits), and iii) sleep aid usage, as measured by self-report.

**Eligibility Criteria:** All patients will be outpatient, though most will still be undergoing long-term treatment: breast cancer patients often receive endocrine therapy; prostate cancer patients often receive androgen deprivation therapy; and HSCT patients will be recovering their immune system from the high-dose chemotherapy that was administered in preparation for their transplant. We will exclude patients actively receiving chemotherapy at the time of enrollment to avoid potential confounding factors. However, post-transplant maintenance chemotherapy will be allowed. We will also exclude night shift workers, where night shift work is defined as working a significant number of hours (i.e. more than half) between the hours of 11PM and 6AM on a regular basis. Participants will be required to be able to read and write English, be at least 18 years old, and report their baseline fatigue level as

moderate (4 or higher on a 10-point scale). Patients must own an iPhone 6s or later (with iOS 14 or later, or willing to update to iOS 14+) and be able to complete surveys on it, or they must agree to utilize a loaner iPhone provided by the study team to use during the study and return at the end of the study.

**Treatment Description:** All participants will be given access to an app into which they enter their research ID number. The research ID number will determine which version of the app is loaded on their phone. Participants will also be given a wearable device and a pair of glasses. Interventional group participants will be given a pair of blue light-blocking glasses. Participants in the control group will be given a pair of glasses that does not block visible light. All participants will wear the wearable device day and night over the course of the 12-week trial. Participants in the interventional group will use a version of the app that gives them personalized lighting recommendations (e.g. "Seek bright light") and a time interval over which the recommendation applies (e.g. "8:30 - 9:45 am").

**Control arm:** Control group participants will use a version of the app that makes recommendations to use the glasses; however, the time intervals recommended will be chosen to occur in the period of time when any change in lighting is expected to have no effect on the circadian clock (e.g. around noon, for many people already entrained to a diurnal schedule). Participants will be informed that they should only wear the glasses if it is reasonable for them to do so.

**Accrual Objective:** We will enroll 138 cancer patients, with half in the intervention arm and half in the control arm. Our primary endpoint is the PROMIS 4-item Fatigue Short Form. The age- and sex-adjusted norm for the Fatigue scale is 50 points, with a standard deviation of 10 points. These statistics have been shown to be largely generalizable to the cancer patient population (mean: 52, standard deviation 7.6). Our study will have power of 0.80, assuming a two-sided Type I error rate of 0.05, to detect an effect size of half the standard deviation between the intervention and control arms if 64 cancer patients are enrolled in each of the control and intervention groups. A mean difference of one-half a standard deviation is clinically meaningful and is considered a medium effect size for clinical trials. During the primary analysis, we will adjust for the fact that there are three cancer populations in our data and will look for a well-defined effect that is marginal within each population. We will accrue a total of 69 patients in each arm to account for attrition of data, assuming a 7% dropout rate from the trial.

**Accrual Period:** The estimated accrual period is 1.5 years

**Study Duration:** Data will be collected from participants for 12 weeks. Passive collection of wearable data through the app will continue for up to one year for each participant who opts-in to continue using the app, and medical records may be accessed for up to five years after the conclusion of the 12-week collection period.

## STUDY SCHEMA: SCHEDULE OF EVENTS

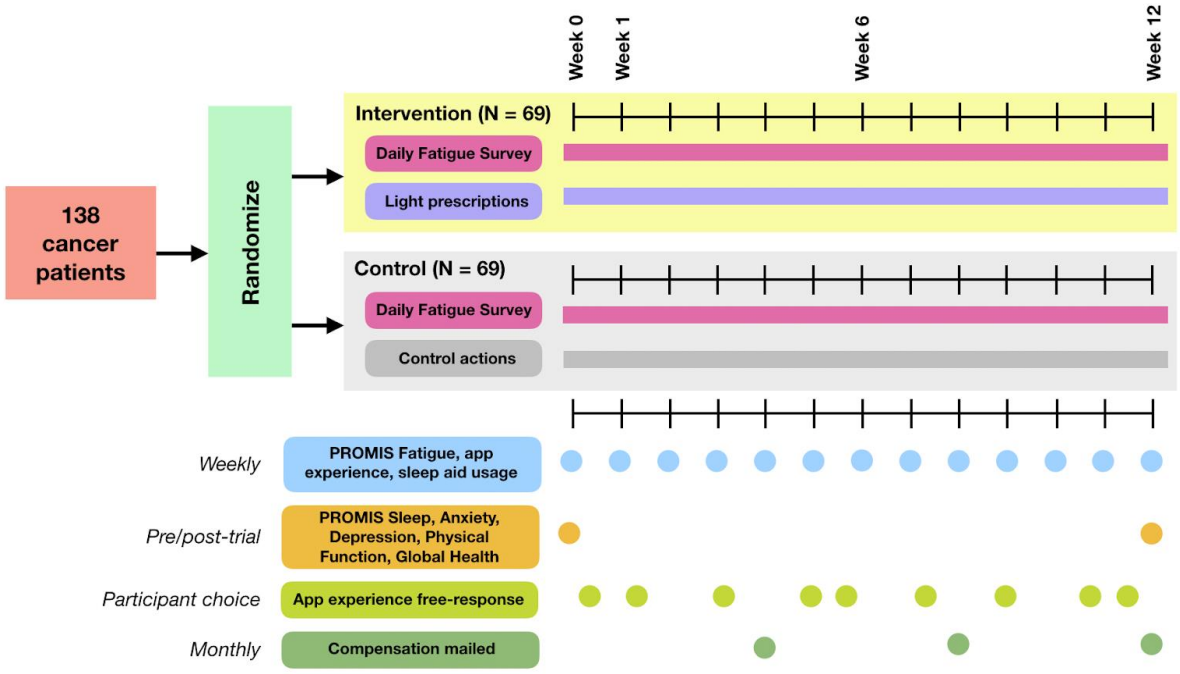



Diagram outlining the survey data collected over the trial. Note: “Control actions” here refers to following “dummy” lighting recommendations that are minimally expected to affect the circadian clock.

## TIME AND EVENTS TABLE

| Patient Events Timeline | | | |
|---|---|---|---|
| *Every day after starting the trial:* | *Every week, starting on the first day of the trial:* | *On the first day and last day of the trial:* | *At any point in time:* |
| Single question daily fatigue survey | PROMIS Fatigue survey, "How is your experience with the app?" questionnaire, sleep aid usage survey | PROMIS Sleep, Anxiety, Depression, Physical Function, Global Health | App experience free response |

| **Study Timeline** | **Year 1** | | | | **Year 2** | | | |
|---|---|---|---|---|---|---|---|---|
| | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| Revise the app to include the capacity to collect survey responses | X | X | | | | | | |
| Begin identifying potential subjects using UofM Health Research website | | X | | | | | | |
| Rolling recruitment, consent, and randomization from all three cancer groups | | | X | X | X | X | X | |
| Re-evaluate study protocol based on the first cohort of participants | | | | X | X | | | |
| Data processing | | | X | X | X | X | X | X |
| Data analysis | | | | X | X | X | X | X |
| Manuscript preparation | | | | X | X | X | X | X |

**Intervention Arm *vs* Control Arm**

| Intervention Arm | Control Arm |
| --- | --- |
| **Wearable sensor:**<br>Patient is given a wearable device to wear for 12 weeks. | **Wearable sensor:**<br>Patient is given a wearable device to wear for 12 weeks. |
| **Blue-blocking glasses:**<br>Patient is given blue-blocking glasses to wear at instructed times. | **Clear glasses:**<br>Patient is given glasses that block no visible light. |
| **Full SYNC app:**<br>Patient downloads the SYNC app and is given light interventions designed to have a targeted, personalized effect on the circadian clock. | **“Dummy” SYNC app:**<br>Patient downloads the SYNC app and is given light interventions designed to have minimal impact on the circadian clock. |

## 1. BACKGROUND AND SIGNIFICANCE

1.1. **Circadian rhythms are chronically disrupted in cancer patients, leading to worsened symptoms and outcomes.** A growing body of evidence links circadian rhythms to human health and disease. These rhythms, which repeat approximately once a day and are kept in sync with the local environment by the timing of light exposure, face constant disruption in the modern era of artificial lighting and smartphones (Wittmann et al. 2006; Roenneberg et al. 2012; Parsons et al. 2015). Sleep, the behavior most famously under circadian control, is not the only process affected: these rhythms feature prominently in nearly every major function in the body, from immune response to metabolism (Eckel-Mahan and Sassone-Corsi 2013; McClung 2013; Paganelli et al. 2018). Yet despite increased awareness of their importance for human health, circadian rhythms are rarely targeted in clinical interventions.

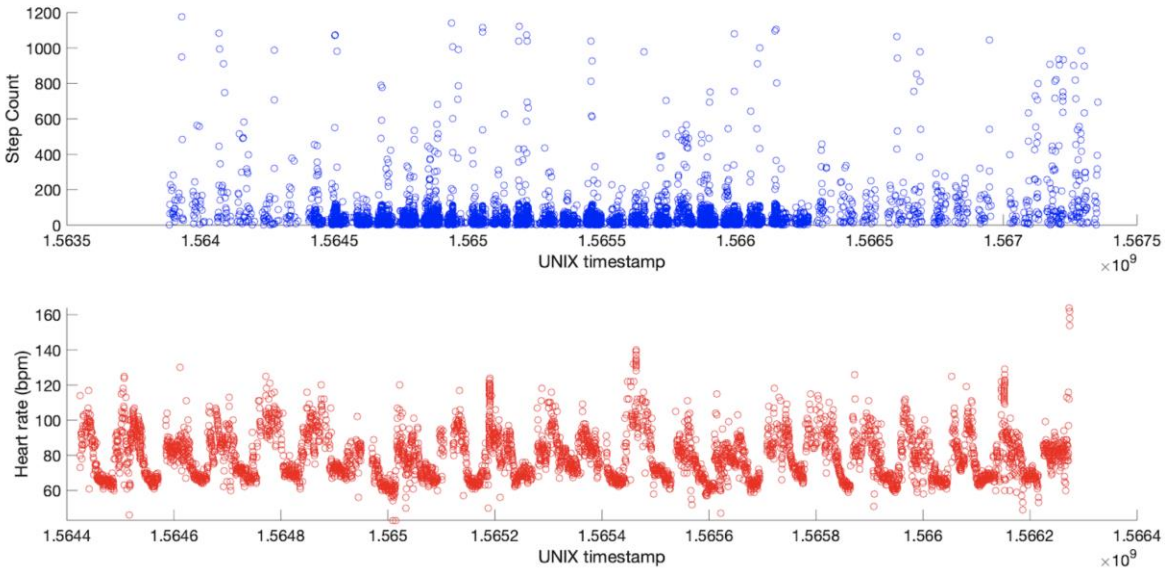
1.2. **Light as a treatment for circadian disruption.** Light therapy, in which people intentionally expose themselves to bright light and/or avoid light at specific times of day, holds promise for reducing circadian rhythm disruption to improve symptoms such as fatigue. However, all intervention studies carried out so far have been one-size-fits-all, with a single light intervention of fixed timing and without real-time personalization to match an individual patient's day-to-day variation in circadian rhythm. Even with these limitations, breast cancer patients exposed to 30 minutes of bright light in the morning experience reduced desynchrony (Neikrug et al. 2012), mitigated fatigue (Ancoli-Israel et al. 2012), and protection from a significant decline in quality of life (QOL) (Jeste et al. 2013). Other studies have found blocking evening light led to improved sleep in healthy populations, though no comparable studies have been carried out in cancer patients (van der Lely et al. 2015, Burkhart and Phelps 2009).

1.3. **Tracking circadian rhythms has historically been challenging in real-world conditions.** There is great promise for lighting interventions as therapy, yet several hurdles stand in the way. The first is awareness. Many patients are unaware of the effects of light on their bodies and how these effects change over the course of the day. In addition, daily exposure to morning light requires habit-formation, which can be burdensome. Importantly, the timing of light interventions in previous work has never been tailored to match the individual's circadian rhythm, instead opting for catch-all instructions; e.g., "on awakening" or "in the morning." This is despite the fact that sleep and circadian rhythms are distinct processes, particularly in people experiencing irregular sleep and light exposure.

1.4. **Mathematical models and wrist-worn wearables can be used to predict circadian time.** The gold standard for estimating circadian time is the costly and time-consuming dim light melatonin onset (DLMO) test. This salivary assessment, which takes hours to collect and costs hundreds of dollars, has made personalizing circadian recommendations impractical in the past. Recent work by our group and others has suggested that circadian rhythms can be tracked by coupling mathematical models to wearable devices that measure activity, light and/or heart rate (Stone et al. 2019; Woelders et al. 2017; Huang et al., In revisions; Bowman et al., in preparation). Building on these methods, it is now possible to deliver light interventions tailored to the individual user, making them both more habit-building and more effective.

1.5. **Prior work: Embedding circadian algorithms in mobile apps.** In our previous work, our team developed a prototype mobile application, SYNC, which tracked the circadian

clock indirectly using wrist-worn wearable sensor data (i.e., minute-by-minute activity/steps and heart rate) as input. The SYNC app makes behavioral recommendations to correct circadian misalignment in patients. The general types of recommendations are: 1) When to seek and avoid light; 2) When to seek and avoid caffeine; 3) Ideal window for sleep. These recommendations are given with associated time periods and tailored to match the user's ability and desire to control their light exposure (e.g. the ability to wear blue-blocking glasses, or be exposed to very bright light) and home time zone. For example, the app will only recommend that the user avoid light by wearing blue-blocking glasses if they have marked that they are willing to use blue-blockers in the Settings page, and will only recommend caffeine timing if the person is a caffeine user.




Sample data from a patient wearing an Apple Watch. The x-axis is time and the y-axis is step count (top) and heart rate (bottom) as recorded by the Apple Watch.

1.6. **Preliminary data suggests strong potential for wearables.** To assess the viability of cancer participants using a wrist-worn wearable and lighting hardware, participants were given a version of the app that passively collected data from an Apple Watch device without making active recommendations, a smart-bulb that could be controlled by the app (to change color to dim red) and red-tinted, blue-blocking glasses, but no specific instructions on how to use these beyond a simple educational primer on how light affects sleep. Overall, users in our Phase I usability trial found the wrist-worn wearable extremely easy to set up (100% found it "Very easy" to Wear and Charge, and 75% found it "Very Easy" to sync with their phone, with the remaining 25% rating it as "Fairly Easy."). The most difficult hardware challenge was connecting the lightbulb, with one participant choosing not to set it up and one person marking it as "Neutral" difficulty. In summary, most participants did not find the hardware overly burdensome to set up. Clear daily patterns of activity and heart rate can be seen over the course of the collected data. While the feasibility of deploying wearables in a patient population was unclear before the usability trial, we found patients were willing and able to reliably wear the device.

1.7. **Study Rationale.** The scientific premise of this protocol stems from the literature presented in the Background and Significance and the large body of prior work by the study PI and Co-Is who have extensive experience examining the information needs of cancer patients. The SYNC app has been tested in one-on-one user interviews and for ease-of-use with lighting and wearable hardware; the next stage of its development is to incorporate greater scientific rigor. The heterogeneity of cancer types and experiences means that an intervention may be effective for one population and not for another. The work proposed in this specific aim is to test the SYNC app, in three separate populations of cancer patients. Patients will be randomized either to use the SYNC app, with its tailored recommendations for use with blue-blocking glasses, or to a control app without tailored recommendations and clear glasses.

1.8. **SYNC 1.0 Development.** The app was developed for iOS devices by Arcascope using a Phase I SBIR grant. A non-interventional version of the app was tested for usability in a prior study. The app was designed based on five in-depth interviews, assessed for usability in four recorded tests with the first prototype, and tested again by eight participants in a long-term study, along with hardware, including blue-blocking glasses and mobile-controlled smart-bulbs. The app was capable of syncing with smart-bulb devices, as well as registering when these devices were used. These features of the app were removed in response to user feedback that they did not like interfacing with the smart lightbulbs.

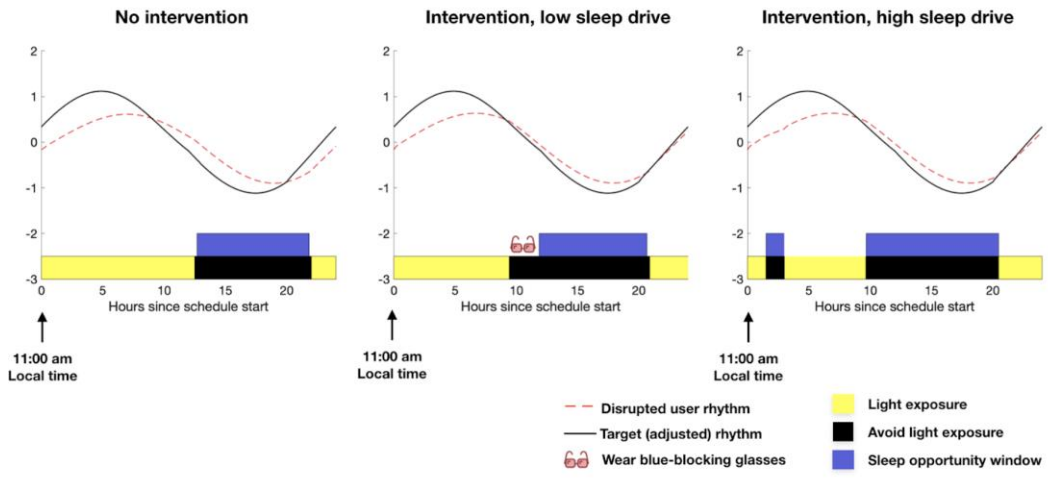



Diagram showing simulations of how the lighting recommendations shift the circadian clock. Purple is expected sleep window, yellow is time spent in light, black is time spent in darkness. (Left) A delayed circadian rhythm remains delayed in the presence of no interventions. (Center) A delayed rhythm with low sleep drive is synchronized by a blue-blocking glasses intervention. (Right) A delayed rhythm with high sleep drive is synchronized by an earlier bedtime and a mid-afternoon nap.

1.9. **Understanding circadian interventions.** To better explain the recommendations by the app, consider the case where a user on a habitual 11:00 pm to 7:00 am sleep schedule has been disrupted by staying up later than normal. The model will track that user's circadian state as disrupted, which is shown by the *x* variable from the limit cycle oscillator model in the figure above as a dashed red line, out-of-sync with the solid black line (again, *x*) of someone entrained to 16 hours of light and 8 hours of dark. Periods of light and dark

are marked as bands of yellow and black, respectively. Predicted windows of sleep (Phillips and Robinson 2007) are marked by purple bands. All simulations start at 11:00 am local time.

The app makes different recommendations based on the user's predicted sleep drive. If the user followed no intervention (leftmost plot), they would end the 24-hour period still out of sync with their target rhythm. If they had accrued a relatively low sleep drive in the days leading up to the disruption, the app would recommend they put on blue-blocking glasses at 8:15 pm, with an anticipated sleep onset at 10:50 pm. If they had a significantly higher sleep drive, the app would recommend a maximum nap opportunity of 1.5 hours between 12:30 and 2:00 pm, and a bedtime at 7:40 pm. For all these sample recommendations, times have been rounded to the nearest five-minute mark. While only two interventions are shown (for "low" and "high" sleep drive), there are many others that would be recommended for different sleep drives and different disruptions.

1.10. *Scientific Premise***.** Fatigue is a major problem for cancer patients, and one that can persist long after treatment ends. Recent work has demonstrated that light therapy may mitigate or reduce fatigue levels in both cancer patients and cancer survivors. This protocol seeks to assess how lighting interventions distributed through a mobile app affect fatigue, sleep, and quality of life across three populations of cancer patients. Our strong preliminary data, coupled with the need to deliver an effective intervention in a population with severe circadian disruption form the scientific premise. *Our central hypothesis is that targeted, personalized light interventions will reduce fatigue in cancer patients.*

# 1. STUDY DESIGN

1.1. *Study Overview***.** This study will use a two-arm randomized study design. Participants will be recruited across three cancer types. Each of the participants will be randomized to an active "intervention" arm (using the full SYNC app) or to a control arm (using a "dummy" version of the SYNC app that gives recommendations for light at times that should not significantly affect the circadian clock). The random allocation of participants to the treatment arm or control arm establishes the basis for testing the statistical significance or difference between the groups in the measured outcome (patient fatigue, assessed by a daily 1-question fatigue survey and the PROMIS 4-item Fatigue). Patient age, gender, and other prognostic baseline characteristics that could potentially confound an observed association, including those that are unknown or unmeasured, will be distributed equally, except through chance alone, through random assignment. Thus, this design is well-suited to our goal of assessing the efficacy of a mobile health intervention, SYNC, on participants.

1.2. *Primary Hypothesis***.** The primary hypothesis is that a mobile-app delivered circadian intervention (SYNC) will reduce patient fatigue.

*1.3. Study Objectives*

1.3.1. Primary Objective. To test the difference between the "intervention" (full SYNC app) arm and the control (limited SYNC app) arm in the measured outcome of patient fatigue, assessed by daily 1 question surveys and weekly 4-item PROMIS questionnaires over the course of 12 weeks.

1.3.2. Secondary Objective. To determine the change in sleep disturbances, anxiety, depression, physical functioning, and global health through PROMIS questionnaires, between baseline and the 12-week assessment in both the control and intervention arms, and to look for differences in this change between the two arms.

1.3.3. Exploratory Objectives

1.3.3.1. Change in patient physical activity through physiological data capture using the wearable sensors in the control versus intervention arm.

1.3.3.2. Change in patient health care utilization (e.g., total count of hospital days, readmissions, and ambulatory care clinic visits) in the control versus intervention arm

1.3.3.3. Change in patient sleep aid usage in the control versus intervention arm.

*1.4. Participant Eligibility*

*1.4.1.* Inclusion Criteria

*1.4.1.1.* Able to provide informed consent and willing to sign an approved consent form that conforms to federal and institutional guidelines.

*1.4.1.2.* Comfortable reading and speaking English.

*1.4.1.3.* Must own an iPhone 6s or later (with iOS 14 or later or willing to update to iOS 14+) and be willing to complete surveys on it, per the protocol. Alternatively, patients without iPhones must be willing to use a loaner iPhone provided by the study team to use during the study and return at the end of the study.

*1.4.1.4.* ≥ 18 years of age.

*1.4.1.5.* Sleep aid usage will be allowed as long as the patient has been on a stable dose for at least 4 weeks prior to enrollment and agrees to continue the same dose during the study.

*1.4.1.6.* A response of at least 4 on a 10-point scale (with 0 = not fatigued at all and 10 = extremely fatigued) to the question "How fatigued did you feel in the last four weeks?"

*1.4.1.7.* Breast cancer population: Diagnosed with stage 1-3 breast cancer in the last 10 years, without metastatic disease. Chemotherapy or radiation therapy, if indicated, must have been completed at least 3 months prior to enrollment. Concomitant anti-HER2 therapy and/or anti-endocrine therapy is permitted.

*1.4.1.8.* Prostate cancer population: Undergoing androgen deprivation therapy (ADT) for at least three months and are anticipated to remain on ADT for the duration of the trial. Concomitant additional anti-androgen therapy (e.g., enzalutamide) is permitted.

*1.4.1.9.* HSCT population: Participants must be from the University of Michigan Blood and Marrow Transplant Program.

1.4.2. Exclusion Criteria

1.4.2.1. The patient cannot be undergoing chemotherapy at the time of enrollment unless it is post-transplant maintenance chemotherapy. Patients undergoing post-transplant maintenance chemotherapy are permitted to enroll.

1.4.2.2. The patient must have no evidence of disease progression or recurrence. Specifically, for the prostate cancer population, the patient must have no evidence of disease progression on their current ADT regimen at the time of enrollment.

1.4.2.3. The patient must not be a night shift worker, where night shift is defined as working a significant number of hours (i.e. more than half) between the hours of 11PM and 6AM on a regular basis.

1.5. *Intervention Plan*

1.5.1. Participants will be consented, enrolled, and randomized remotely with a Research Coordinator prior to beginning the trial. A review of inclusion/exclusion criteria will be conducted to determine the patient's eligibility for enrollment. Study procedures will be reviewed with the patient, and documentation of informed consent will be obtained. After signing the informed consent form (ICF) either in person or electronically using SignNow or other process approved by the University of Michigan IRBMED, patients will be assigned a unique study ID number in sequential order. Those who are found to be ineligible will be replaced.

1.5.2. After providing informed consent, the participant will be provided, in the clinic or via mail, a wearable device and a pair of glasses, which will be either blue-blocking (intervention group) or clear (control group). Both of these are described in detail in **Appendix A**. When both are in the participant's possession, the study coordinator will schedule a second meeting with the participant to onboard them to the specifics of the study.

1.5.3. The study coordinator will walk the participant through setting up the app and entering their Research ID number. They will ensure that the participant is able to connect to the wearable device via their phone and will explain to the subject that they should not wear the blue-blocking glasses while driving or if their vision will be impaired by them in a way that challenges their mobility.

1.5.4. Participants will be allowed to use sleep aids over the course of the trial. There will be no restriction on their usage; however, subjects will be asked to report on a weekly basis what sleep aids they consumed, as well as the number of alcoholic drinks they consumed. This survey will be carried out in the app.

1.5.5. Once the trial has begun, study coordinators will track completion of surveys, and in the event of missing data will follow-up with subjects to assess challenges to encourage survey completion. SYNC software will be maintained in collaboration with Arcascope, Inc. After randomization, subjects will complete baseline assessments, as outlined in the metrics Appendix. They will be asked to wear the wearable device day and night for twelve weeks. During this time, the app will deliver ecological momentary assessments of fatigue daily at random times of day and the validated 4-item PROMIS Fatigue questionnaire weekly to both the control and interventional groups. At the end of the twelve-week period, the subjects will remotely complete end-of-trial assessments.

1.5.6. Intervention arm (SYNC app): Participants randomized to the intervention arm will be instructed on how to download the app on their mobile phones (iOS) and how to operate the wearable device. The app will record when the user opens the app, as well as when they check off having completed an assigned task; e.g. “getting bright light exposure”. Please see **Appendix A** to view the components of the wearable device. Please see **Appendix B** to view specifications of the mobile app. Any PHI information will be stored on University of Michigan servers in a secure way. Only non-PHI information will be stored and collected via the Sync app. The SYNC will be downloaded onto patient mobile phones and can be used freely throughout the intervention period because it contains no PHI data.

1.5.7. Control arm: Participants randomized to the control arm will be instructed on how to download the SYNC app and how to operate the wearable sensor. Their research ID will trigger the “control” recommendations from SYNC, which are chosen to minimize circadian effect. Any PHI information will be stored on University of Michigan servers in a secure way. Only non-PHI information will be stored and collected via the Sync app. The SYNC will be downloaded onto patient mobile phones and can be used freely throughout the intervention period because it contains no PHI data.

1.5.8. Light-blocking and “dummy” glasses: Participants will be provided either blue-blocking glasses (intervention group) or clear glasses that do not block visible light (control). The blue-blocking glasses are meant to reduce the circadian effect of light at certain times for participants. Both pairs of glasses will be capable of being worn over regular glasses for vision impairment. Participants will be informed not to wear the glasses while driving, or when doing motor activity that risks injury with vision impairment. They will also be informed that they are not required to wear the glasses if doing so makes them feel uncomfortable; e.g. if they are out in public.

1.5.9. Wearable sensor device: Each participant will be given a wearable sensor to wear throughout the treatment period, except while in water or when charging. The goal is to collect objective, continuous, multi-parameter physiological data (e.g., total

hours of sleep, sleep quality, total number of steps) on patients throughout the treatment period to correlate with their subjective, snapshot participant-reported outcomes collected over the course of the trial. The de-identified wearable data will be stored on servers purchased by the small business partner, Arcascope. For troubleshooting, detailed instructions will be provided for all participants, and customer support will be available 8AM – 5PM CST. Our team is available by pager after hours, if needed.

## 3. STUDY ENDPOINTS

3.1. *Primary Endpoint***.** The primary endpoint is **fatigue,** as assessed by a daily fatigue questionnaire and a weekly 4-item PROMIS fatigue questionnaire.

3.2. *Secondary Endpoint***.** The secondary endpoints are sleep disturbance, anxiety, depression, physical function and global health, as measured via the following PROMIS validated instruments:

- PROMIS Sleep Disturbance (8-item)
- PROMIS Anxiety (7-item)
- PROMIS Depression (8-item)
- PROMIS Physical Function (8-item)
- PROMIS Global Health (10-item)

3.3. *Exploratory Endpoints***.**

3.3.1. Activity data. Patient activity (steps) and sleep will be measured continuously from the start to the end of the trial through wearable sensors.

3.3.2. Health care utilization data. Patient health care utilization data (e.g., total count of hospital days, emergency department visits, readmissions, and ambulatory care clinic visits) will be captured through the electronic health record as well as self-report (i.e., if the patient is readmitted at an outside hospital other than Michigan Medicine).

3.3.3. Sleep aid utilization data will be collected via self-report in the app once a week.

## 4. PATIENT ENROLLMENT AND EVALUATION

4.1. Study participants will be recruited through the following means:

(1) The University of Michigan Rogel Cancer Center physicians, advanced practice providers, and nurse coordinators.
(2) The University of Michigan health system's electronic health record (EHR) is based on the Epic software (MiChart), which allows researchers, with IRB approval, to contact (via email, flyers, phone calls, or in-person) individuals who meet specific criteria and may be eligible to participate in the study. For example, with IRB-approval, Drs. Choi, Alumkal, and Henry and their Research Staff can access the daily clinic schedules, which will enable them to identify potential participants and meet them in-person during a corresponding patient encounter.
(3) With IRB-approval, we will distribute flyers in the outpatient clinics for our three cancer populations to inform potential individuals about the study. We will also distribute emails to potential study participants via the University of Michigan's UMHealthResearch (https://umhealthresearch.org) service.
(4) The Michigan Institute for Clinical and Health Research (MICHR), supported by the NIH Clinical and Translational Science Award Program, will assist our team with developing and reviewing recruitment materials, and identifying obstacles that may affect participant recruitment and retention.

4.2. *Randomization*: Once the patient is deemed eligible and has provided written informed consent, the Research Coordinator will confirm eligibility. The study statistician, Walter Dempsey, will create a randomization list before the study begins enrollment using the statistical package R. Dr. Dempsey will then forward the list to the Data Manager, who will be responsible for enrolling patients and assigning them to the correct study arm.

4.3. *Pre-Intervention Evaluation*: PROMIS Patient-Reported Outcomes (PROs) – Well-being or HRQOL assessments will be obtained at baseline, pre-intervention. The surveys will be completed directly through the SYNC app on mobile phones. Based on prior work, our Study Team has experience administering PROMIS PROs on mobile devices.

4.4. *Post-Intervention Evaluation*: PROMIS Patient-Reported Outcomes (PROs) – Well-being or HRQOL assessments will be completed at 12 weeks, post-intervention. This survey must be completed within two weeks after the 12-week intervention period.The surveys will be obtained directly through the SYNC app on mobile phones. Based on prior work, our Study Team has experience administering PROMIS PROs on mobile devices.

4.5. *Participant Withdrawal*: At any time, a participant may request that her or his data no longer be collected. The participant may make this request to the Research Coordinator or to any member of the Study Team. A note will be made in the patient chart documenting the reason the patient withdrew from the study. Participants may also be removed for the following reasons: development of disease recurrence or progression, in the event that the IRB or sponsor decides to close the study, or if the treating physician thinks it is no longer in the best interest of the patient.

4.6. *Study Regulations*: The trial will be performed in accordance with all applicable regulatory requirements and laws.

4.7. *Risks*.

4.7.1. Wearable Sensor Device: Patient Subjects who agree to wear the device(s) for data collection may experience mild skin irritation, which will be monitored by the care team. The subject can decline to wear the device(s) or request to try a different device(s) that may be more comfortable. Subjects who decline to wear the wearable device will be replaced and not included in the statistical analysis. All subjects will be instructed to remove the device before any scans or radiation therapy.

4.7.2. Confidentiality: There is a possible risk of loss of confidentiality. However, every effort will be made to keep your medical information confidential. We will code data by assigning a number to each individual patient and then store the data by that number. No mention of patient subject identities is made in analyses of the data or in any publications, which result from such research.

4.8. Adverse Event Reporting Requirements.

Adverse events related to this intervention are not expected, as the focus of this intervention (if randomized to the intervention group) is on lighting and minimal-risk behavioral interventions. However, any adverse events resulting from research procedures will be reported to IRBMED per institutional guidelines. In the event an AE does occur, the PI will determine the attribution/relatedness of each AE. Expected side effects from anti-hormonal therapies, anti-HER2 therapy, GVHD will not be reported for this trial.

4.9. *Participant Data Security and Compliance*. All identifiable information about the patient will be stored on a secure, password-protected core image laptop computer in Dr. Sung Won Choi's Laboratory (MPB) following rules for secure data storage (e.g., M+Box or Dropbox). Research devices will not interface with MiChart. All study personnel will be HIPAA and PEERRS certified. All study information will be stored in password-protected encrypted files and identified by case number. The technologies proposed in this proposal have all been carefully reviewed, and approved by the governing bodies at Michigan Medicine. All regulatory and security requirements have been met and have been fully documented in accordance with the policies and best practices that govern the use of technology for patient care and research at Michigan Medicine. The MiChart web services were built and are supported by HITS, and their use for this project has been approved by HITS. All standard procedures and protocols for security and data integrity that apply to this project are being followed. All PHI will be stored in the HITS Oracle Database.

4.10. *Data Safety Monitoring Plan*. This study will be monitored in accordance with the NCI approved University of Michigan Rogel Cancer Center Data and Safety Monitoring Plan. The study team will meet every six months or more frequently depending on the activity of the protocol. The discussion will include matters related to the safety of study participants (SAE/UaP reporting), validity and integrity of the data, enrollment rate relative to expectations, characteristics of participants, retention of participants, adherence to the protocol (potential or real protocol deviations) and data completeness. At these regular meetings, the protocol specific Data and Safety Monitoring Report form will be completed and signed by the Principal Investigator or by one of the co-investigators. Data and Safety Monitoring Reports will be submitted to the University of Michigan Rogel Cancer Center Data and Safety Monitoring Committee (DSMC) every six months for independent review.

## 5. STATISTICAL CONSIDERATIONS

5.1. *Study Design***.** The clinical trial is a two-arm randomized controlled trial. After completion of the intervention, data analysis will be conducted according to the statistical analysis plan outlined below. Descriptive statistics will be performed prior to conducting the statistical analyses. An intention-to-treat (ITT) analysis of the results will be based on the initial assignment of the randomized participants. With the ITT approach, participants will be analyzed according to the treatment assignment, even if the participant drops out of the study. The ITT approach minimizes biased comparisons among the treatment arms. Missing data will be imputed using the last collected data from the subject prior to dropout.

5.2. *Accrual*. It is estimated that 18-months will be necessary to enroll the targeted sample size. Accrual will be reported by race, ethnicity, gender, and age.

5.3. *Study Duration***.** Survey results and wearable data will be actively collected from participants over the course of 12 weeks. At the conclusion of the 12 weeks, passive collection of wearable data through the app will continue for up to one year for each participant who opts-in to continue using the app. Medical records may be accessed for up to five years after the conclusion of the 12-week collection period.

5.4. *Randomization***.** Blocked randomization will be used to limit bias and achieve an equal distribution of participants to the intervention and control arms of the study (69 randomized, 69; with 23 from each cancer population in each arm). This approach will recruit participants in small blocks to ensure that half of the participants within each block will be allocated to the treatment and the other half to the control. The size of the blocks will be permuted to limit selection bias, and within each block, the order of patients will be random. The study statistician will create a randomization list before the study begins enrollment using the statistical package R. This list will be used by the study group in assigning patients to the correct study arm.

5.5. *Blinding***.** Study arm assignments cannot be blinded to the investigators or the rest of the study team because it will be known whether participants have SYNC on their mobile device or not (due to technical purposes).

5.6. *Primary Endpoint***.** The primary objective of the study is to test the effects of SYNC in a randomized controlled clinical trial design. Patients will be randomly assigned to the treatment arm or the control arm. The primary objective is to quantify the effects of the light interventions delivered by SYNC on patient fatigue.

5.7. *Sample Size Considerations***.** We will enroll 138 cancer patients, with half in the intervention arm and half in the control arm. Our primary endpoint is the PROMIS 4-item Fatigue Short Form. The age- and sex-adjusted norm for the Fatigue scale is 50 points, with a standard deviation of 10 points. These statistics have been shown to be largely generalizable to the cancer patient population (mean: 52, standard deviation 7.6). Our study will have power of 0.80, assuming a two-sided Type I error rate of 0.05, to detect an effect size of half the standard deviation between the intervention and control arms if 64 cancer patients are enrolled in each of the control and intervention groups. A mean difference of one-half a standard deviation is clinically meaningful and is considered a medium effect size for clinical trials. During the primary analysis, we will adjust for the fact

that there are three cancer populations in our data and will look for a well-defined effect that is marginal within each population. We will accrue a total of 69 patients in each arm to account for attrition of data, assuming a 7% dropout rate from the trial.

5.8. PROMIS® measures use Item Response Theory (IRT), a family of statistical models that link individual questions to a presumed underlying trait or concept of global health represented by all items in the scale. PROMIS® instruments are scored using item-level calibrations. The most accurate way to score a PROMIS® instrument is to use the Health Measures Scoring Service, which our Study Team has experience with. This method of scoring uses "response pattern scoring," which uses responses to each item for each participant. Response pattern scoring is especially useful when there is missing data (i.e., a respondent skipped an item), or different groups of participants responded to different items).

There are four key features of the score for PROMIS® Fatigue:

1. Reliability: The degree to which a measure is free of error. It can be estimated by the internal consistency of the responses to the measure, or by correlating total scores on the measure from two time points when there has been no true change in what is being measured (for z-scores, reliability = $1 - SE^2$).
2. Precision: The consistency of the estimated score (reciprocal of error variance).
3. Information: The precision of an item or multiple items at different levels of the underlying continuum (for z-scores, information = $1/SE^2$).
4. Standard Error (SE): The possible range of the actual final score based upon the scaled T-score. For example, with a T-score of 52 and a SE of 2, the 95% confidence interval around the actual final score ranges from 48.1 to 55.9 (T-score ± (1.96*SE) = 52 ± (1.96*2) = 48.1 to 55.9)

The final score is represented by the T-score, a standardized score with a mean of 50 and a standard deviation of 10 points.

5.9. *Interim Analysis***.** There will be no interim analyses for efficacy or futility for this trial.

5.10. *Patient Characteristics***.** Patient characteristics will be summarized for all participants. Patient characteristics to be examined may include: age, gender, race/ethnicity, treatment and pathology information (including dates), and clinical outcomes; e.g. survival, relapse, and toxicities.

5.11. *Analysis Populations and General Analysis Guidelines***.**

5.11.1. Primary Analysis Population. All participants enrolled, consented, and completing at least the baseline outcome measures will be included in the primary analysis population. Analyses for the primary and secondary endpoints will use the primary analysis population: The primary analysis will occur once all patients have been followed for the duration of the 12-week trial, data adjudication completed, and data are locked.

5.11.2. General Analysis Guidelines. Primary analyses for the primary, secondary, and exploratory endpoints will use the primary analysis population. Analyses of each endpoint in each population will follow the

analysis plans, as described below. We expect minimal missing data (<5%) for the primary endpoint and secondary endpoints based on past experience with mobile app studies.

5.12. *Analysis of Primary Endpoint***.** Analysis will be an intent-to-treat analysis that includes all participants. Mean Global Health scores at the end of the trial will be compared using a two-sample *t*-test (or Wilcoxon Rank Sum test if non-normality is apparent) with a significance level of 0.05. Linear regression models will be performed to complement the results of the *t*-test and adjust for specific baseline participant's characteristics (e.g., demographic, social, environmental) to increase the precision of our inference. There is a possibility that patient characteristics will be unbalanced since our randomization scheme will be applied to participants. Thus, our models also will assess potential moderating or mediating effects.

5.13. *Analysis of Secondary Endpoint***.**

Mean PROMIS scores (PROMIS sleep disturbances, anxiety, depression, physical function, and global health) for each arm at the end of the trial will be compared using a two-sample *t*-test (or Wilcoxon Rank Sum test if non-normality is apparent) with a significance level of 0.05. Linear regression models will be performed to complement the results of the *t*-test and adjust for specific baseline participant's characteristics (e.g., demographic, social, environmental) to increase the precision of our inference. There is a possibility that patient characteristics will be unbalanced since our randomization scheme will be applied to participants. Thus, our models also will assess potential moderating or mediating effects.

5.14. *Analysis of Exploratory Endpoints***.**

5.14.1. Patient activity. The accelerometer data of each subject will be transformed into a low-dimensional representation using motif discovery algorithms.[79] Such techniques are completely data-driven, and search for motifs (i.e., patterns) in the data that occur more often than chance. A signal can then be represented by the number of times a particular motif occurs. Others have successfully used such techniques for representing a variety of waveform data, including accelerometer and continuous glucose data.[80-82] The accelerometer data will be processed to derive estimates of total sleep duration (i.e., hours per night), wake after sleep onset, and sleep efficiency (i.e., ratio of sleep to wake). The variables will be compared between arms.

5.14.2. Patient health care utilization. The total count of hospital days, ED visits, readmissions, and ambulatory care clinic visits during the trial, with adjustment for follow-up, will be compared between arms using a Poisson regression model, with adjustment for potential mediating or moderating effects of patient characteristics, if needed. The data will be captured at the time of PRO assessments.

5.14.3. Patient sleep aid utilization. The total number of sleep aids being used by the patients, as well as the types, will be collected via weekly surveys over the course of the trial.

## APPENDIX A: DESCRIPTION OF DEVICES

Participants in both arms will be given a pair of glasses. In the control group, participants will be given a pair of clear safety glasses. They will be given one of two types of clear glasses, depending on whether or not they wear reading glasses and comfort considerations.

The first type of glasses for the control group are those meant for participants who do not wear reading glasses. To account for changing availability of specific glasses models on the Amazon website, any pair of clear safety glasses that is similar to the model below may be used.

Example of control glasses for participants who do not wear reading glasses:

Crews BK310 BearKat 3 Polycarbonate Clear Lens Safety Glasses with Non-Slip Hybrid Black Temple Sleeve


| | |
|---|---|
| Manufacturer | **MCR Safety** |
| **Part Number** | **1** |
| **Item Weight** | **0.32 ounces** |
| **Package Dimensions** | **9 x 2.6 x 1.6 inches** |

| | |
|---|---|
| **Item model number** | **BK310** |
| **Color** | **Clear Lens** |
| **Style** | **Duramass Coated Lens** |
| **Finish** | **Scratch-resistant** |
| **Pattern** | **Safety Glasses** |
| **Item Package Quantity** | **1** |
| **Batteries Required?** | **No** |

The second type of glasses available to participants in the control group are larger and meant for participants who also wear reading glasses. To account for changing availability of specific glasses models on the Amazon website, any pair of clear safety glasses that is similar to the model below may be used.

Example of control glasses for participants who do wear reading glasses:

Safety glasses Industrial Goggles with Anti-fog Lens, Clear Safety glasses with Anti-Scratch Lens Goggles Inside Eyeglasses (Transparent)

| | |
|---|---|
| Manufacturer | MEIGIX |
| Part Number | MEIGIX-GOGGLES2 |
| Item Weight | 2.82 ounces |
| Package Dimensions | 9.09 x 4.53 x 2.8 inches |
| Finish | Scratch-resistant, Anti-fog, Uv-protection |
| Material | Plastic |
| Batteries Required? | No |

Participants in the intervention arm will be given a pair of blue-blocking glasses. This will be one of two types depending on whether they wear reading glasses or not, as well as comfort considerations.

Participants in the intervention arm with reading glasses will receive blue-blocking glasses that fit over their other glasses. To account for changing availability of specific glasses models on the Amazon website, any pair of blue-blocking glasses that is similar to the model below may be used.

Example of intervention glasses for participants who do wear reading glasses:

Uvex ASTRO Over-The-Glass (OTG) Blue Light Blocking Computer Glasses with SCT-Orange Lens.

| | |
|---|---|
| Manufacturer | Honeywell |
| Part Number | S2515 |
| Item Weight | 2.32 ounces |
| Package Dimensions | 6.81 x 2.83 x 2.6 inches |
| Item model number | S2515 |
| Style | ASTRO OTG |
| Item Package Quantity | 1 |
| Included Components | 1 safety eyewear |

| | |
|---|---|
| Batteries Required? | No |

Participants in the intervention arm without reading glasses will receive smaller blue-blocking glasses that would not fit over other glasses. To account for changing availability of specific glasses models on the Amazon website, any pair of blue-blocking glasses that is similar to the model below may be used.

Example of intervention glasses for participants who do not wear reading glasses:

Uvex Skyper Blue Light Blocking Computer Glasses with SCT-Orange Lens.

| | |
|---|---|
| Manufacturer | Uvex |
| Part Number | S1933X |
| Item Weight | 1.6 ounces |

| | |
|---|---|
| Product Dimensions | 2.7 x 2.2 x 7 inches |
| Item model number | S1933X |
| Is Discontinued By Manufacturer | No |
| Size | 1-Pack |
| Color | Sct-orange Lens |
| Style | Skyper |
| Finish | Anti-fog |
| Item Package Quantity | 1 |
| Included Components | 1 Pair of Glasses |
| Batteries Included? | No |
| Batteries Required? | No |
| Warranty Description | Lifetime Frame Guarantee |

Participants in both arms will be given a wearable device. This device will be either a Fitbit Charge 3 or an Apple Watch.

In the event that Fitbit Charge 3s are the selected wearable device for the study, a description of the device follows below.

The Fitbit Charge 3 is a smart watch capable of measuring heart rate, exercise amount, and sleep levels. There is a retail version available, and that is the model we will be using for our study. The data collected by the Fitbit Charge 3 is transferred from the smart watch to the Fitbit application installed on the patient's phone via Bluetooth Low Energy (BLE), a form of Bluetooth specifically designed to lower power consumption without compromising range. The app then transmits the data to Fitbit's information management system securely and without identifiable information. The smart watch can be worn on either wrist to give accurate measurements. The Charge 3 is made of safe-to-use aluminum and flexible, non-elastic elastomer material common in fitness watches.

Participant Fitbits will be managed through Fitbit's proprietary management system. The user will grant the SYNC app permission to access their heart rate and steps data during the onboarding step. The subject will wear the Charge 3 as often as they like. This will begin the collection of the subject's data. The smart watch will upload the data to the patient's phone every 15 minutes via BLE. The data is then sent to the Fitbit, where it is housed in secure Microsoft Azure servers, compliant with ISO/IEC 27001:2006 industry standards of encryption.

In the event that the Apple Watch is the selected wearable device for the study, a description of the device follows below.

The Apple Watch is a smart watch capable of measuring heart rate, steps, and sleep levels. The retail version will be used in the study. The data from the Apple Watch is transferred via Bluetooth Low Energy to the participant's phone and stored in the Apple Health App. The smart watch can be worn on either wrist. The strap is made from liquid silicone rubber or nylon weave for wearing comfort.

Information collected by the watch can be accessed by the app after the user has granted permission via the Apple Health app.

The Apple Watch series used in this trial may range from Series 3 to Series 6 and may include Series SE.

Detailed descriptions of both the Fitbit Charge 3 and the Apple Watch use and care are below.

## Fitbit Charge 3

Place Charge 3 around your wrist. If you need to attach a different size band, or if you purchased another band, see the instructions in "Change the band" on page 13.

Placement for all-day wear vs. exercise

When you're not exercising, wear Charge 3 a finger's width above your wrist bone.

For optimized heart-rate tracking while exercising:

During a workout, experiment with wearing your tracker a bit higher on your wrist for an improved fit. Many exercises, such as bike riding or weight lifting, cause you to bend your wrist frequently, which could interfere with the heart- rate signal if the tracker is lower on your wrist.

Wear your tracker on top of your wrist, and make sure the back of the device is in contact with your skin.

Consider tightening your band before a workout and loosening it when you’re done. The band should be snug but not constricting (a tight band restricts blood flow, potentially affecting the heart-rate signal).

*Handedness:*

For greater accuracy, you must specify whether you wear Charge 3 on your dominant or non-dominant hand. Your dominant hand is the one you use for writing and eating. To start, the Wrist setting is set to non-dominant. If you wear Charge 3 on your dominant hand, change the Wrist setting in the Fitbit app:

From the Today tab in the Fitbit app, tap your profile picture > Charge 3 tile > Wrist > Dominant.

*Change the band:*

Charge 3 comes with a small band attached and an additional large, bottom band in the box. Both the top and bottom bands can be swapped with accessory bands, sold separately on fitbit.com. For band measurements, see "Band size" on page 48.

*Remove a band:*

1. Turn over Charge 3 and find the band latches.
2. To release the latch, press down on the flat button on the band.
3. Gently pull the band away from the tracker to release it.
4. Repeat on the other side.

*Attach a new band:*

To attach a new band, press it into the end of the tracker until you feel it snap into place.

If you have trouble attaching the band or if it feels loose, gently move the band back and forth to make sure it's attached to the tracker.

*Notifications: Charge 3 can show call, text, calendar, and app notifications from your phone to keep you informed. Keep your tracker within 30 feet of your phone to receive notifications.*

Set up notifications

Check that Bluetooth on your phone is on and that your phone can receive notifications (often under Settings > Notifications). Then set up notifications:

1. From the Today tab in the Fitbit app, tap your profile picture > Charge 3 tile.
2. Tap Notifications.
3. Follow the on-screen instructions to pair your tracker if you haven't already. Call, text, and calendar notifications are turned on automatically.
4. To turn on notifications from apps installed on your phone, including Fitbit and WhatsApp, tap App Notifications and turn on the notifications you want to see.

Note that if you have an iPhone or iPad, Charge 3 shows notifications from all calendars synced to the Calendar app. If you have an Android phone, Charge 3 shows calendar notifications from the calendar app you choose during setup.

*See incoming notifications:* A notification causes your tracker to vibrate. If you don't read the notification when it arrives, you can check it later by swiping down from the top of the screen.

*Manage notifications:* Charge 3 stores up to 10 notifications, after which the oldest are replaced as you receive new ones.

To manage notifications:

Swipe down from the top of the screen to see your notifications and tap any notification to expand it.

To delete a notification, tap to expand it, then swipe to the bottom and tap Clear.

To delete all notifications at once, swipe to the top of your notifications and tap Clear All.

*Turn off notifications:* Turn off certain notifications in the Fitbit app, or turn off all notifications in the quick settings on Charge 3. When you turn off all notifications, your tracker won't vibrate and the screen won't turn on when your phone receives a notification.

To turn off certain notifications:

1. From the Today tab in the Fitbit app on your phone, tap your profile picture > Charge 3 tile > Notifications.
2. Turn off the notifications you no longer want to receive on your tracker.
3. Sync your tracker to save your changes.

To turn off all notifications:

1. Press and hold the button on your tracker and swipe left to reach the quick settings screen (on Fitbit Pay-enabled trackers).
2. Tap DND to turn on do not disturb. The DND icon dims to indicate that all notifications, including goal celebrations and reminders to move, are turned off.

Note that if you use the do not disturb setting on your phone, you don't receive notifications on your tracker until you turn off this setting.

*Answer or reject phone calls:*

If paired to an iPhone or Android (8.0+) phone, Charge 3 lets you accept or reject incoming phone calls. If your phone is running an older version of the Android OS, you can reject, but not accept, calls on your tracker.

To accept a call, tap the check mark on your tracker's screen. Note that you can't speak into the tracker—accepting a phone call answers the call on your nearby

phone. To reject a call, tap the icon on your tracker's screen.

Respond to messages

If paired to an Android (8.0+) phone, Charge 3 lets you respond directly to text messages and notifications from certain apps on your tracker with preset quick replies.

To respond to a message:

1. Tap the notification on your tracker. To see recent messages, swipe down from the clock face.
2. Tap Reply. If you don’t see an option to reply to the message, replies aren’t available for the app that sent the notification.
3. Choose a text reply from the list of quick replies or tap the emoji icon to choose an emoji.

For more information, including how to customize quick replies, see help.fitbit.com.

*Activity and Sleep:*

Charge 3 continuously tracks a variety of stats whenever you wear it. Data automatically syncs when in range of the Fitbit app throughout the day.

*See your stats:*

Swipe up from the clock face on your tracker to see your daily stats, including:

| | |
|---|---|
| **Core stats** | **Steps taken today, distance covered, floors climbed, calories burned, and active minutes** |

| | |
|---|---|
| **Hourly steps** | **Steps taken this hour, and the number of hours you met your hourly activity goal** |
| **Heart rate** | **Current heart rate and heart-rate zone, and resting heart rate** |
| **Exercise** | **Number of days you met your exercise goal this week** |
| **Cycle track** | **Information on the current stage of your menstrual cycle, if applicable** |
| **Sleep Duration and quality of your sleep** | |

Find your complete history and other information detected by your tracker, such as sleep data, in the Fitbit app.

*Track a daily activity goal:* Charge 3 tracks your progress toward a daily activity goal of your choice. When you reach your goal, your tracker vibrates and shows a celebration.

Choose a goal: Set a goal to help you get started on your health and fitness journey. To begin, your goal is to take 10,000 steps per day. Choose to change the number of steps, or pick a different activity goal depending on your device.

Track progress toward your goal on Charge 3. For more information, see "See your stats" on the previous page.

*Track your hourly activity:*

Charge 3 helps you stay active throughout the day by keeping track of when you're stationary and reminding you to move.

Reminders nudge you to walk at least 250 steps each hour. You feel a vibration and see a reminder on your screen at 10 minutes before the hour if you haven't walked 250 steps. When you meet the 250-step goal after receiving the reminder, you feel a second vibration and see a congratulatory message.

*Track your sleep:* Wear Charge 3 to bed to automatically track basic stats about your sleep, including your time asleep, sleep stages (time spent in REM, light sleep, and deep sleep), and

sleep score (the quality of your sleep). Charge 3 also tracks your estimated oxygen variation throughout the night to help you uncover potential breathing disturbances. To see your sleep stats, sync your tracker when you wake up and check the Fitbit app, or swipe up from the clock face on your tracker to check the Sleep tile in Fitbit Today.

*Fitness and Exercise*

Choose to automatically track exercise, or to track activity with the Exercise app and see real-time stats and a post-workout summary.

Sync Charge 3 with the Fitbit app and share your activity with friends and family, see how your overall fitness level compares to your peers, and more.

Track your exercise automatically

Charge 3 automatically recognizes and records many high-movement activities which are at least 15 minutes long. Sync your device to see basic stats about your activity in the Exercise tile in the Fitbit app.

For more information, including how to change the minimum duration before an activity is tracked, see help.fitbit.com.

Track and analyze exercise with the Exercise app

Track specific exercises with the Exercise app on Charge 3 to see real-time stats, including heart-rate data, calories burned, elapsed time, and a post-workout

summary on your wrist. For complete workout stats, and a workout intensity map if you used GPS, tap the Exercise tile in the Fitbit app.

Note: Charge 3 uses the GPS sensors on your nearby phone to capture GPS data.

*Check your heart rate*

Heart-rate zones help you target the training intensity of your choice. See your current zone and progress toward your maximum heart rate on your device next to your heart-rate reading. In the Fitbit app, you can see your time spent in zones during a particular day or exercise. Three zones based on American Heart Association recommendations are available, or you can create a custom zone if you have a specific heart rate you're targeting.

*Default heart-rate zones:*

Default heart-rate zones are calculated using your estimated maximum heart rate. Fitbit calculates your maximum heart rate with the common formula of 220 minus your age.

| Icon | Zone | Calculation | Description |
|---|---|---|---|
| Icon Zone Calculation Description | | | |
| | Below Zones | Below 50% of your maximum heart rate | Below the fat burn zone, your heart beats at a slower pace. You're likely at rest or doing light activities such as taking a stroll. |
| | Fat Burn Zone | Between 50% and 69% of your maximum heart rate | In the fat burn zone, you're likely in a moderate activity such as a brisk walk. Your heart rate and breathing might be elevated, but you can still carry on a conversation. |
| | Cardio Zone | Between 70% and 84% of your maximum heart rate | In the cardio zone, you're likely doing a vigorous activity such as running or spinning. |
| | Peak Zone | Greater than 85% of your maximum heart rate | In the peak zone, you're likely doing a short, intense activity that improves performance and speed, such as sprinting or high-intensity interval training. |

*Custom heart-rate zones*

Instead of using these 3 heart-rate zones, you can create a custom zone to target a specific heart-rate range in the Fitbit app.

## Apple Watch

To use your Apple Watch Series 3 or later with watchOS 7, you need to pair your Apple Watch with an iPhone 6s or later with iOS 14 or later. Setup assistants on your iPhone and Apple Watch work together to help you pair and set up your Apple Watch.

WARNING: To avoid injury, read Important safety information for Apple Watch before using your Apple Watch.

Turn on, pair, and set up your Apple Watch

1. Put your Apple Watch on your wrist. Adjust the band or choose a band size so your Apple Watch fits closely but comfortably on your wrist.
   For information about changing the band on your Apple Watch, see Remove, change, and fasten Apple Watch bands.
2. To turn on your Apple Watch, press and hold the side button until you see the Apple logo.
3. Bring your iPhone near your Apple Watch, wait for the Apple Watch pairing screen to appear on your iPhone, then tap Continue.
   Or open the Apple Watch app on your iPhone, then tap Pair New Watch.

4. When prompted, position your iPhone so that your Apple Watch appears in the viewfinder in the Apple Watch app. This pairs the two devices.
5. Tap Set Up Apple Watch. Follow the instructions on your iPhone and Apple Watch to finish setup.

Tip: If you have difficulty seeing your Apple Watch or iPhone, VoiceOver or Zoom can help—even during setup. See Set up Apple Watch using VoiceOver or Use Zoom on Apple Watch. While it’s pairing with your iPhone, your Apple Watch provides tips on how to interact with it. Tap Display, Digital Crown, and Side Button to learn more.

You can activate cellular service on your Apple Watch during setup. If you don’t wish to, you can activate it later in the Apple Watch app on your iPhone. See Use Apple Watch with a cellular network.

Your iPhone and Apple Watch must use the same cellular carrier. However, if you set up an Apple Watch for someone in your Family Sharing group, you may use a cellular carrier different from the one used on the iPhone you manage it with.
Cellular service not available in all regions.


Trouble pairing?

- *If you see a watch face when you're trying to pair:* Your Apple Watch is already paired to an iPhone. You need to first erase all Apple Watch content and reset settings.
- *If the camera doesn't start the pairing process:* Tap Pair Apple Watch Manually at the bottom of the iPhone screen, and follow the onscreen instructions.
- *If Apple Watch isn't pairing with iPhone:* See the Apple Support article If your Apple Watch isn't connected or paired with your iPhone.

Unpair Apple Watch

1. Open the Apple Watch app on your iPhone.
2. Tap My Watch, then tap All Watches at the top of the screen.
3. Tap ⓘ next to the Apple Watch you want to unpair, then tap Unpair Apple Watch.

Pair more than one Apple Watch

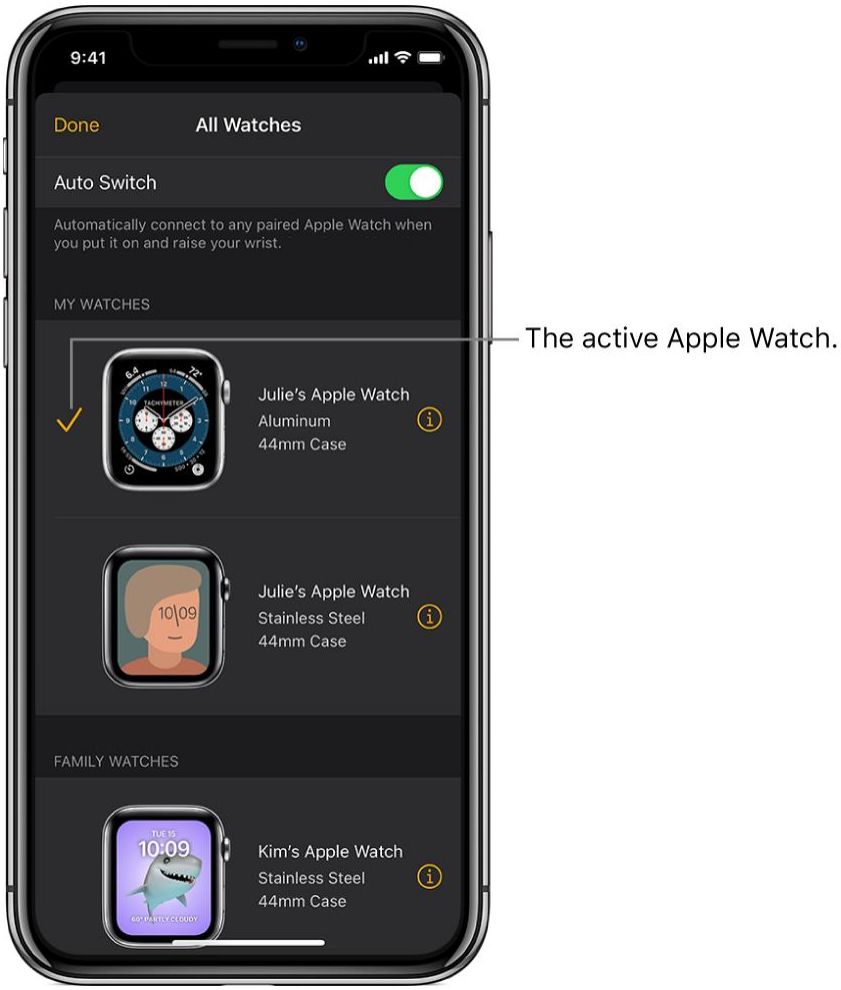
You can pair another Apple Watch in the same way you paired your first one. Bring your iPhone near your Apple Watch, wait for the Apple Watch pairing screen to appear on your iPhone, then tap Pair. Or follow these steps:

1. Open the Apple Watch app on your iPhone.
2. Tap My Watch, then tap All Watches at the top of the screen.
3. Tap Pair New Watch, then follow the onscreen instructions.

See the Apple Support article Use more than one Apple Watch with your iPhone.
To learn how to set up a watch for someone in your Family Sharing group, see Set up Apple Watch for a family member.
Quickly switch to a different Apple Watch
Your iPhone detects the paired Apple Watch you're wearing and automatically connects to it. Just put on a different Apple Watch and raise your wrist.
You can also choose an Apple Watch manually:

1. Open the Apple Watch app on your iPhone.
2. Tap My Watch, then tap All Watches at the top of the screen.
3. Turn off Auto Switch.

To see if your Apple Watch is connected to your iPhone, touch and hold the bottom of the watch screen, swipe up to open Control Center, then look for the Connected status icon .




Pair Apple Watch to a new iPhone
If your Apple Watch is paired to your old iPhone and you now want to pair it with your new iPhone, follow these steps:

1. Use iCloud Backup to back up the iPhone currently paired to your Apple Watch (see the iPhone User Guide for more information).

2. Set up your new iPhone. On the Apps & Data screen, choose to restore from an iCloud backup, then select the latest backup.
3. Continue iPhone setup and, when prompted, choose to use your Apple Watch with your new iPhone.

When iPhone setup completes, your Apple Watch prompts you to pair it to the new iPhone. Tap OK on your Apple Watch, then enter its passcode.

For more information, see the Apple Support article How to pair your Apple Watch with a new iPhone.

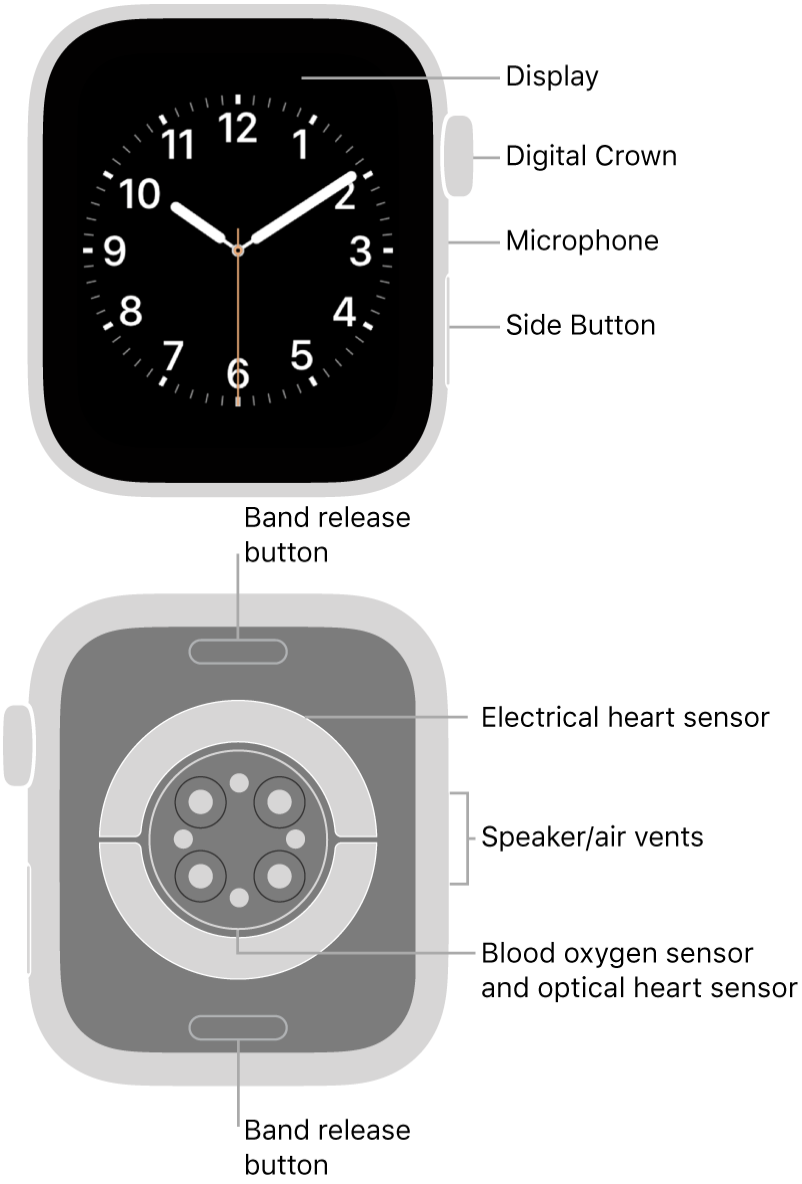
Transfer an existing cellular plan to a new Apple Watch

You can transfer your existing cellular plan from your Apple Watch with cellular to another Apple Watch with cellular by following these steps:

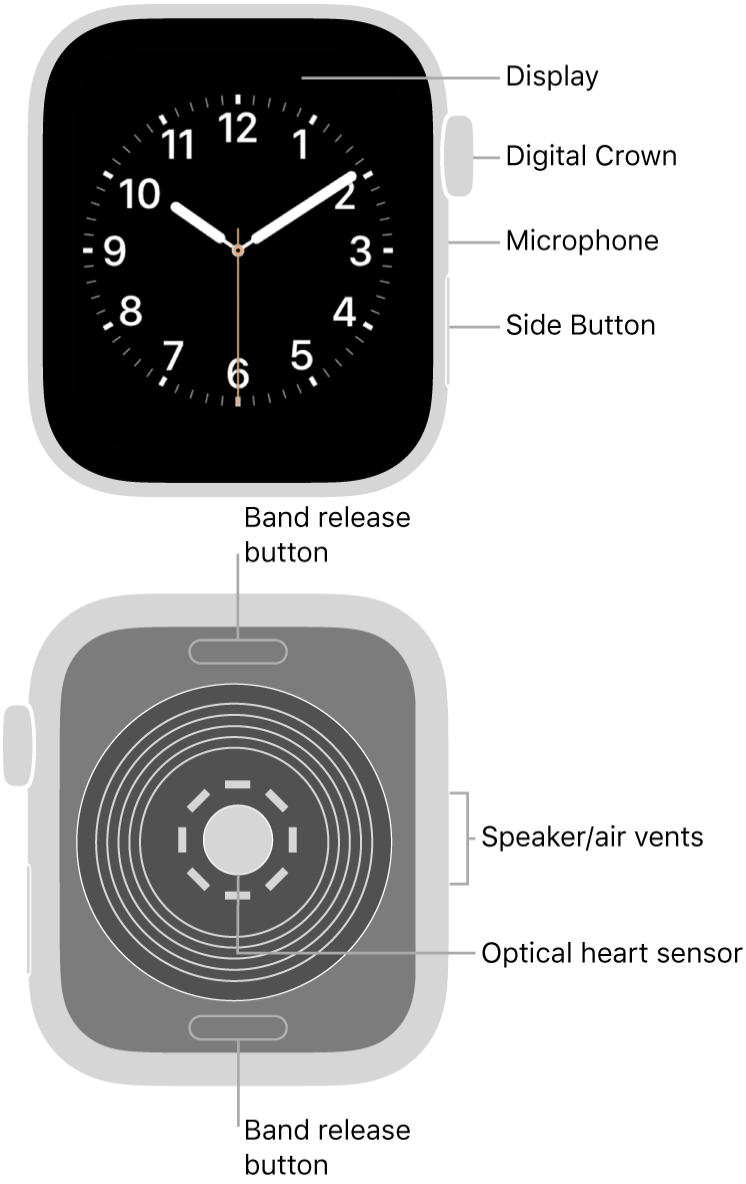
1. While wearing your Apple Watch, open the Apple Watch app on your iPhone.
2. Tap My Watch, tap Cellular, then tap  next to your cellular plan.
3. Tap Remove [*name of carrier*] Plan, then confirm your choice.
   You may need to contact your carrier to remove this Apple Watch from your cellular plan.
4. Remove your old watch, put on your other Apple Watch with cellular, tap My Watch, then tap Cellular.
   Follow the instructions to activate your watch for cellular.

For more information about setup and pairing, see the Apple Support article Set up your Apple Watch.

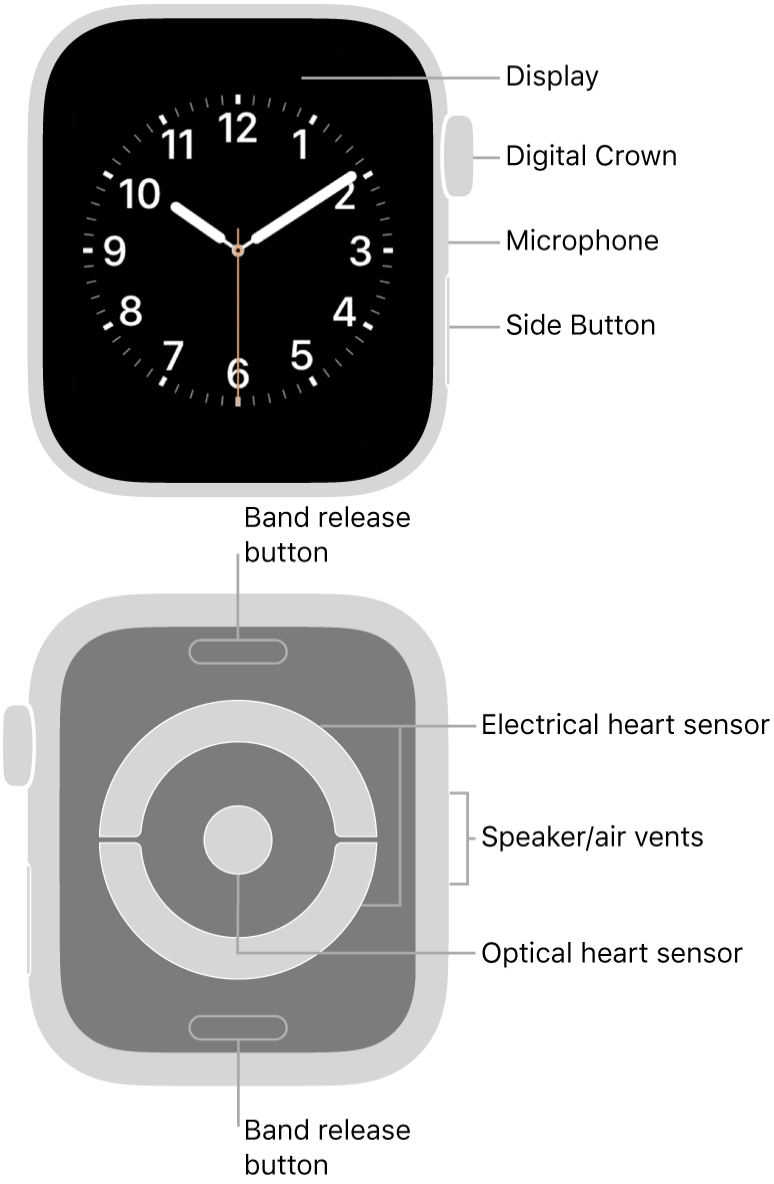
If you need to charge your Apple Watch before setup, see Charge Apple Watch.



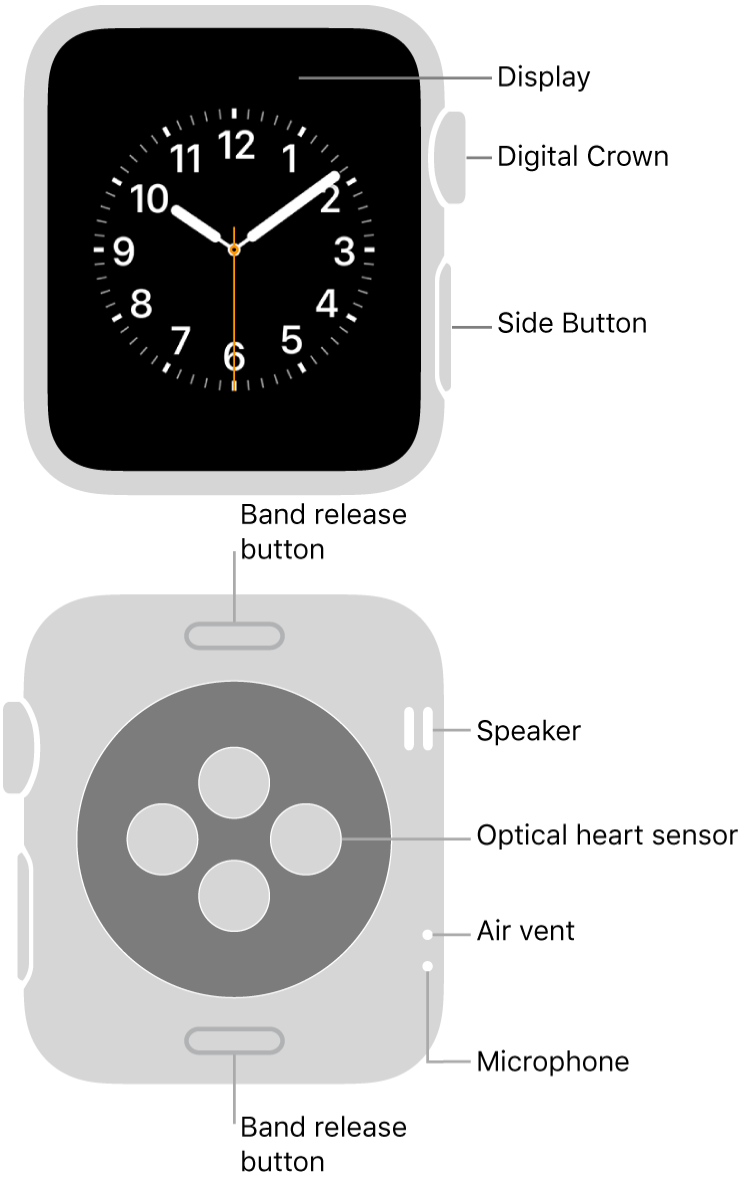

Apple Watch SE




Apple Watch Series 4 and Apple Watch Series 5




Apple Watch Series 3




Charge Apple Watch

Set up the charger

1. In a well-ventilated area, place the included Apple Watch Magnetic Charging Cable or Apple Watch Magnetic Charging Dock on a flat surface.
2. Plug it into the power adapter (sold separately).
3. Plug the adapter into a power outlet.

Begin charging Apple Watch

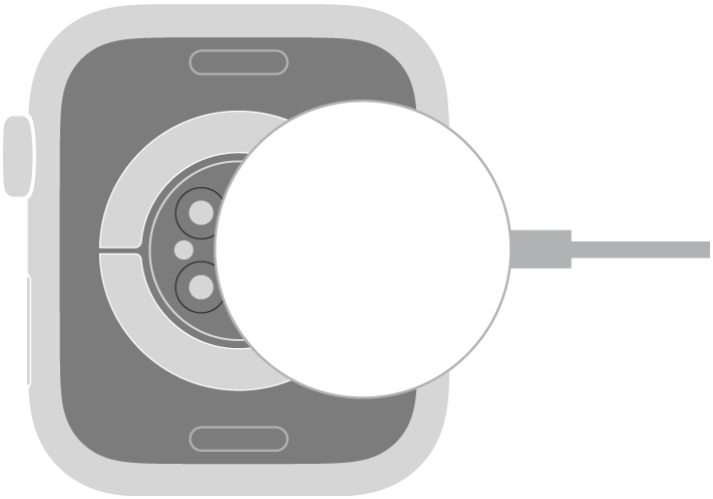
Place the Apple Watch Magnetic Charging Cable on the back of your Apple Watch. The concave end of the charging cable magnetically snaps to the back of your Apple Watch and aligns it properly.

You hear a chime when charging begins (unless your Apple Watch is in silent mode) and see a charging symbol on the watch face. The symbol is red when Apple Watch needs power and turns green when Apple Watch is charging.

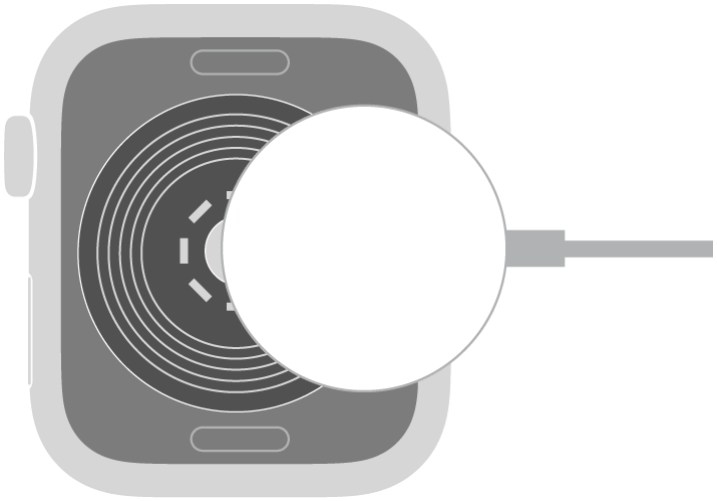
You can charge your Apple Watch in a flat position with its band open, or on its side.

- *If you're using the Apple Watch Magnetic Charging Dock:* Lay your Apple Watch on the dock.
- *If your battery is very low:* You may see an image of the Apple Watch Magnetic Charging Cable and the low battery symbol on the screen. For more information, see the Apple Support article If your Apple Watch won't charge or it won't turn on.

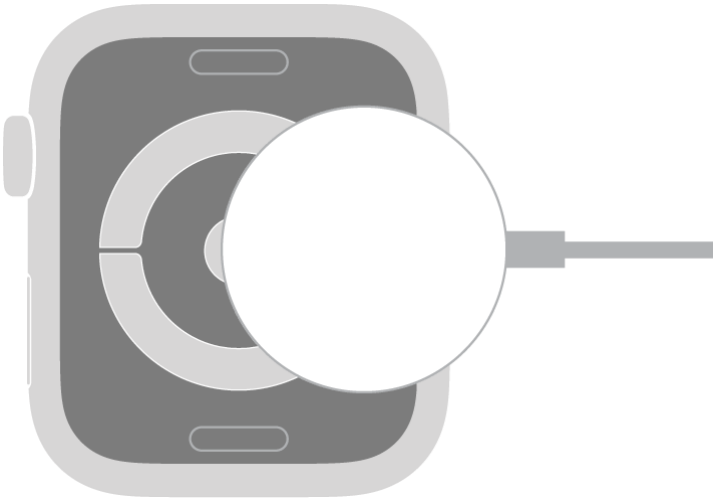
Apple Watch Series 6



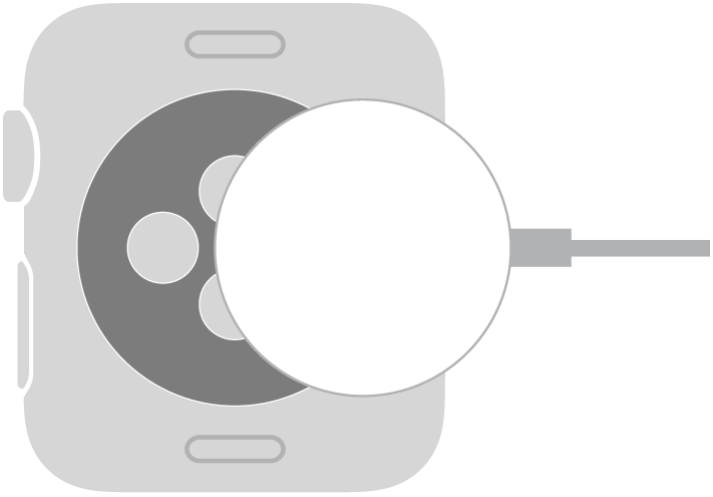
Apple Watch SE



Apple Watch Series 4 and Apple Watch Series 5



Apple Watch Series 3



WARNING: For important safety information about the battery and charging Apple Watch, see Important safety information for Apple Watch.

Check remaining power

To see remaining power, touch and hold the bottom of the screen, then swipe up to open Control Center. To more quickly check the remaining power, add a battery complication to the watch face. See Customize the watch face.


Save power when the battery is low

You can put your Apple Watch in Power Reserve mode to stretch the remaining battery power. Your Apple Watch still displays the time, but you can’t use apps.

1. Touch and hold the bottom of the screen, then swipe up to open Control Center.
2. Tap the battery percentage, then drag the Power Reserve slider to the right.


Tip: If you have battery-powered devices such as AirPods connected to your Apple Watch through Bluetooth, their remaining charge appears on this screen.

When battery charge drops to 10 percent or lower, your Apple Watch alerts you and gives you the opportunity to enter Power Reserve mode.


When your Apple Watch is almost out of power, it enters Power Reserve mode automatically.
Tip: For tips on maximizing battery life, see Maximizing Battery Life and Lifespan at the Apple website.
Return to normal power mode
Restart your Apple Watch—press and hold the side button until the Apple logo appears.
The battery must have at least 10 percent charge for your Apple Watch to restart.
Check time since the last charge

1. Open the Settings app on your Apple Watch.
2. Tap Battery.
   The Battery screen shows the remaining battery percentage, a graph that details the recent history of the battery charge, and information about when the battery was last charged.


You can also check the time since last charge on iPhone. Open the Apple Watch app on iPhone, tap My Watch, then go to General > Usage.
Check battery health
You can find out the capacity of your Apple Watch battery relative to when it was new.

1. Open the Settings app on your Apple Watch.

2. Tap Battery, then tap Battery Health.

To reduce battery aging, Apple Watch learns from your daily charging routines so it can wait to finish charging past 80 percent until you need to use it.

Apple Watch alerts you if battery capacity is significantly reduced, allowing you to check your service options.

Track important health information with Apple Watch

Your Apple Watch can help you meet your sleep goals, track important information related to your heart, check your blood oxygen levels, and encourage you to wash your hands.


Prioritize your sleep

Apple Watch can help you create a sleep schedule, track your sleep, then report your sleep trends over time. To get started, open the Health app on iPhone and create a sleep schedule. Then wear your watch to bed and Apple Watch does the rest.


Get heart health notifications

You can enable notifications from the Heart Rate app on your Apple Watch to alert you to high or low heart rates. The irregular heart rhythm notification on the Apple Watch can also alert you if an irregular rhythm suggestive of Atrial fibrillation is identified. Open the Apple Watch app on your iPhone, go to My Watch, then tap Heart. Turn on High Heart Rate or Low Heart Rate, then set a heart rate threshold, also turn on irregular rhythm notifications.


*Check your blood oxygen levels (Apple Watch Series 6 only)*

Use the Blood Oxygen app to measure your blood oxygen levels directly from your wrist. See the most recent measurement on your Apple Watch and a record of all your readings in the Health app on iPhone.


*Wash your hands thoroughly*

Turn on Handwashing in the Apple Watch app on iPhone, and your Apple Watch encourages you to keep going for 20 seconds, the time recommended by global health organizations. Your watch can also notify you if you haven't washed your hands within a few minutes of returning home.


*Track your menstrual cycle*

Use the Cycle Tracking app to log daily information about your menstrual cycle. The app uses that information to provide period and fertility window predictions.

# APPENDIX B: SYNC COMPONENTS

Study participants randomized to the Intervention Arm will use a version of SYNC that makes behavioral recommendations to correct circadian misalignment. Those in the Control Arm will use a "dummy" version of the app that makes behavioral recommendations that should minimally affect the circadian clock.

The full version of SYNC has the following features:

- Light exposure recommendations; e.g. times to sit near a window or go outside
- Light avoidance recommendations; e.g. times to wear blue-blocking glasses
- Caffeine avoidance recommendations
- Ideal times to sleep
- Ideal times to exercise for peak performance
- Ideal times to exercise to shift the circadian clock
- Surveys embedded for daily tracking of fatigue and other metrics
- Personalized educational information about the circadian clock

The dummy version of SYNC has the following features:

- Light exposure recommendations, timed to avoid shifting circadian rhythms
- Surveys embedded for daily tracking of fatigue and other metrics

The abovementioned recommendations are calculated using mathematical models of the circadian clock which read in data from the user's wearable device. The times are expected to shift every day, as the user's circadian clock shifts.

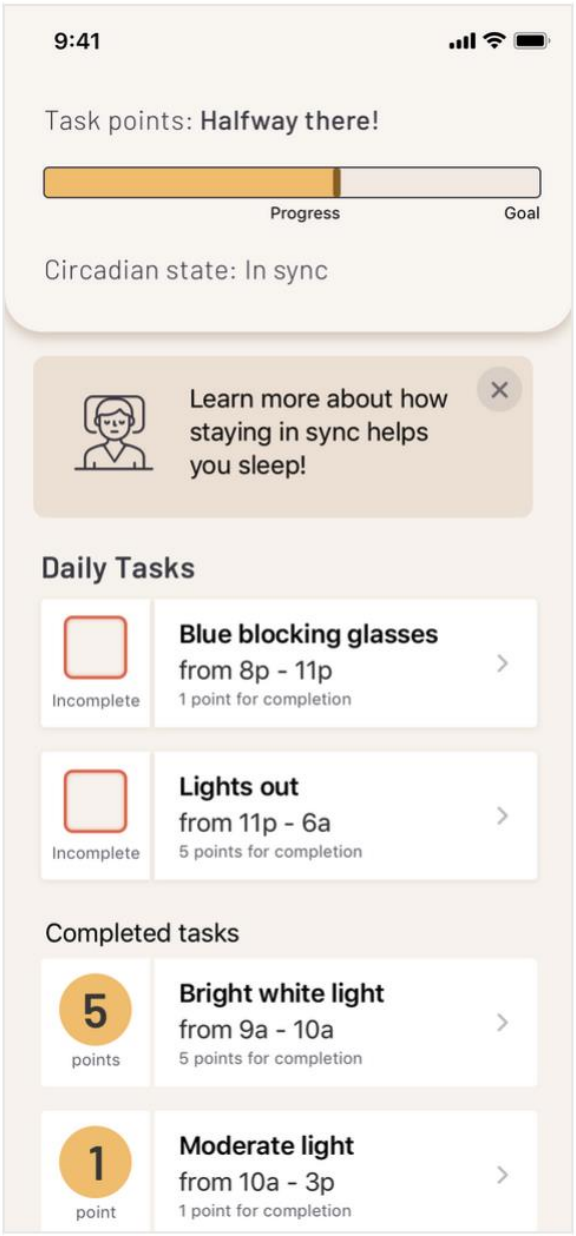
Sample behavioral recommendations from the full app include:

- *"Sit near a window or go outside from 8:30 am - 9:45 am"*
- *"Put on your blue-blocking glasses at 7:05 pm"*
- *"To fall asleep earlier tonight, do a workout between 6:45 am and 9:30 am"*
- *"Your peak window of athletic performance is from 7:45 pm - 9:45 pm"*
- *"Taking a nap from 1:00 - 1:45 pm today shouldn't keep you from falling asleep tonight."*

The dummy version of the app will make the following recommendations:

- "*Put on your study-provided glasses from 12:00 pm - 1:00 pm*"
- "*Be in a room with normal lighting from 1:00 pm - 1:30 pm*"

A screenshot of the app, currently in revision, is provided below for context:


9:41
Task points: Halfway there!
Progress
Goal
Circadian state: In sync
Learn more about how staying in sync helps you sleep!
Daily Tasks
Incomplete
Blue blocking glasses
from 8p - 11p
1 point for completion
Incomplete
Lights out
from 11p - 6a
5 points for completion
Completed tasks
5
points
Bright white light
from 9a - 10a
5 points for completion
1
point
Moderate light
from 10a - 3p
1 point for completion

# APPENDIX C: USER-REPORTED OUTCOME MEASURES

## Baseline Survey/Exit Survey

PROMIS® Item Bank v1.0 – Sleep Disturbance – Short Form 8a

### Sleep Disturbance – Short Form 8a

**Please respond to each question or statement by marking one box per row.**

| | **In the past 7 days…** | **Very poor** | **Poor** | **Fair** | **Good** | **Very good** |
|---|---|---|---|---|---|---|
| Sleep109 | My sleep quality was ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| | **In the past 7 days…** | **Not at all** | **A little bit** | **Somewhat** | **Quite a bit** | **Very much** |
| Sleep116 | My sleep was refreshing. ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| Sleep20 | I had a problem with my sleep ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| Sleep44 | I had difficulty falling asleep ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| Sleep108 | My sleep was restless ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| Sleep72 | I tried hard to get to sleep ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| Sleep67 | I worried about not being able to fall asleep ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| Sleep115 | I was satisfied with my sleep. ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |

## Emotional Distress - Anxiety – Short Form 7a

**Please respond to each item by marking one box per row.**

**In the past 7 days...**

| | | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|---|
| EDANX01 | I felt fearful | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDANX05 | I felt anxious | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDANX30 | I felt worried | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDANX40 | I found it hard to focus on anything other than my anxiety | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDANX46 | I felt nervous | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDANX53 | I felt uneasy | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDANX54 | I felt tense | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |

## Emotional Distress – Depression – Short Form 8a

**Please respond to each question or statement by marking one box per row.**

| | In the past 7 days... | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|---|
| EDDEP04 | I felt worthless | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP06 | I felt helpless | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP29 | I felt depressed | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP41 | I felt hopeless | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP22 | I felt like a failure | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP36 | I felt unhappy | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP05 | I felt that I had nothing to look forward to | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| EDDEP09 | I felt that nothing could cheer me up | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |

## Physical Function – Short Form 8b

**Please respond to each question or statement by marking one box per row.**

| | | Without any difficulty | With a little difficulty | With some difficulty | With much difficulty | Unable to do |
|---|---|---|---|---|---|---|
| PFA11 | Are you able to do chores such as vacuuming or yard work? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| PFA21 | Are you able to go up and down stairs at a normal pace? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| PFA23 | Are you able to go for a walk of at least 15 minutes? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| PFA53 | Are you able to run errands and shop? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| | | **Not at all** | **Very little** | **Somewhat** | **Quite a lot** | **Cannot do** |
| PFC12 | Does your health now limit you in doing two hours of physical labor? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| PFB1 | Does your health now limit you in doing moderate work around the house like vacuuming, sweeping floors or carrying in groceries? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| PFA5 | Does your health now limit you in lifting or carrying groceries? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| PFA4 | Does your health now limit you in doing heavy work around the house like scrubbing floors, or lifting or moving heavy furniture? | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |

PROMIS® Scale v1.2 – Global Health

## Global Health

**Please respond to each question or statement by marking one box per row.**

| | Excellent | Very good | Good | Fair | Poor |
|---|---|---|---|---|---|
| In general, would you say your health is: ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| In general, would you say your quality of life is: ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| In general, how would you rate your physical health? ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| In general, how would you rate your mental health, including your mood and your ability to think? ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| In general, how would you rate your satisfaction with your social activities and relationships? ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| In general, please rate how well you carry out your usual social activities and roles. (This includes activities at home, at work and in your community, and responsibilities as a parent, child, spouse, employee, friend, etc.)..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| | **Completely** | **Mostly** | **Moderately** | **A little** | **Not at all** |
| To what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair? ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |

**In the past 7 days…**

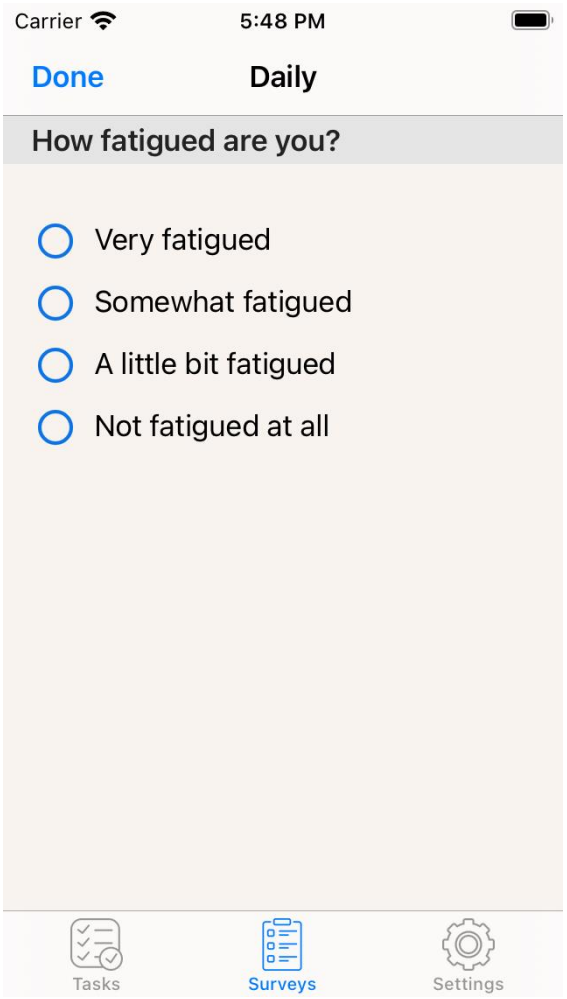
| | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|
| How often have you been bothered by emotional problems such as feeling anxious, depressed or irritable? ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| | **None** | **Mild** | **Moderate** | **Severe** | **Very severe** |
| How would you rate your fatigue on average? ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| How would you rate your pain on average? ..... | ☐ 0 **No pain** | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | ☐ 8 | ☐ 9 | ☐ 10 **Worst pain imaginable** |

Morningness-Eveningness Questionnaire:

1. One hears about “morning” and “evening” types of people. Which one of these types do you consider yourself to be?
    a. Definitely a morning type
    b. More of a morning than evening type
    c. More of an evening than morning type
    d. Definitely an evening type
2. Considering only your own “feeling best” rhythms, at what time would you get up if you were entirely free to plan your day?
    a. 5 am - 6:30 am
    b. 6:30 am - 7:45 am
    c. 7:45 am - 9:45 am
    d. 9:45 am - 11 am
    e. 11 am - 12 noon
3. During the first half hour after awakening in the morning, how tired do you feel?
    a. Very tired
    b. Fairly tired
    c. Fairly refreshed
    d. Very refreshed
4. At what time in the evening do you feel tired and in need of sleep?"
    a. 8 pm - 9 pm
    b. 9 pm - 10:15 pm
    c. 10:15 pm - 12:30 am
    d. 12:30 am - 1:45 am
    e. 1:45 am - 3 am
5. At what time of the day do you think that you reach your “feeling best” peak?
    a. 10 pm - 5 am
    b. 5 am - 8 am
    c. 8 am - 10 am
    d. 10 am – 5 pm
    e. 5 pm – 10 pm

Daily Fatigue Survey



# Weekly Survey

PROMIS Fatigue Short Form 4a

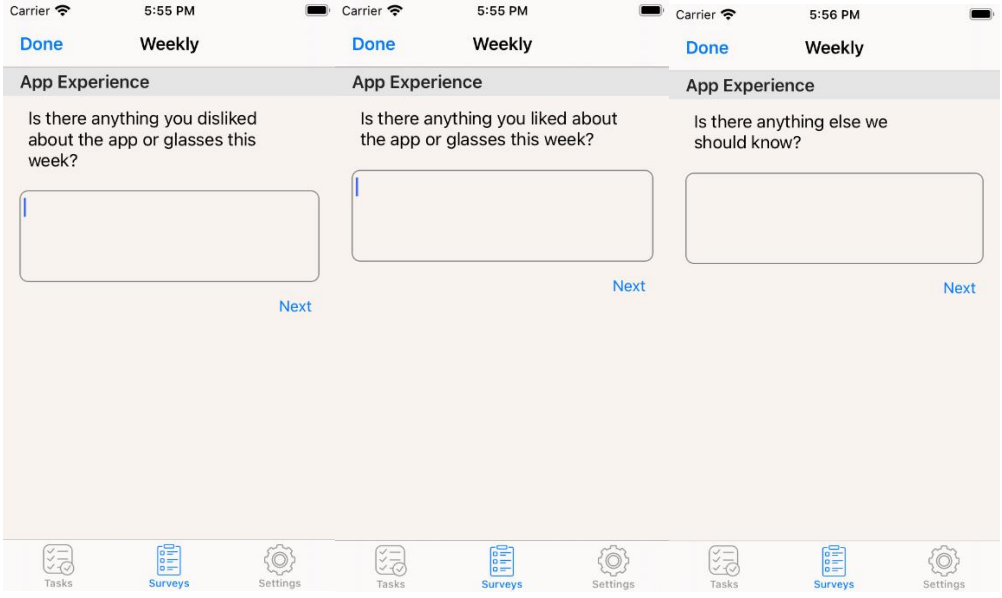
PROMIS® Item Bank v1.0 –Fatigue – Short Form 4a

**Fatigue – Short Form 4a**

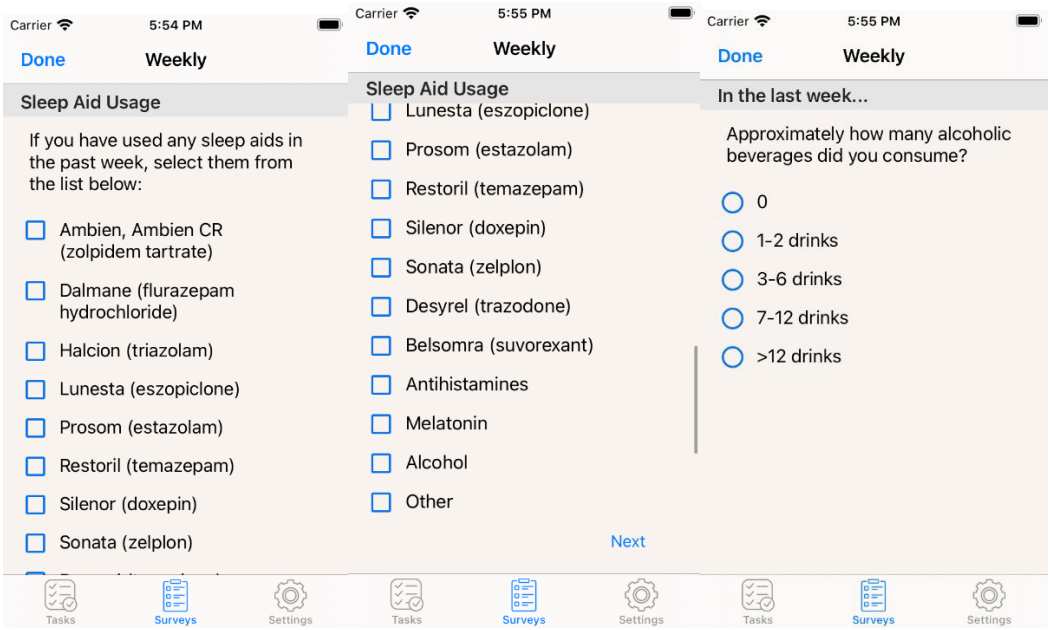
**Please respond to each question or statement by marking one box per row.**

| | **During the past 7 days…** | **Not at all** | **A little bit** | **Somewhat** | **Quite a bit** | **Very much** |
|---|---|---|---|---|---|---|
| HI7 | I feel fatigued ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN3 | I have trouble starting things because I am tired..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| | **In the past 7 days…** | | | | | |
| FATEXP41 | How run-down did you feel on average? ... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| FATEXP40 | How fatigued were you on average? ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |

"How is your experience with the app?" questionnaire



Sleep aid usage survey




Weekly travel questionnaire:

1. Did you travel across time zones this week?"

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