Series of virtual light therapy interventions for fatigue: a feasibility pilot study protocol for a series of personalised (N-of-1) trials

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INTRODUCTION

Fatigue is one of the most commonly recorded patient symptoms that can result in deficits in aspects of psychomotor functioning, cognition, work performance and mood. Research shows that bright light and dim light therapy may be an efficacious way to reduce symptoms of fatigue. Still, the feasibility, scalability, individual treatment effects and adverse event heterogeneity of these treatments are unknown.

Methods and analysis The current study evaluates the feasibility, acceptability and effectiveness of a series of personalised (N-of-1) interventions for virtual delivery of bright light therapy and dim light therapy versus usual care treatment for fatigue in 60 participants. We hypothesise that this study will provide valuable information about implementing virtual, N-of-1 randomised controlled trials (RCTs) for fatigue. It will also offer results about determining participants’ ratings of usability and satisfaction with the virtual, personalised intervention delivery system; evaluating participants’ improvement of fatigue symptoms; and, in the long term, identify ways to integrate N-of-1 light therapy trials into patient care.

Ethics and dissemination This trial was approved by the Northwell Health Institutional Review Board. The trial results will be published in a peer-reviewed journal. All publications resulting from this series of personalised trials will follow the Consolidated Standards of Reporting Trials extension for N-of-1 trials CENT 2015 reporting guidelines.

Registration details This trial is registered in www.ClinicalTrials.gov (number NCT04707846).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This trial provides a virtual, personalised intervention delivering bright light and dim light therapy for fatigue.
⇒ This trial will ask participants to evaluate usability and satisfaction with the intervention and thereby provide information about the acceptability of the intervention and feasibility of its integration into patient care.
⇒ This trial will use ecological momentary assessment, online survey measures and Fitbit Charge 3 devices to accurately assess the effect of the intervention on participant’s fatigue, pain, stress, confidence, concentration, mood, activity and sleep in real-world contexts.
⇒ This trial’s personalised (N-of-1) design allows for examination of heterogeneity of intervention effects.
⇒ This study will enrol 60 participants and assess them for a duration of 14 weeks.

INTRODUCTION

Fatigue is one of the most commonly recorded patient symptoms in conversations with primary care providers. Practitioner surveys indicate that 25% of patients endorse fatigue as a complaint, while 6.5% name fatigue symptoms as their primary reason for seeking treatment. The consequences of fatigue include deficits in aspects of psychomotor functioning (eg, attention and vigilance), cognition (eg, memory and reasoning), work performance and mood. In the general population, fatigue is associated with increased workplace accidents, highway mortality and reduced quality of life. Despite the high prevalence of fatigue symptoms, therapies are without clear guidelines by which to address these symptoms.

Fatigue may stem from many causes, one of which is disruption of circadian rhythms that control the sleep–wakefulness cycle. Reviews indicate that bright-light therapy can reduce fatigue via two circadian rhythm mechanisms: (a) light influences the suprachiasmatic nucleus (SCN), a region in the hypothalamus that controls circadian rhythms; and (b) light has alerting effects, which in turn facilitate thalamic and cortical connections. The SCN acts as the pacemaker for circadian rhythm within the brain, with light exposure helping to trigger mammalian sleep and wake states.
in mammals have found that blue light exposure can alter the functioning of the circadian clock in the SCN, linking the exposure to increased alertness and wakefulness. In addition, light exposure has also been shown to activate the posterior thalamus, a region associated with alertness, and in the parietal, temporal and occipital lobes of the cortex. Intervention trials have also found that brief morning exposure to bright light (BL) improves subjective symptoms and performance in nurses with rapidly rotating shifts—individuals who are particularly at risk for circadian rhythm disruption.

Based on the effect of light on the circadian rhythm, bright-light therapy has emerged as a potentially viable treatment for fatigue but has been found to have small to moderate effects. A meta-analysis examining 53 studies of BL treatment found that BL exposure was associated with reduced general levels of sleep problems, circadian rhythm sleep disorders, insomnia and sleep disruptions related to Alzheimer’s disease. However, this same meta-analysis showed heterogeneity of treatment effects for light therapy that potential moderator variables (such as sex, age and study design) have not explained. Further complicating findings, dim light (DL) has also demonstrated varying levels of effectiveness on fatigue and called into question the use of solely BL therapy. This research indicates that, though the use of light therapy for fatigue has been studied, the utility of BL and DL therapy for individual patients is still unknown.

Personalised (N-of-1) trials are a patient-centred research approach that can provide important clinical information for patients in selecting which treatments work best for them. In a personalised trial design, individual patients are assessed using multiple crossover trials with objective data collected continuously throughout the trial with alternating time periods of treatment, alternative treatment and placebo therapies in randomised blocks. Personalised trials are specifically designed to help patients make healthcare decisions informed by high-integrity, evidence-based information uniquely relevant to the outcomes and values important to them. Prior series of personalised trials led participants to changes in treatment, cessation of treatment or confirmation of the initial treatment. Despite the utility of personalised trials at the patient level, N-of-1 personalised designs are seldom used in clinical practice. In surveys that examined attitudes about personalised trials, respondents concluded that the potential benefits of personalised designs did not match the cost and effort required for implementation. However, personalised trials have often been initiated with clinicians serving as the target audience for results rather than patients. If personalised N-of-1 trials are conducted with patients as the target audience and conducted in a cost-effective manner, this will increase the use of personalised designs to determine individual-level patient benefits and harms.

Most studies on the effects of BL therapy on fatigue have involved between-subject RCTs. Although such trials often report significant benefits on average, not all individuals show substantial gains and may instead experience modest or no effects. The heterogeneity of effects is of concern and fails to confirm a common assumption of clinical trialists that between-subject treatment change will be roughly equivalent to within-subject treatment change. A personalised trial involving a single, within-subject experimental approach can evaluate the optimum treatment for a single patient. Since each patient serves as their own control, these crossover trials eliminate confounding by covariates. Given the previously shown heterogeneity in studies examining the effects of light therapy on fatigue, the N-of-1 personalised design is ideal for assessing the effects of light therapy on participants suffering from fatigue. Furthermore, this intervention is designed for a single patient and so estimates the fatigue improvements and side effects quantitatively for that single patient. This allows a clinician and patient to determine if a treatment has net benefit for that patient, rather than trying to guess the benefit for the patient based on data obtained from other trial participants and averaged and summarised in published articles.

The current study evaluates the feasibility, acceptability and effectiveness of a series of N-of-1 interventions for virtual delivery of BL therapy, DL therapy or usual care treatment for fatigue symptoms in 60 participants. By using new wearable technologies (such as Fitbit devices) and commercially available light therapy devices (such as AYO), the current study allows for continuous data collection and virtually conducted assessment. Furthermore, virtual delivery of the intervention allows each participant to receive treatment and be assessed for fatigue in their own home. Results from this study will determine whether virtual delivery of these interventions is feasible and acceptable for participants with fatigue and allow clinicians to identify for which patients virtual delivery of light therapy can effectively treat fatigue.

METHODS

Study design
The study is a series of 60 randomised N-of-1 trials examining the effects of BL and DL versus usual care on fatigue. The intervention will be delivered virtually to participants across the USA over 14 weeks. Participants will be provided with a Fitbit Charge 3 device and two AYO light therapy devices.

Worn similarly to glasses, AYO is a commercially available wearable light therapy device that uses blue (470 nm±2 nm wavelength) light of±100 Lux and irradiance of±250 μW/cm². A device emitting a blue light wavelength of 470 nm was preferable to similar devices, as those emitting this wavelength may offer increased ocular protection. AYO rests above the eyes and emits light down into the user’s eyes via four light-emitting diodes. Figure 1 displays the proper position for wearing the AYO device. Using a short ‘lens’, the AYO diffuses light and thereby reduces glare and increases the comfort of device use. Unlike desktop or free-standing light therapy, the
AYO allows users to continue with their everyday tasks while completing their light therapy sessions. AYO devices were specifically chosen to address safety concerns and concerns raised by participants during alpha-piloting of the light-therapy-fatigue study. AYO light therapy glasses can easily turn on/off and have a charging case that connects directly to a power source. In addition, the diffused LED light was more comfortable on the eyes than alternative wearables and adheres to safety recommendations for luminosity. Smartphone activation allows participants to start their light therapy session from their phone, and automatic shut-off eliminates the need to set a separate timer to end the session. Furthermore, Bluetooth capability allows research staff to remotely monitor sessions to ensure participants’ safety and proper adherence to study protocol.

The first 2 weeks of the study will be a baseline assessment period. Participants will not be able to use any light therapy during this time. During baseline assessment, each study participant will be asked to both engage in their usual methods of managing fatigue symptoms and wear their Fitbit device at all times, including during sleep. Participants will also be asked to rate an ecological momentary assessment (EMA) of their fatigue symptoms, pain, concentration, stress, mood and confidence three times daily via text message. Each evening, participants will answer a survey questionnaire assessing their symptoms of fatigue from that day. Each weekend, participants will complete a longer survey measure asking them to reflect on their fatigue symptoms over the week. Participants will be encouraged to wear their Fitbit devices day and night and will be asked to sync their device with the Fitbit application on their phone at least every 2 days and charge their Fitbit device at least every 4 days.

After successfully completing the baseline period, participants will be randomised into two arms with six 2-week treatment blocks of BL AYO therapy, DL AYO therapy or usual care. During BL and DL intervention periods, participants will be discouraged from receiving additional light therapy or fatigue treatments outside those provided during the study. Only the commercial ‘high’ light setting on the AYO device will be used for BL periods within this study. During DL periods, an additional non-commercial version of the AYO—using 1% of regular intensity, less than 2lux—will be used. During usual care periods, no treatment will be provided to participants, and they will be discouraged from engaging in light therapy treatment on their own. At the end of the 14 weeks, each participant will be provided with a satisfaction survey and report containing their analysed data. This report will be sent within 3 months of study completion. After the satisfaction survey is completed, study coordinators will reach out to each participant to interview them about their experience with the personalised trial. Study recruitment began in December 2020, and the study completion is anticipated to occur in December 2021.

Study population
Participants in the current study, including employees within the Northwell Health system, will be volunteer subjects from across the USA. Comprised of approximately 77 000 employees, Northwell Health offers a large pool of potential participants affiliated with the organisation. To expand beyond the Northwell Health system, recruitment will also use the US’s internet and social media users. All participants in the study will self-identify as having a minimum threshold of fatigue. Due to the high prevalence of fatigue and the potential reach of our outreach methods (69% of US adults report ever using Facebook, 18% report using Reddit and 93% report using the internet), the potential study population is anticipated to be quite sizeable. After consultation from an ophthalmologist expert, the study will exclude participants with a family history of Stargardt’s disease and exclude those with diabetes for eye vision safety reasons.

Inclusion criteria
Participants must meet the following criteria to be included in the study:
- Are 18–59 years of age.
- Are fluent in English.
- Have self-reported fatigue scores of ≥12 on a modified Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue Short Form 8a scale.
- Are able to participate in blue light therapy.
- Possess a smartphone capable of receiving text messages.
- Possess an email account that can be regularly accessed.
- Live in the USA.

Exclusion criteria
Persons who meet the following criteria will be excluded:
Have had a previous diagnosis of a serious mental health condition or psychiatric disorder that could be exacerbated by exposure to light therapy or that would compromise their ability to engage with full consent in this trial or adhere to the protocol.

Recruitment

Potential participants will primarily be recruited via advertising and posting across Facebook, Instagram, Google and Reddit. Several iterations of Facebook and Google advertising campaigns will be used to identify the best methods and target different subpopulations (namely by gender or US state of residence). Various formats of recruitment information (including videos, images and text posts) will be posted in online interest group communities on Facebook and Reddit. In addition to word of mouth, recruitment methods will also include emails sent out to all Northwell Health employees and individuals who previously expressed interest in Personalized Trials and the Northwell Health Clinical Trials Listing. Interested persons will be directed to an online information screen with details about the pilot study and asked to complete an initial screening measure containing questions regarding study inclusion and exclusion criteria. This information will be reviewed by study staff to determine participant eligibility prior to consent. If a potential participant is deemed ineligible or is waitlisted due to high demand, study staff will reach out to the participant to notify them within two business days. If the participant is deemed eligible, they will be asked to select times when they are available for a 30 min educational phone call with a study staff member. A study staff member will confirm the scheduled time with the participant within two business days. After the phone call, the study staff will send the eligible participant a message containing the electronic consent form and additional information.

Consent

Persons who are eligible to participate after the screening and educational phone call will receive a message from study staff with a link to access an electronic copy of the consent form and a short video explaining key details of the study protocol and consent form. A four-question screening measure will assess participant understanding of the protocol and consent process. Consent will be obtained electronically, and a copy of the consent will be mailed to the participant and the study instructions and devices. Signed consent forms will be stored electronically on a Health Insurance Portability and Accountability Act (HIPAA) compliant, Northwell Health approved shared drive accessible only to the IRB-approved study staff. An example consent form can be found in appendix 1—sample patient consent.

Potential participants will have the opportunity to choose from within a provided list of start dates during their enrolment process. No more than 20 potential participants will begin their baseline period on the same day. Enrolment will be ongoing until up to 60 participants have been randomised after baseline.

Assignment of interventions

Of those participants who are enrolled in the study, approximately 30 will be randomised by the study statistician to receive the protocol in the following order of balanced 2-week treatment periods: BL, DL, usual care, usual care, DL and BL. The other participants will be randomised in the following order of 2-week treatment periods: usual care, DL, BL, DL and usual care. In each treatment arm, participants alternate between BL, DL and usual care periods. Randomisation of participants to one of the two treatment orders will be conducted in six blocks using a readily accessible randomisation website. This randomisation to treatment order can be viewed in the participant timeline in figure 2.

Interventions

Once a participant successfully completes baseline data collection and is found to meet all eligibility criteria, that participant will be randomised into the study and will be mailed two AYO light therapy glasses. One pair of glasses will be labelled ‘Bright’, indicating it has been hard-coded to emit the BL therapy treatment (blue light with 470nm±2 nm wavelength, ±100 Lux, and irradiance of±250 μW/cm²). The other pair of glasses will be labelled as ‘Dim’, indicating it has been hard-coded to emit the DL therapy treatment (1% regular intensity; less than 2lux.). Participants are not blind to treatment condition during their 2-week treatment periods. Participants will also receive a treatment schedule indicating when they are to use BL glasses, when they are to use DL glasses and when they are to avoid light therapy treatments. Participants will be instructed to download a unique research study application that will initiate light therapy sessions at a predetermined session length of 30 min. During intervention weeks and within an hour of their self-reported wake time, participants will receive morning text message reminders instructing them to complete a 30 min session of either BL or DL each day depending on where they are in the protocol. During usual-care treatment periods, participants will be asked to refrain from participating in any light therapy and instead manage their fatigue using the methods they usually would. During all treatment
but those who respond to 80% of the EMA and survey measures.

**OUTCOMES**

**Primary outcome**

In this study, the System Usability Scale (SUS) will be used to assess the primary outcome of this design, feasibility of the intervention. The primary outcome of the current study will be the mean usability score as measured using the SUS. This scale is a validated 10-item questionnaire that asks users to score each item on a Likert scale from strongly disagree (0) to strongly agree (4). Individual item scores are multiplied by 2.5 and summed to generate a total score ranging from 0 to 100, with higher scores indicating a greater level of usability. This measure has been used and validated in multiple contexts.

**Secondary outcomes**

Secondary outcomes in the current study will include self-reported daily fatigue, self-reported weekly fatigue, EMA self-reported fatigue ratings, EMA self-reported pain ratings, participant satisfaction, EMA self-reported concentration ratings, EMA self-reported stress ratings, EMA self-reported mood ratings, EMA self-reported confidence ratings, Fitbit device – recorded daily steps and Fitbit device – recorded nightly sleep duration. We will also measure participant adherence to survey measures, EMA assessment measures, the Fitbit device and adherence to both BL and DL therapy. Finally, potential side effects during the BL and DL therapy phases will be assessed daily.

The PROMIS fatigue scales are used to measure daily levels of participant fatigue over the past 24 hours (PROMIS Item Bank V.1.0 Fatigue 7b Daily) and weekly levels of participant fatigue over the past 7 days (PROMIS Item Bank V.1.0 Fatigue 8a). All items are rated on a scale of 1–5, with higher scores indicating higher fatigue levels. PROMIS fatigue measures are collected every evening and on the weekends, and EMAs are collected daily via surveys using the N1Thrive platform, a Northwell Health approved and HIPAA-compliant system used for patient engagement and collecting and storing research data. An N1Thrive workflow was constructed for this study to include automated messaging pathways delivered via text message directly to the participant’s smartphone. For both PROMIS scales, scores will be converted to T-scores using methods from the PROMIS scoring manual based on item response theory. These will allow scores to be compared with previously established population norms. With an SD of 10, a T-score of 50 is the average for the US general population. A higher T-score represents higher levels of fatigue. The reliability and validity of the PROMIS fatigue scales have been well supported. In the current study, the effect of BL and DL on the PROMIS fatigue scales (relative to usual care) will be used to determine the effectiveness of each intervention.
Daily self-reported fatigue, pain, concentration, stress, mood and confidence ratings will be assessed via EMA using a measure adapted from the Numeric Pain Rating Scale. These assessment measures are single-item assessments administered three times daily via text message asking participants to rate their fatigue, pain, concentration, stress, mood and confidence in the current moment on a scale of 0–10. The timing of the text messages will be randomised between a participant’s self-reported wake and sleep times. For fatigue, the text stated ‘I feel fatigued’ and ratings of 0 indicate no feeling of fatigue while scores of 1–3, 4–6, 7–9 and 10, respectively, indicate a little, some, significant and extreme feeling of fatigue. Interpretations of scores remain the same for pain, concentration, stress and confidence. For mood, ratings of 0 indicate poor mood with scores of 1–3, 4–6, 7–9 and 10, respectively, indicating a fair, good, very good and excellent mood. As with the PROMIS fatigue scales, changes in the EMA measures will be examined to determine the effectiveness of each intervention.

Measures of participant satisfaction will be used to determine the acceptability of the trial.

Patient satisfaction with the trial will be assessed using a satisfaction survey administered on completion of the treatment. The survey will assess participant satisfaction with elements of the trial, including the onboarding process, the consenting process, the AYO device, the Fitbit device, the N-of-1 trial design, assessment measures and the participant report. Participant satisfaction with the interventions (both BL and DL therapy) will also be assessed. Participants will be asked to rate their satisfaction on a scale of 1 (‘not very satisfied’) to 5 (‘very satisfied’).

Daily steps and nightly sleep duration will be assessed using non-near field communication (non-NFC) Fitbit Charge 3 devices. Both physical activity and sleep duration have been linked with fatigue, indicating these may be important secondary outcomes. During baseline assessment (2 weeks) and all treatment weeks (12 weeks), participants will be asked to continue wearing their Fitbit device each day and night (for a total of 14 weeks, overall). All enrolled participants will be provided with a Fitbit study account that the research team has created with no identifying information. A file linking the Fitbit identifier to the study participant will be housed in a Northwell-approved drive to store protected health information. It will be accessible solely to members of the study team listed in the IRB application. Participant Fitbit data will be retrieved using Fitabase, a secure online portal. Participants’ study accounts will then be linked to an identification number in the Fitabase system. No identifying information will be stored in the Fitabase dataset, and Fitabase will stop tracking participant data at the end of the trial. As an added security measure, participants will be instructed to remove the Fitbit study account from their smartphone device to keep the Fitbit.

**Analysis**

**Sample size calculation**

The sample size of 60 participants was chosen to ensure a sufficient number of participants to obtain a preliminary assessment of the feasibility of this series of N-of-1 trials of BL and DL therapy for fatigue. In the current study, feasibility is determined by participant scores on the SUS. The numbers of assessment measures and treatment repetitions per trial were based on expert recommendations by a statistician and their estimations about the maximal duration of the trial to maintain patient engagement. The primary endpoint is trial completion in the first 3 months. We aim to demonstrate a trial completion rate greater than 50% in randomised participants. With n=60 and use of a 1-sample binomial test at 2.5% significance 1-sided, we will have approximately 90% power if the true completion rate is 70%. With 60 randomised participants, expecting a trial completion rate of 70%, we anticipate SUS data are available in about 42 participants, thus giving an SE no greater than 8% in estimating the rate of SUS ≥85, an exceptional level of usability. The SE will be the largest when the trial completion rate is at 50%. Data will be reported transparently so that individual-level heterogeneity can be assessed.

**Primary analysis**

The primary analysis will examine the feasibility of the trial measured by participant scores on the SUS. Ratings from all enrolled participants (n=60) on the SUS will be summarised via descriptive statistics including mean, median, SD and IQR. We will also visualise the distribution using histogram. The SUS data will be compared with established usability standards in the SUS literature to determine the relative usability of the intervention protocol. If scores on the SUS are greater or equal to 70, defined as an acceptable rating, the current intervention will be judged to be feasible. To determine whether SUS ratings differ by participant characteristics, we will examine mean SUS ratings by age, sex, race and ethnicity.

**Secondary analyses**

Means and SDs for PROMIS daily fatigue scores, PROMIS weekly fatigue scores, self-reported EMA fatigue scores, self-reported EMA pain scores, self-reported EMA concentration scores, self-reported EMA stress scores, self-reported EMA mood scores, self-reported EMA confidence scores, Fitbit-assessed daily steps and Fitbit-assessed nightly sleep will be reported for the baseline assessment period (2 weeks) and each treatment period (six blocks of 2 weeks) and depicted graphically. Means and SDs for patient satisfaction with the trial will be calculated and reported. Higher average scores will be interpreted as higher levels of satisfaction with the trial overall and specific trial elements. We will also calculate mean and SD values for each secondary outcome across treatment periods for BL, DL and usual care. For example, we will sum all outcome measures for both 2-week massage treatment periods to derive an overall mean value for BL.
(The same process will be followed for DL and usual-care periods.) We will then compare overall means of secondary outcomes for BL, DL and usual care periods with baseline means using paired-sample t-tests.

Finally, the effects of each treatment on daily fatigue, weekly fatigue and self-reported EMA fatigue will be assessed using generalised linear mixed models with an autoregressive (AR1) model that accounts for possible autocorrelation and linear trends between fatigue ratings across time. We will consider ‘week’ as a linear term and a factor in the mixed model to explore the non-linear time effects of each treatment. More specifically, to determine whether BL therapy or DL therapy was superior to usual care and the other light therapy for reducing fatigue among individual patients, treatment effects will be assessed using an AR model that includes the type of light therapy as the main exposure, adjusted for time (eg, days since enrolment) linearly as a covariate and accounted for autocorrelations of the order 1.

PATIENT AND PUBLIC INVOLVEMENT STATEMENT
Pilot data with participants was used to help determine which light therapy device to select for the current trial. We did not directly involve participants in any other elements of the design or conduct of this trial.

DATA MONITORING
A Data and Safety Monitoring Board (DSMB) will be assigned to periodically review and evaluate project data for participant safety, scientific integrity and the trial’s progress. The DSMB will have four members from different disciplines with varying areas of expertise, such as biostatistics and behavioural medicine. The DSMB will review data for accuracy, completeness and timeliness of submission. DSMB reviews will examine for evidence of potential harms, including adverse treatment events and loss of confidentiality. Based on the data reviewed, the DSMB will be responsible for making recommendations regarding the continuation, modification and termination of the project in reports provided to the study’s principal investigator (PI). The study team will provide the DSMB with access to study data for monitoring and regulatory inspection.

HARMS
Treatment adverse events
Bright blue light therapy, which poses a low risk of physical harm to participants, is a typical treatment for symptoms of fatigue. It has been associated with several transient side effects, including jumpiness/jitteriness, headache and nausea, and mania has been infrequently observed in patients with bipolar disorder. These side effects have been observed to resolve quickly after the cessation of light therapy.

Study exclusion criteria were designed to prevent participants at greater risk of harm from participating in the study, such as found for participants with certain mental disorders or vision disorders. Light therapy protocol adherence is monitored throughout the trial, and participant re-education is conducted as needed. Participants are asked daily to report to the study team any side effects they experience that may be due to light therapy each intervention day of the study via the daily evening survey. Participants are informed that they can discontinue blue light therapy at any point during the trial.

Loss of confidentiality or privacy
One potential risk of participating in this study is loss of confidentiality or privacy. All identifying information will be stored in a secure, password-protected, Northwell Health approved, HIPAA-compliant database. Neither personal nor identifying information will be stored on any of the study devices used in the study. Furthermore, identifying information will be destroyed once a participant completes their study involvement. All research team members with access to identifiable and deidentified data will be trained and included on the IRB submission for approval. Regular meetings will occur with the PI and other study team members to ensure protocol adherence and data accuracy. The participant will be made aware of all data collected and the companies/technology employed to collect the data via the consent process.

Costs
This research study is funded by the National Institutes for Health (R01LM012836). All study-related equipment, devices, procedures and BL and DL treatments will be provided to participants at no cost. Participant insurance will not be billed. This study uses text messaging to deliver notifications, reminders and study questionnaires. Standard message and data rates from the participant’s wireless carrier may apply to the study participant. Study participants will not be compensated for any costs related to data usage or sending or receiving text messages by the study or by members of the study team.

COMPENSATION
After completing all components of the study (ie, submission of a satisfaction survey and completion of a follow-up interview), study participants will be mailed a $100 payment card (Clincard). Additionally, to thank study participants for their participation, we will let them keep their Fitbit Charge 3 ($120.00) and 1 AYO light therapy device ($299.00).

ETHICS
All amendments to the protocol will be submitted to the ethics committee and Northwell Health IRB for approval.
DISSEMINATION
The trial results will be published in a peer-reviewed journal. All publications resulting from this series of personalised trials will follow the CONSORT extension for N-of-1 trials CENT 2015 reporting guidelines.36 Trial results will be reported to study collaborators and participants following study completion.

Acknowledgements We are grateful for the contributions and support of the Northwell Health System and AVO by Novology for providing the investigators with the support and tools for the development and implementation of this trial.

Contributors KWD, SD and YC contributed to the development of the trial idea. KWD, SD, CL, DM, AP and YKC contributed to development of the trial protocol. MB, SD, JS, CL, DM, AP and KWD drafted the manuscript, and all authors contributed to its revision and gave final approval. YKC and TC provided statistical expertise.

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Disclaimer The funder had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; or decision to submit the manuscript for publication. The views expressed in this paper are those of the authors and do not represent the views of the National Institutes of Health, the US Department of Health and Human Services or any other government entity. KWD is a member of the US Preventive Services Task Force (USPSTF). This article does not represent the views and policies of the USPSTF.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Northwell Health Human Research Protection Program Approval # 20-0835. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement As this is a protocol, no data is collected and available.

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REFERENCES


41 Lewis JR. The system usability scale: past, present, and future. *Int J Hum Comput Interact* 2018;34:577–90.


APPENDIX 1 – Sample Consent Form

Northwell Health

Consent for Participation in a Research Study

Study Title: Re-engineering Precision Therapeutics Through N-of-1 Trials: Feasibility Study of Personalized Trials of Light Therapy for Fatigue

Principal Investigator: Karina W. Davidson, PhD, MASc

Sponsor: National Institutes of Health (NIH)

About this research
You are being asked to participate in a research study pilot. A pilot study is a small-scale study that explores the reasonableness of doing the type of research.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Important Information
This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

<table>
<thead>
<tr>
<th>Why am I being asked to provide my consent?</th>
<th>This is a pilot research study, which is different than personal medical care. Scientists do research to answer important questions which might help change or improve the way we do things in the future.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do I have to join this research study?</td>
<td>No. Taking part in this pilot research study is voluntary. You may choose not to take part in the pilot study or may choose to leave the pilot study at any time. Deciding not to participate, or deciding to leave the pilot study later, will not result in any penalty or loss of benefits to which you are entitled.</td>
</tr>
<tr>
<td></td>
<td>This study may enroll employees of Northwell Health. Employee participation or non-participation will have no bearing on an employee’s position at Northwell Health.</td>
</tr>
<tr>
<td></td>
<td>This study may also enroll students, including those that may attend Hofstra University. Student participation or non-participation will have no bearing on a student’s grades nor academic standing.</td>
</tr>
</tbody>
</table>
**Why is this research study being done?**

The main purpose of this pilot study is to test the feasibility and satisfaction of methods used for Personalized Trials (meaning your own personal response or N-of-1), including:

- Methods used to remotely recruit and enroll participants,
- Using online web and social media advertising to recruit and enroll participants in research study
- Methods used to collect and assess symptoms in response to a health and wellness strategy (in this case, blue light).

Our main goal is to see if an N-of-1 study design, or what we are terming Personalized Trials, can have widespread use in future research and clinical practice. We are not testing the safety or the effectiveness of the light therapy devices.

**What will happen to me during the study?**

In this pilot study, you will test the effects of two types of light therapy devices for chronic fatigue, a bright light and a dim light. Some weeks, you will use the bright light glasses for 30 minutes each morning, and some weeks you will wear the dim light glasses for 30 minutes each morning. Other weeks you will be instructed not to participate in any light therapy, and instead asked to treat your fatigue as you normally would. Each day you will answer questions about the fatigue you are experiencing, and some questions about your fatigue, sleep, stress, pain, concentration, confidence, and mood. You will also wear a Fitbit® each day and night to track your activity and sleep. You will receive a participant report that summarizes your observed response while you used both light therapy interventions. At the end of the study, we will send you a satisfaction survey and ask you to participate in a phone interview to share your opinions about your Personalized Trials experience.

**How long will I participate?**

The Personalized Trial will take place over the course of 14 weeks. You will be asked to complete a satisfaction survey after you receive your summary results (within 3 months of the Personalized Trial being complete). You will also be asked to participate in a 1-hour phone interview to talk about your opinions about your experience. Study participation will end upon completion of the phone interview.

**Will taking part expose me to risks?**

Some people may experience mild side effects from light therapy. Possible side effects may include headache, dry-mouth, eyestrain, nausea, or hyperactivity. Hyperactivity means being unusually active. These side effects normally go away quickly on their own. If you experience severe side effects, you should immediately stop light therapy and contact a member of the study team.

There may be a chance that blue light may worsen glaucoma, a condition of increased pressure in the eyeball causing gradual loss of sight.
Although there is no evidence of this happening to humans, some scientists have seen a worsening of glaucoma in controlled animal studies with mice. Even though we believe the blue light used in this study does not carry the same risk as the blue light used the mice studies, individuals with glaucoma are not eligible to participate.

Another risk of taking part in this pilot study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy. Their plans for keeping your information private are described in the sections below.

Are there any benefits to participation?

A Personalized Trial of Light Therapy for Fatigue is not designed to benefit you directly. You may or may not experience anything when wearing either pair of glasses but in receiving your observed data trends when using either pair of glasses, you will find out information about your own personal response to light therapy which may give you information on how to manage your fatigue. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include demonstrating that a Personalized Trial design can help doctors and scientists discover new ways to help patients in the future.

What are my alternatives to participation?

You do not need to participate in this pilot study to try light therapy. There are many light therapy devices available for purchase online, including the AYO light therapy glasses used in this study.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether to participate in this research.

Introduction

You are being asked to join a pilot research study. The purpose of a pilot research study is to answer specific questions.

You do not have to be in this pilot study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the pilot study by emailing ____________ or calling __________.

Why is this research study being done?

The main purpose of this pilot study is to assess the feasibility and satisfaction of methods used for Personalized Trials, including:

- Methods used to remotely recruit and enroll participants,
- Using online web and social media advertising to recruit and enroll participants in research study

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Methods used to collect and assess symptoms in response to a health and wellness strategy (in this case, light therapy).

This data will be used to inform future Personalized Trials, and it will help us understand the needs for a future technology platform to conduct these trials. We are testing these methods and technology to help determine if a Personalized Trial design, or a research study that occurs in only one patient, can have widespread use in future research and clinical sessions.

This particular pilot study will test a Personalized Trial design to see if it can be useful in observing trends in light therapy for symptoms of fatigue. We are not testing the safety or the effectiveness of the light therapy devices. You are being asked to participate in this pilot study because you have self-identified as someone who often has symptoms of fatigue.

You will not be able to participate in this study if:

- You are 60 years old or older or younger than 18 years of age
- You are pregnant
- You have had a diagnosis of a serious mental health condition or psychiatric disorder, such as bipolar disorder
- You have had a previous diagnosis of eye disease, such as cataracts, glaucoma, macular degeneration, Stargardt or family history of Stargardt, retinitis or retinopathy, or other retinal disorders
- You have had a previous diagnosis of diabetes
- You have sensitivity to light or use of medication causing sensitivity to light
- You have epilepsy or a history of seizures
- You participate in shift work (evening/night shifts, early morning shifts, rotating shifts, etc.)
- You live outside of the United States

How many people will take part in this study?
This pilot research study hopes to enroll up to 150 people. Up to 60 participants will be randomized (like the flip of a coin) to complete research procedures.

How long will I be in this study?
If you are selected to take part in this pilot study, the Personalized Trial procedures will last for 14 weeks. When all of your data is collected, you will be sent a custom participant report along with a satisfaction survey. Once you complete the satisfaction survey, you will be asked to take part in a follow-up phone interview to discuss your experience with a member of the study team.

If you will be traveling outside of the United States during the pilot study period, or if you will not have access to text-messaging or internet for more than a few days during the pilot study period, you should talk to a member of the study team to determine your eligibility for this study.

What will happen in this research study?

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After filling out this consent form, you will be asked to provide the research team some more information about yourself. This will include your cell phone number, cell phone carrier, and home address. This pilot study uses text-message reminders to help you through the study protocol. Completing the surveys will require cellular data if you are not connected to Wi-Fi. You will not be reimbursed for text messages or data charges, and standard carrier rates may apply.

If you are selected as a potential research participant in this pilot research study, you will be mailed your first study kit. This will include a Fitbit Charge 3™ and printed materials to help guide you through this pilot study. You will be asked to download an app to your personal phone in order to use the Fitbit Charge 3™. You will be sent an email to confirm your pilot study start date, and you will also receive a text message the day that your study begins. You will be asked to download the Fitbit® app to your phone to collect your data. Any e-mail correspondence that you send to the study team or the study team sends to you during your participation in the study, other than the custom report of your trial experience, will be unencrypted. This means that others may be able to access the information and read it once it is transmitted over the internet. Any e-mail correspondence sent by the study team will reference “the fatigue study” or “the personalized trial of blue light for fatigue.” The fact that you have fatigue and are participating in the study constitutes protected health information. Other than the reference to the study title, e-mail correspondence from the study team will not contain protected health information.

The first two weeks of the study is considered your baseline period. The purpose of this baseline period is to help us determine your usual activity and how you normally feel, without using any blue light. You will not receive any light therapy during your baseline period. Each evening you will receive a survey asking you a few questions about your fatigue that day, and your previous night’s sleep. This survey will take approximately 5 minutes to complete. At three random times each day, you will receive a text message asking you to rate your pain, fatigue, stress, mood, confidence, and concentration levels at that exact moment. This survey will take approximately three minutes of your time. On Sunday evenings, you will receive a slightly longer survey asking you to reflect on your fatigue that week. This survey will take less than 10 minutes to complete.

You will be asked to wear your Fitbit Charge 3™ all day and night, even while you are sleeping. Your Fitbit® can be charged during periods of extended sitting, like when you are in your car or sitting at a desk, or while you are showering. Every two days you will need to sync your Fitbit® device. You can sync your device by opening the Fitbit® app and waiting for your data to load.

It is very important that you wear your Fitbit® device all day and night, that you sync your Fitbit® device at least every two days, and that you answer the survey questions sent to you each day. You will be able to select the best times to send you these messages before your baseline period begins, and you will have the opportunity to change these times if there is a change in your schedule. You may be asked to discontinue your participation in this study if you are not wearing your Fitbit® long enough, or if you do not answer enough survey questions each day.
This is often referred to as adherence or compliance, and will be measured by at least 80% satisfactory completion.

If there is enough data collected during your baseline period, you will be contacted by a member of our pilot study team by email with your treatment schedule for the rest of the study. You will be mailed a second study kit, which will include two AYO light therapy glasses. The glasses will be labeled “bright light” or “dim light” and will be used during your light therapy treatment weeks. Both bright and dim light glasses have four (4) light emitting diodes (LEDs) that put out light within the visible spectrum of blue light at 470 nanometers (nm), with different levels of energy output (irradiance). You will be asked to download a study app to your personal phone in order to use the AYO light therapy glasses. You will be assigned a random order of 6 treatment periods. Each treatment period will last 2 weeks. A treatment period may consist of bright blue light therapy, dim blue light therapy, or usual care. Usual care is a treatment period where you will be asked to not use either pair of light therapy glasses, but still answer questions and wear your Fitbit®. You will receive a calendar and text message reminders that tell you when you are assigned to each intervention or usual care. We will also be able to monitor your use of the light therapy devices. If we see that you are not using the glasses appropriately, we will contact you by text message to remind you of your assigned treatment schedule and duration of use.

During treatment weeks, you will be also be asked to continue wearing your Fitbit® device each day and night. You will continue to receive 4 text messages every day with survey questions about your fatigue, sleep, pain, stress, mood, concentration, and confidence levels. You will also be asked about any treatment-related side effects you may be experiencing. If you are concerned about any side effects, you may stop doing light therapy at any time and contact a member of the research team for more information about continuing your study participation. You will also continue to receive a slightly longer weekly survey at the end of each week reflecting on your fatigue from the last week.

During the pilot study period, you may also receive additional text messages to remind you of next steps for this study, or to ask you to sync your data if it is not appearing correctly. We will send a maximum of 6 text messages per day during the study, including these reminders and the survey questions outlined above.

The treatment portion of the study will end once you have completed one baseline period (two weeks), two periods of bright light therapy (two weeks each), two periods of dim light therapy (two weeks each), and two periods of usual care (two weeks each), or 14 weeks total. Your participation in this pilot research study is voluntary. You may stop participating at any time by the methods described in the relevant section below. Alternatively, you may be asked to end your study participation by a member of our research team for any reason.

We will ask you to return 1 of the AYO light therapy glasses at the end of the study. The light therapy glasses can be returned in the padded envelope you received in your second personalized
trials box using the return slip that was also provided to you. No personal information, such as your name or address, will be printed on these materials.

We will compile the data from your questionnaires, the AYO light therapy glasses, and your Fitbit®. Any identifying information about you will be removed. A statistician will then analyze your coded data. Only the research team will have the key to identify you based on your research code. We will then turn this analysis into a report of your observed data and symptoms over the study period. Creating this type of report helps us to see if a Personalized Trial design works or is feasible. You will be sent this report in an encrypted email by our study team. This report is not meant to offer medical advice, but you may find that the information is useful for your own knowledge because it could help you understand your personal response to each light therapy. You will be sent a satisfaction survey within one week of receiving your report.

Within one month from your study ending, regardless of when that takes place, you will receive a phone call from a member of our study team to talk about your experience as a research participant. We will ask you several questions about what it was like to participate in the study. We will also ask about your opinion on Personalized Trials.

Your trial is complete after you completed 14 weeks of data collection and you have completed your satisfaction survey and phone interview. Upon full completion of the trial, including submission of your satisfaction survey and phone interview, you will receive a $100 pay card (ClinCard) as a thank you for your participation. You can use this card like a credit or debit card anywhere MasterCard is accepted, including online.

**What are the risks of the research study? What could go wrong?**

Although this is a minimal risk pilot study, there are some potential risks to participating.

**Treatment Side Effects**

Blue light therapy was selected for this study because it has been shown to be safe and commonly used by consumers to address fatigue with minimal side effects. There may be a chance that blue light may worsen glaucoma, a condition of increased pressure in the eyeball causing gradual loss of sight. Although there is no evidence of this happening to humans, some scientists have seen a worsening of glaucoma in controlled animal studies with mice. Even though we believe the blue light used in this study does not carry the same risk as the blue light used the mice studies, individuals with glaucoma are not eligible to participate.

There may be risks to prolonged exposure of blue light that are unknown at this time. You should use the blue light glasses as directed to lessen the chance of any unknown risks.

Common side effects some people may experience are headache, dry mouth, eye-strain, nausea, or hyperactivity. Hyperactivity means being unusually active. These side effects are normally very mild and brief.
If you are concerned about any of these side effects or any others you may experience, you should immediately stop doing light therapy and contact a member of the study team. You may still be able to continue with the study with modified light therapy treatments, or you may be asked to end your participation in the study.

**Loss of Confidentiality or Privacy**
One risk of taking part in this pilot study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy by only sharing necessary information about you to those outlined in the “Who else will see your information?” section below.

Any information collected during this study that can identify you by name will be kept confidential. We will separate your personal information (name, address, cell phone number) from all the information you provide us (this is called giving a “code” to your data). The key to your identifiable information will be stored separately in a secure, password-protected, HIPAA compliant database. Your personal or identifiable information is not stored on any of the study devices used in this study.

Your questionnaire responses will be obtained by a text message link from a secure web application that is used to collect survey data. We will do everything we can to keep your data secure, however, complete confidentiality cannot be promised.

**What are the benefits of this research study?**
This Personalized Trial of Light for Fatigue is not designed to benefit you directly. You may or may not experience anything when wearing either pair of glasses but in receiving your observed data trends when using either pair of glasses, you will find out information about your own personal response to light therapy which may give you information on how to manage your fatigue. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include demonstrating that a Personalized Trial design can help doctors and scientists discover new ways to help patients in the future.

**Will I receive my results?**
Although the main purpose of this pilot study is to assess the methods for future Personalized Trials, the data we collect from you during study activities could impact how you treat your symptoms of fatigue. For this reason, much of the information collected about you during the study will be analyzed and provided back to you. You will receive this data in the form of a participation report. The data included in the participation report will include graphs and statistics about your self-reported fatigue, self-reported stress, self-reported pain, mood, confidence, and concentration, activity patterns, sleep patterns, and adherence (or how closely you followed the study procedures). This data will be shown in relation to weeks you had bright blue light therapy, the weeks you had dim blue light therapy, and the weeks you had usual care. This report is meant to summarize your observed data trends and self-reported symptoms, and should not be considered medical advice.
If you do not want to take part in this research study, what are your other choices?
Since this project is assessing the Personalized Trial study design, the alternative is not to participate.

If you are interested in learning about effective treatments for your symptoms of fatigue, or if you want to learn more about your personal results, you may wish to meet with professionals with expertise to help you learn more about available treatments. The study team/study will not cover the costs of any follow-up consultations or actions.

Are there any costs for being in this research study?
This pilot research study is funded by the National Institutes for Health (NIH). All study related devices will be provided to you at no cost. This includes the Fitbit Charge 3™ and AYO light therapy glasses. Neither you nor your insurance company will be billed for your participation in this research.

This pilot study uses text messages to deliver links to notifications, reminders, and study questionnaires. Standard message and data rates from your wireless carrier may apply. You will not be compensated for any costs related to data usage or sending or receiving text messages by the study or by members of the study team.

Will you receive any payments for participating in this research study?
After successfully completing all aspects of this study, you will be mailed a $100 payment card called a ClinCard that can be used like a credit or debit card anywhere MasterCard is accepted, including online. As a thank you for participation, you will also be able to keep your Fitbit Charge 3™ (a value of $120), and one of the sets of light therapy glasses (a value of $299).

What are your rights as a research participant?
Your participation in this project is voluntary. The quality of your medical care and/or employment or enrollment status will be the same, whether you join, refuse to join, or decide to leave the pilot study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care and/or employment at Northwell Health.

This study may enroll employees of Northwell Health. Participation or non-participation will have no bearing on your position at Northwell Health.

This study may also enroll students, including those that attend Hofstra University. Student participation or non-participation will have no bearing on your grades or standing at your academic institution.
Could you be taken off the study before it is over?
It is also possible that your participation in this pilot study may end without your consent. This decision may be made by a researcher, study sponsor or the Institutional Review Board, (the committee that oversees research at this institution).

Reasons for withdrawal may include:

- Failure to follow instructions, including maintaining less than 80% adherence to survey responses and Fitbit® use
- Failure to complete your light therapy treatments
- Significant cell phone carrier issues that prevent you from receiving study text messages
- It is not in your best interest to continue on this pilot study, or
- The pilot study is stopped

If you withdraw from this pilot study or if you are withdrawn from the pilot study, any data already collected will continue to be used. However, no new data will be collected.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this pilot study may be obtained again.

What information will be collected and used for this study?
If you agree to be in this pilot study, we will collect information that identifies you. We may collect the results of questionnaires, interviews, Fitbit® activity and sleep, light therapy use via AYO, and video views. We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information.

**Fitbit®**
Data collected by Fitbit® includes activity data (steps, activities, intensity, heart rate, floors climbed), sleep data (total sleep minutes, sleep stage estimates, sleep and wake times), and device data (last sync date and Fitbit® battery level). No information that can be used to identify you will be associated with your Fitbit® study account. We will only collect this data through the 14-week pilot study period. Once your study period is complete, you will be sent instructions on how to un-link your Fitbit® device from the account.

**AYO**
Data collected by the AYO light therapy glasses includes session number, date and time a device was used, the type of device that was used (in other words, bright blue or dim blue), and how long the device was used. No information that can be used to identify you will be associated with your AYO study account. We will only collect this data through the 14-week study period. Once your study period is complete, you will be sent instructions on how to continue using the AYO glasses after the study ends if you so choose.
N1Thrive
Survey data will be collected via a secure web browser and stored in a HIPAA-compliant, Northwell approved database. Text messages will alert you to a new message from “N1Thrive” and contain a link to open this secure browser directly on your phone. No identifying information will be shared via text message.

What information will be shared outside of Northwell Health?
Your privacy is important to us. We will only share information that is necessary to complete the study.

AYO
If you agree to be in this pilot study, and if you are selected as a participant, you will be sent two pairs of AYO light therapy glasses. You will also be sent instructions on how to connect the device to a study application account. General user IDs that have been created for this research study have been used to create AYO study accounts without any information that could identify you. Only the research team will have the key to connect you to your general AYO User ID. It is important that you use the AYO account provided during the study to protect your information, and to allow us to collect your data. The research team will not share any of your personal information with AYO.

Fitbit®
If you agree to be in this pilot study, and if you are selected as a participant, you will be sent a Fitbit Charge 3™. You will also be sent instructions on how to connect the device to a study account. General email addresses that have been created for this research study have been used to create these study accounts without any information that could identify you. It is important that you use the Fitbit® account provided during the study to protect your information, and to allow us to collect your data. The research team will not share any of your personal information with Fitbit®. At the end of the study, you will be asked to remove the study account from your phone. If you would like to keep the Fitbit Charge 3™, you will be sent instructions on how to create your own Fitbit® account to connect the device.

Fitabase™
Data will be shared from your Fitbit® to the research team using an online portal called Fitabase™. The study account given to you to connect your Fitbit Charge 3™ will be linked to an identification number in the Fitabase™ system. No information that could be used to identify you will ever be shared with Fitabase™. Only the research team will have access to data that will be able to connect a research participant to their Fitabase™ ID. Fitabase™ will stop sharing your data at the end of your study, but as an added step, you will be asked to remove the study account from your device if you would like to keep your Fitbit Charge 3™.

N1Thrive
N1Thrive, the company the study team is partnering with to develop the technology to analyze data for current and future Personalized Trials, will send study messages via a HIPAA-compliant manner on behalf of the study team. The study team will have direct access to the data shared...
through N1Thrive. At the end of the study, your identifying information will be removed from the N1Thrive database.

**Who else will see your information?**
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside Northwell Health, except as detailed below.

Investigators will share information collected from this pilot research study with:
- Study sponsor (NIH) and/or its agents,
- Other researchers,
- Accrediting agencies,
- Data safety monitoring board.

The following reviewers may access your study records to make sure that this study is being done properly:
- Representatives from federal and state government oversight agencies, such as the Department of Health and Human Services, and the National Institutes of Health
- Representatives from Northwell Health’s Human Research Protection Program, (a group of people that oversee research at this institution)

In the future, we may publish results of this pilot study in scientific journals and may present it at scientific meetings. If we do, we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

**Can you change your mind?**
If you change your mind about being in the pilot study, you may withdraw at any time. If you want to withdraw from the study, you need to send an email to the researcher at the following address: _________________. Alternatively, you can send a letter to the researcher at the following address:

Dr. Karina W. Davidson  
Center for Personalized Health

Your email or letter needs to say that you have changed your mind and do not want to continue to participate. You may also need to leave the pilot research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

**Will information about this study be available to the public?**
The researcher also plans to share information about the pilot study, including de-identified data, on the following data sharing website: https://cos.io/. The Open Science Framework is a free, open-source web application built to provide researchers with a free platform for data and materials sharing. There will be no identifiable data (like your name) posted to this website or used in future studies.

In addition, a description of this clinical trial will be available on http://www.Clinical Trials.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 website at any time.

Certificate of Confidentiality
To help us protect your privacy, this research is covered by a Certificate of Confidentiality from the US Department of Health and Human Services (DHHS). The Certificate of Confidentiality means that researchers cannot be forced to identify you, even under a court subpoena. The Certificate does not mean the Secretary of DHHS approves or disapproves of the project. It adds special protection for the research information about you. You should know, however, that researchers may provide information to appropriate individuals or agencies if harm to you, harm to others or child abuse becomes a concern. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. However, if an insurer, employer or other person learns about your participation and gets your consent to receive research information, then the researchers will have to provide your information.

Will my information be used for research in the future?
Information collected from you for this research may be used for future research studies or shared with other researchers for future research. If this happens, information which could directly identify you will be removed before any information is shared. Since identifying information will be removed, there will not be an additional consent for future research. By consenting to participate in this study you are agreeing to allow your coded data to be used by future researchers without additional consent.

Some information collected during this pilot study that can identify you will be kept on file. This information may be used in the future to contact you for future participation in Personalized Trials. This information will be stored on a secure database. It will only be accessible by trained members of the study team. If you change your mind about being contacted in the future, you may follow the procedures outlined above to notify the researcher.

Does the investigator of this study receive money if you take part?
The investigators on this pilot study receive money to conduct the study, but do not financially benefit from your participation. The money they receive is to pay them back for the costs of conducting the research study. Funding for this research study is provided by the National Institutes of Health (NIH).
Who can answer your questions about this study?
If you have any questions about the pilot study, you may call Alexandra Perrin, Clinical Research Assistant, at ___________ or email ___________. If you have questions about side effects or injury caused by research you should call Joan Duer-Hefele RN, MA, CCRC, Director of Clinical Research, at ___________. If you need emergency care, dial 911 or go to the nearest Emergency Room. If you have questions about your rights as a research participant, concerns about being in the study, or would like to offer input, you may contact the Office of the Institutional Review Board at _____________.

A signed copy of this consent form will be mailed to you.

[Signature Page Follows]
Please respond to the following questions to demonstrate your understanding of study procedures and your rights as a research participant.

1. As a participant, I will need to wear my Fitbit® 24 hours a day, even while I am sleeping.
   - True
   - False

2. As a participant, I will use light therapy glasses every morning for 8 weeks out of the 14 week study, as instructed.
   - True
   - False

3. As a participant, I can remove myself from the pilot study at any time by contacting the researcher.
   - True
   - False

4. As a participant, I will receive at most 6 text messages a day, unless there is an unexpected problem with my data.
   - True
   - False

**Summation/Signature**

- I consent to be a part of the n1thrive Personalized Trial of Light Therapy for Fatigue Research Study

By checking the box and signing this form, you are consenting to the information found at personalizedhealth.org/fatigue-consent-form-11-20-2020. You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

___________________________________________________             ____________________
Electronic Signature                                                                                         Date & Time
Stamp

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