What a difference a year makes: Objective rest/activity patterns, circadian phase markers, and sleep quality before and during the COVID-19 pandemic

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Abstract

Objectives: The COVID-19 pandemic led to numerous changes in sleep duration, quality, and timing. The goal of this study was to examine objective and self-reported changes in sleep and circadian timing before and during the pandemic.

Methods: Data were utilized from an ongoing longitudinal study of sleep and circadian timing with assessments at baseline and 1-year follow-up. Participants had baseline assessment between 2019 and March 2020 (before pandemic) and 12-month follow-up between September 2020 and March 2021 (during pandemic). Participants completed 7 days of wrist actigraphy, self-report questionnaires, and laboratory-collected circadian phase assessment (dim light melatonin onset).

Results: Actigraphy and questionnaire data were available for 18 participants (11 women and 7 men, Mean = 38.8 years, SD = 11.8). Dim light melatonin onset was available for 11 participants. Participants demonstrated statistically significant decreases in sleep efficiency (Mean = −4.11%, SD = 3.22, P = .001), worse scores on Patient-Reported Outcome Measurement Information System sleep disturbance scale (Mean increase = 4.48, SD = 6.87, P = .017), and sleep end time delay (Mean = 22.4 mins, SD = 44.4 mins, P = .046). Chronotype was significantly correlated with change in dim light melatonin onset (r = 0.649, P = .031). This suggests that a later chronotype is associated with a greater delay in dim light melatonin onset. There were also non-significant increases in total sleep time (Mean = 12.4 mins, SD = 44.4 mins, P = .255), later dim light melatonin onset (Mean = 25.2 mins, SD = 1.15 hrs, P = .295), and earlier sleep start time (Mean = 11.4 mins, SD = 48 mins, P = .322).

Conclusion: Our data demonstrate objective and self-reported changes to sleep during the COVID-19 pandemic. Future studies should look at whether some individuals will require intervention to phase advance sleep when returning to previous routines such as returning to office and school settings.

Introduction

The National Institutes of Health in 2019 reported that more than 40 million Americans suffer from chronic, long-term sleep disorders. Insufficient sleep is a risk factor for weight gain and obesity dietary habits occurrence and outcome of depression. Furthermore, the stresses of the COVID-19 in 2020 caused significant disruptions to routines, including sleep. The pandemic led to a significantly negative impact on the physical and mental sub-dimensions of the quality of life with sleep and disruption of circadian rhythms likely playing a role. Given the associations between sleep and circadian rhythms with physical and mental health, we seek to examine changes in sleep during the pandemic.

Multiple studies demonstrated self-reported changes in sleep as a result of the pandemic, particularly in the first few months. In the early stages of the COVID-19 pandemic, a survey in China found increased levels of anxiety and stress and decreased general self-efficacy were dependent on sleep quality. An Italian study reported...
that over half of respondents experienced poor sleep during the pandemic, indicating that the COVID-19 pandemic appeared to be a risk factor for sleep disorders and diagnosed psychological diseases in this population.\textsuperscript{10} In a cohort study done in the United Kingdom, from months before the pandemic to the full lockdown in May 2020, there were improvements in exercise, diet, and consumption of alcohol, but a deterioration in sleep. The associations between poor mental health and adverse health behaviors were larger during the May 2020 lockdown than pre-pandemic.\textsuperscript{11} In Spain, a study comparing data obtained at baseline on March 2020 to data gathered once the restrictions began to be eased on May 2020, found that the lockdown period due to COVID-19 had a negative impact on the physical activity levels, sleep quality and well-being in a group of physically active Spanish adults.\textsuperscript{12} During the initial lockdowns in Portugal, from March 30 to April 20, 2020, the study found that home confinement without working, female gender, and sleep-disordered breathing may predict a higher risk of reporting sleep difficulties.\textsuperscript{13} Changes and disruption of sleep appear to affect both healthy individuals and those with high risk of sleep difficulty.

A limitation to the prior studies is that they are cross-sectional and utilize self-report measures. Self-reported measures can be susceptible to self-report bias, and cross-sectional analysis can only elucidate sleep variables at one moment in time. Only one study has examined both objective and subjective sleep-related changes during the pandemic, but results were collected in an adolescent sample. The Australian study found significant sleep offset delay and increases in total sleep times and found significant sleep onset delay. They reported that remote learning, or later school times, may extend sleep duration and improve subjective symptoms in adolescents, compared with in-person school.\textsuperscript{14} Although the study focused on an adolescent population and in school settings, notable is their use of objective markers of sleep such as dim light melatonin onset (DLMO). However, a limitation is that the study conducted in adolescence likely does not generalize to adults due to many reasons, including developmental changes in sleep across the lifespan and work versus school schedules.

Therefore, in our study, we seek to address this gap in the literature by adding measures of objective biological markers of circadian timing in a longitudinal study of adults before and during the COVID-19 pandemic. In addition to self-reported measures, we analyzed actigraphy and DLMO to evaluate changes in sleep time, quality, and circadian timing. DLMO is the quantitative measure of melatonin in human saliva and is a well-accepted measure of the timing of the circadian rhythm.\textsuperscript{15} Similarly, actigraphy represents a useful diagnostic tool by providing objective information about daily variability in sleep timing and quality, recording information in the home sleep environment, avoiding recall bias, or memory impairments.\textsuperscript{16}

The goal of this study is to further understand how sleep changed, both subjectively and objectively, during the COVID-19 pandemic. Given the associations between sleep with multiple aspects of health, our primary aims were to 1) understand if there were any changes in sleep and 2) test where objective and subjective data inform each other in our findings. Since age and sex are related to sleep duration and timing,\textsuperscript{17,18} our secondary aims were to conduct exploratory analyses to determine whether age and sex predict any potential sleep changes. Our laboratory was collecting data for a longitudinal study prior to the outbreak of the pandemic, and this timing provided an opportunity to compare these data with that collected months after the lockdowns and restrictions created by the pandemic. Consistent with the previous findings of more disturbed sleep, we hypothesized that sleep in our sample would become more disturbed across time, which would manifest as 1) decreased sleep efficiency, 2) worsening scores on self-reported sleep quality measures, and as seen in the Australian study, we would find 3) delays in sleep and circadian timing. Although the analysis has been done 2 years into the pandemic, the study is important due to the lasting changes in work and school schedules. It is also helpful in understanding sleep changes in the pandemic to inform future public health emergencies.

**Methods**

This was a secondary analysis of a parent study that is currently evaluating how circadian timing and misalignment relate to risk factors for cardiovascular disease in healthy adults. Participants were adults with body mass index (BMI) ranging from 25 to 34.9.\textsuperscript{19} The study participants were a subset of the larger parent study (R01 HL141706). This study was approved by the University of Utah IRB (IRB_00117438), and all participants provided written informed consent.

**Screening**

The following were the study inclusion criteria: 1) Enrolled between 2019 and before March 2020; 2) age 25-60 years; 3) habitual sleep onset time between 10:00 PM and 3:00 AM on wrist actigraphy; 4) able to read and write in English; and 5) BMI 25-39.9 kg/m\(^2\), which fell in the overweight category.

Exclusion criteria were as follows: 1) high risk for or presence of sleep disorders (obstructive sleep apnea [OSA] STOP > 3), restless legs syndrome (RLS > 11), or insomnia (ISI > 7) assessed by their respective questionnaires\textsuperscript{16-18} as well as an overnight OSA screening using ApneaLink\textsuperscript{21} if their STOP score was 1 or 2; 2) diagnosed with diabetes or HbA1c > 7% at screening or taking medications known to affect glucose; 3) self-reported history of cognitive or neurological disorders; 4) presence of any major psychiatric disorder (serious or unstable psychiatric bipolar, schizophrenia spectrum disorders, and participants with elevated depressive symptoms Patient Health Questionnaire (PHQ) > 10;\textsuperscript{22} 5) current alcohol or substance abuse as determined by screening questionnaires or self-report; 6) unstable or serious medical illness; 7) overnight shift work; 8) travel over 2 time zones in the past 2 months; 9) self-reported use of hypnotic, stimulant or other medications known to affect melatonin concentrations such as beta blockers or daily nonsteroidal anti-inflammatory drug (NSAIDs); 8) current smoker; 10) daily caffeine intake > 300 mg; 11) pregnant or lactating; and 12) currently on a restrictive or special diet.

We used multiple methods of recruitment, including sending letters and phone calls to existing primary care patients at University of Utah Health who met preliminary study criteria (age, diagnoses, medications), posting flyers, and online recruitment.

**Procedure**

**Baseline visit**

Potentially eligible participants that completed initial screening measures were invited to a baseline screening visit to complete informed consent, height, and weight measurement to determine BMI. If participants attended the screening visit, they completed one night of home sleep apnea screening (Apnea Link, ResMed Inc) and 7 days of actigraphy. In total, 18 study participants either completed the study or had data available from their 6-month visit. Additionally, the Munich-Chronotype Questionnaire was collected at baseline only, while all the other variables were collected at both baseline and follow-up.

**DLMO session**

As part of the larger study protocol, eligible participants (N = 18) completed a circadian phase assessment in the laboratory. Saliva samples were collected via 13 salivettes, 6.5 h before subjects’ average bedtime and subsequently every 30 min according to standard procedures according to Burgess.\textsuperscript{25} DLMO can be obtained.
noninvasively from half-hourly or hourly saliva samples, collected in the 6.5 h before habitual sleep onset. Lights in the phase assessment room were dimmed (< 5 lux) as light is known to suppress melatonin secretion. Dimming of lights occurred 30 min before the first saliva sample and until after the last saliva sample collected. The last sample collected represented each participant’s average bedtime during the prior week. Average bedtime was estimated using wrist actigraphy. All subjects refrained from caffeine and alcohol in at least the 24 h before saliva collection, refrained from nonsteroidal anti-inflammatory drugs for at least 72 h before saliva collection.

Follow-up visit

Following similar procedures used at baseline, actigraphy, DLMO, and self-reported questionnaire data were collected at 12 months (N = 15 actigraphy, N = 18 self-reported questionnaires, N = 11 for DLMO). Study staff scheduled the follow-up visit and mailed an Actiwatch to participants beforehand in order to collect actigraphy data 7 days prior to the visit. DLMO and questionnaires were completed at a visit to the sleep lab. Not all participants’ data were collected at the follow-up visit. We utilized actigraphy at the 6-month visit for 3 participants who were lost to follow-up at 12 months. This was done to maximize the number of participants, as our focus was to see changes in sleep patterns during the pandemic. These participant’s data were not significantly different from the 12-month follow-ups. Furthermore, 7 participants did not participate in DLMO because they declined an in-person visit due to COVID-19-related concerns.

Measures

Sleep

Sleep/wake patterns were estimated using 7 days of wrist actigraphy at screening and 7 days prior to their 12-month visit using the Actiwatch Spectrum (Philips/Respironics, Inc, Bend, OR, USA). Actiwatches were worn on the non-dominant wrist and set with 30 s epoch length and medium sensitivity. Actigraphic sleep parameters were calculated using Actiware-Sleep 6.0 software with default setting and included the following variables: total sleep time, sleep start time, sleep end time, and sleep efficiency. Sleep efficiency is defined as the percentage of time a participant was asleep while in bed. Sleep efficiency above 80% is considered normal for healthy adults. Off-wrist time was excluded based on the Spectrum’s off-wrist detection. A day was not considered valid if there was any off-wrist time during the sleep period reported in the software. To be included in the analyses, participants needed at least 5 days of valid actigraphy data. The average number of actigraphy days per participant was 11 days, including both baseline and follow-up. Actigraphy-based sleep parameters were derived from averaging the mean days of measurement from each participant. No participants were excluded from analyses due to insufficient actigraphy data.

Circadian timing (DLMO)

Saliva samples were frozen and shipped in dry ice to Solidphase, Inc (ME) who centrifuged the samples and performed direct RIA assay. The Novolyltix Direct Saliva Melatonin Radio Immunoassay (RIA) test was used for the direct, quantitative determination of melatonin in human saliva. The RIA kit measured melatonin by a double-antibody RIA based on the Kennaway G280 anti-melatonin antibody (Novolyltix). Upon receipt of the assay results, the DLMO was calculated as the clock time (with linear interpolation) when the melatonin concentration exceeded the mean of 3 low consecutive daytime/early evening values plus twice the standard deviation of these points. This low threshold more closely tracks the initial rise of melatonin when the central circadian clock, or suprachiasmatic nucleus triggers the release of melatonin from the pineal gland.

Demographics

A demographic questionnaire included age, sex, race, ethnicity, income, employment, and marital status.

PROMIS item bank v1.0 sleep disturbance – short form 8a

Patient-Reported Outcome Measurement Information System (PROMIS) Health Organization and PROMIS Cooperative Group constitute of 8 items that were reflective of insomnia-like items and assess one’s perception of sleep quality and restoration associated with sleep, perceived sleep difficulties and concerns with falling and staying asleep, and perceptions of adequate and satisfactory sleep. The PROMIS questionnaires have been developed for adults and have shown good psychometric properties. It is important to note that these item banks do not measure symptoms of specific sleep disorders, as the intent is to gain a more general overview of self-perception of sleep problems and how these problems hinder daily functioning. The T-scores are interpreted as follows: less than 55 = none to slight, 55.0-59.9 = mild, 60.0-69.9 = moderate, 70 and over = severe. Higher scores demonstrate worse sleep, the general population mean being 50 and 1 SD being 10.

Munich Chronotype Questionnaire

The Munich Chronotype Questionnaire (MCTQ) included 14 items that assess one’s work schedule, workdays, sleep timing preceding workdays, work-free days, and use of an alarm clock. Chronotype was defined by the timing of sleep onset and wakfulness. The MCTQ calculates the mid-sleep point, halfway between onset and end on work-free days (MSF [Mid-sleep point, halfway between onset and end on work-free days]), which is then corrected for potential oversleep on free days compensating for sleep debt accumulated over the workweek (MSFsc). Morning types (M-types) prefer to go to sleep and wake up earlier and perform better in the mornings, whereas individuals who are evening types (E-types) prefer to go to sleep and get up later and performed better in the afternoon. MSFsc or MSF below 2.17 were classified as extreme M-types, and MSFsc or MSF above 7.25 were classified as extreme E-types. These criteria were defined 2.5% at each end of the distribution as extreme chronotypes based on the distribution of MSFsc as suggested by Kühnle. Although the MCTQ includes items similar to a sleep diary, we did not require participants to fill in daily diaries or sleep logs to reduce burden.

Data analysis

Using SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp), we calculated descriptive statistics to characterize our sample. Next, we evaluated change in self-reported sleep quality, objective sleep variables, and circadian timing using paired t-tests for within person change. We used linear regression to examine predictors of change in total sleep time, sleep efficiency, sleep start time, sleep end time, perceived sleep quality, and DLMO based on demographic and baseline characteristics. We conducted the analyses with an α level of 0.05.

Results

Participant characteristics

A total of 106 participants were pre-screened on the phone or by online survey, and 36 completed the baseline assessment. Although 36 participants completed the baseline visit, 18 participants were mostly due to pandemic-related concerns. Actigraphy and self-report data were available for 18 adults (11 women and 7 men, average age = 38.8, SD = 11.8, Table 1), PROMIS measures were available for 17 adults due to 1 missing data. To be included in the
Sleep time, sleep efficiency, DLMO, or perceived sleep quality. Age at whether age predicted changes in sleep start time, end time, total sleep time (Mean = 11.4 mins, SD = 48 mins, \( P = .001 \)), worse scores on the PROMIS sleep disturbance (T-score Mean = 4.48, SD = 6.87, \( P = .017 \)), and sleep end time delay (Mean = 22.4 mins, SD= 44.4 mins, \( P = .046 \)). There were also non-significant increases in total sleep time (Mean = 12.4 mins, SD = 44.4 mins, \( P = .255 \)), later DLMO (Mean = 25.2 mins, SD = 1.15 hrs, \( P = .295 \)), and earlier sleep start time (Mean = 11.4 mins, SD = 48 mins, \( P = .322 \)). Fig. 1 is provided for visualization of these changes across time.

Predictors of change in sleep

As part of our secondary aims, we used linear regression to look at whether age predicted changes in sleep start time, end time, total sleep time, sleep efficiency, DLMO, or perceived sleep quality. Age did not predict change in any of the variables. We then used Mann-Whitney U Tests to determine if there were meaningful differences in sleep variables between sexes. Sex differences in change scores in total sleep time were not significant (\( P = .29 \)); men on average slept 3 min less (SD = 19.8 m) and women 22.8 min more (SD = 53.4 m) from baseline to 12-month follow-up. Likewise, sex differences in sleep efficiency were not statistically significant (\( P = .66 \)), men had an average sleep efficiency decrease of 4.12% while women had an average decrease of 4.11% suggesting similar changes in sleep efficiency across time. DLMO changes were also not significant (\( P = .93 \)), with a DLMO average increase of 24 min in men and 25.8 min in women, also suggesting similar changes in DLMO across time. Perceived sleep quality scores were different between sex, but not significant (\( P = .48 \)), with men reporting a 6.1 score point increase, while women reported an average increase of 3.3 score points.

Chronotype and DLMO

We found that chronotype collected at baseline was moderately correlated with change in DLMO (\( r^2 = 0.42, P = .031 \)). We did not find correlations between chronotype and DLMO at baseline or follow-up. However, findings from the change in DLMO suggest that a later sleep timing as measured by MCTQ (MSFsc, higher chronotype) was associated with a greater delay in DLMO (Fig. 2).

Baseline chronotype and actigraphy

We also found that certain variables collected via actigraphy at baseline to be significantly associated with the questionnaire-based chronotype, finding a moderate correlation between chronotype and total sleep time (\( r^2 = 0.56, P = .03 \)) and sleep end time (\( r^2 = 0.68, P = .01 \)). Sleep start time (\( r^2 = 0.40, P = .12 \)) and sleep efficiency (\( r^2 = 0.43, P = .09 \)) were not statistically significantly correlated with chronotype. These findings further demonstrate the ability and concordance of actigraphy-based chronotyping.
Discussion

The longitudinal design of our ongoing study allowed us an opportunity to examine objective changes in sleep and circadian timing before and during the COVID-19 pandemic in overweight adults who were free of diabetes, as well as sleep and psychiatric disorders. Participants were carefully screened for confounds, most notably sleep apnea and depression, which are often associated with later circadian timing. Consistent with our hypotheses 1) decrease in sleep efficiency and, 2) worse scores on the self-reported measures. From baseline to follow-up, participants had a statistically significant decrease in sleep efficiency, increase in sleep end time, and worse scores on the self-reported PROMIS measure. We also observed a non-significant later DLMO, increased total sleep time, and earlier sleep start times. Our third hypothesis was only partially supported: there were significant delays in sleep end time but not sleep start time. We did not observe significant age or sex differences in changes in total sleep time, sleep efficiency, sleep start time, sleep end time, or DLMO from baseline to 12-month follow-up. While we found a relationship between changes in DLMO timing and chronotype, we did not see this relationship between baseline DLMO and chronotype. This could be due to the fact that the small sample size may have created a restricted range in the DLMO. We also found statistically significant correlations between the MCTQ and actigraphy at baseline which supports evidence of the ability and usefulness of actigraphy-based chronotyping.

This study reports on the effects of the COVID-19 pandemic on sleep. It demonstrates that sleep patterns are not immune to the disruptions caused by world events. Furthermore, it demonstrates that during a world pandemic, typical sleep is not guaranteed in any population. While participants reported worse scores on the PROMIS questionnaire, our sample reported lower sleep disturbance scores than the general population mean at baseline and follow-up. This may be because they were selected as individuals without depression or sleep disorders. Additionally, we observed a worsening of sleep in this generally healthy population, meaning that the effects of the pandemic were robust, given the sample participants without pre-pandemic sleep disorders. Likewise, the decrease in sleep efficiency may not be clinically relevant as sleep efficiency of 80% or higher is often used as a cutoff for quality sleep, but a 4% change in sleep efficiency is clinically fairly large, and improvements of 6%-10% are seen among clinical populations with the treatment with Cognitive Behavioral Therapy for Insomnia (CBT-I).

Although this study found that sleep efficiency and sleep quality decreased while total sleep time increased, it is possible that participants did not struggle to reach sleep needs, but rather due to having more time available at home. Furthermore, the results of this study may not apply to the general population due to the small sample size.

This present study also enhances previous self-reported studies by using biological markers to objectively track changes in sleep. For example, a Canadian study found that respondents, relative to the pre-pandemic baseline, had wake-up times that were significantly delayed, and clinically meaningful sleep difficulties significantly increased. Although we were not able to collect more data on predictors of changes in sleep, a study with responders from 49 countries identified the female sex, being in quarantine, livelihood adversely affected by the crisis, and reduction in physical activity to be negatively associated with changes in sleep quality. Our study also supports the findings of the only other study looking at objective changes in sleep-wake patterns and circadian timing in adolescents during the pandemic. While they also found longer total sleep times and sleep end times, they also found later sleep start times. Conversely, our adult sample on average reported earlier sleep start times. Their findings may be due to the overall patterns of later sleeping times across adolescence.

This naturalistic study allowed us to objectively measure circadian timing, phase markers, and sleep quality change in adults before and during the COVID-19 pandemic. These results are significant because, as previously mentioned, insufficient sleep, poor sleep quality, and disturbances of sleep-wake schedules have been associated with both physical and emotional morbidity in several epidemiological studies. Moreover, the perception of poorer sleep quality despite later bedtimes and wake-up times and longer hours in bed appears to be related to a higher symptomatic level of depression, anxiety, and stress. Although symptoms of depression and anxiety were not measured in this study in relation to sleep, this study did find the perception of sleep and efficiency to have meaningfully decreased. Furthermore, it would be beneficial for government institutions to look at developing interventions that include lifestyle guidelines in sleep and mental health. The goals of these lifestyle guidelines are to mitigate the effects of suboptimal sleep and therefore improve the well-being of the population. Effective public health policies should identify and promote protective factors in healthy sleep that can be applied in public health emergencies.

Strengths and limitations

Strengths of this study include the use of objective measures of sleep, eliminating potential self-report bias. This is, to the best of our knowledge, the only study to measure DLMO changes in adults during the COVID-19 pandemic. Additionally, this is one of very few studies with available objective data of people’s sleep prior and during the pandemic. This study merges and demonstrates the complementarity of objective and subjective sleep data.

Since the nature of this study was naturalistic and not prospective, a power calculation was not undertaken. Due to the small sample size, this study is limited by its ability to statistically detect a true difference in the population. The sample size of 18 (actigraphy), 17 (PROMIS), and 11 (DLMO) limits the ability to generalize the results to the general population. Another limitation is that the sample was generally healthy but overweight (class 1 obesity, or class 2 obesity), so this might not be representative of populations that were excluded from our study, such as those experiencing diabetes, sleep-related disorders, depression, or other mental health conditions.

Due to limited occupational variability in our sample, our data did not allow us to examine correlations in characteristics of occupation. For example, 78% of the sample worked full time and remained so from baseline to follow-up. Changes in sleep may have been substantially different in essential and/or front-line employees. Another limitation was that only about half of participants who had enrolled pre-pandemic returned for the follow-up during the pandemic and 3 participants’ actigraphy data were not collected at the 12-month mark, but rather at the 6-month mark due to loss to follow-up. Finally, there is a large time range for follow-up assessments. Conditions with the pandemic were changing rapidly and
may have influenced sleep based on current orders. This variability thus diminishes the consistency among participants, and is confined to the specific social distancing policies of the state the study was conducted in.

Conclusion

Our data demonstrate objective changes to sleep during the COVID-19 pandemic for healthy, overweight patients, including decreases in sleep efficiency, sleep end time delay, correlation between later chronotype and later DLMO, and increases in self-reported sleep disturbance. Future research should evaluate whether these changes in sleep are related to risk factors in other patient populations that are known to have sleep comorbidities, such as patients with depression, cardiovascular disease, or HIV/AIDS. Further studies should also look at protective factors that can reduce the negative changes in objective and subjective sleep quality due to public health emergencies. Evidence that detrimental sleep metrics persist suggest that interventions may be needed to phase advance sleep. Phase advance sleep may be necessary due to schools, jobs, and other occupations increasingly returning to pre-pandemic routines and the potential conflict with the sleep end time delays. Earlier wake times may be needed for successful reintegration to the school/workforce.

Declaration of conflict of interest

Dr Burgess serves on the scientific advisory board for Natriot, LLC, and Moving Mindz, Pty Ltd, and is a consultant for F. Hoffmann-La Roche Ltd. Other authors declared no competing interests.

Funding

This work was supported by the National Heart, Lung, and Blood Institute [SRO1HL141706]. The research reported in this publication was supported in part by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number (s) UL1TR002538. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Acknowledgments

This work was supported by the National Heart, Lung, and Blood Institute, the University of Utah, and the Department of Family and Preventive Medicine. We would like to thank the following for their contributions to this study.

Research collaborators: Andrea Baxter, MPH, Andrew Rivera. Students: Su Rin Choi, MSPH, Doug Van, Alana Mudrow, Julianna Tran, Max Byck, Talmage Sanders, Jessica Nguyen.

Author contributions


All authors have read and agreed to the published version of manuscript.

References


