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TITLE: A Head-to-Head Comparison of the 2B-Alert Caffeine Optimization Algorithm Versus Standard Caffeine Dosing on Performance During Sleep Deprivation

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Abstract:
The present study is running a head-to-head comparison of the 2B-Alert app against standard caffeine dosing recommendations to improve performance and minimize side effects in service members. A total of 150 participants will complete multiple psychomotor vigilance tests (PVTs) daily for 13 days at-home, recording their nightly sleep duration and daily caffeine intake to the 2B-Alert app. Then participants will complete 4-days in lab and will be assigned to 1 of 5 conditions: Placebo/Placebo, Placebo/Standard, Placebo/Optimized, Standard/Standard, Standard/Optimized. Individuals in the placebo conditions will receive 0mg of caffeine through a placebo version of the Military Energy Gum (MEG) every hour between 0200-0800. Individuals in the standard conditions will receive 200mg of caffeine (2 pieces of MEG) at 0200 and 0600 and placebo at all other hours between 0200-0800. Individuals in the optimized condition will have the amount of caffeine dosed to them based on their performance on the PVTs. Dosing for this condition can vary from 0mg-300mg every hour without exceeding a max of 800mg in 24 hours. It is anticipated that participants in the optimized conditions will perform better than those in other conditions on the following PVTs that are administered during the 62-hour total sleep deprivation phase of the study. In order to monitor sleep and potential effects on recovery sleep after the total sleep deprivation phase participants will undergo polysomnography during the baseline and recovery nights of sleep to monitor sleep quality, latency, and duration.

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1. INTRODUCTION:

Warfighters often need to complete mission critical tasks in harsh environments and without sufficient opportunity for restorative sleep. This lack of sleep can lead to degraded readiness and lethality, potentially placing the mission and personnel at risk. Caffeine can be an effective countermeasure to fatigue and sleep loss that can be used to temporarily sustain Warfighter performance. However, the effectiveness of caffeine depends on the duration of sleep deprivation and the phase of the circadian rhythm of alertness. Moreover, there are also significant inter-individual differences in how people are affected by sleep deprivation and their sensitivity to caffeine. The 2B-Alert Caffeine Optimization algorithm was developed by collaborators at the U.S. Army Biotechnology HPC Software Applications Institute (BHSAI) to provide individualized caffeine recommendations for a specific time of day or "mission window." The 2B-Alert algorithm utilizes a mathematical prediction model based on the user's sleep history, circadian phase, caffeine history, and repeated performances on a psychomotor vigilance test. The performance of the app was recently validated in a series of studies showing its effectiveness at optimizing caffeine dosing. In those studies, the recommended caffeine dosing by the 2B-Alert app was effective at optimizing psychomotor vigilance performance and side effects. However, it remains to be determined whether the precision medicine approach of the 2B-Alert optimization provides significantly better outcomes than simply taking a standard dose of caffeine according to a general prescribed schedule such as Table 11-1 of FM7-22. The present study will determine whether the 2B-Alert Caffeine Optimization algorithm provides greater performance optimization, side effect minimization, and quality of recovery sleep during sleep deprivation compared to the standard published U.S. Army recommendations for caffeine use during two nights of sleep deprivation. The objective is to conduct a head-to-head comparison between the 2B-Alert app versus a commonly recommended caffeine dosing regimen published by the U.S. Army with respect to their effects on sustaining optimal performance during sleep deprivation and minimizing side effects and subsequent sleep disruption. The specific aims are to: 1) Determine the effectiveness of 2B-Alert versus standard caffeine dosing or placebo on psychomotor vigilance, subjective sleepiness, and cognition on single and multiple nights of sleep deprivation; 2) Determine the effectiveness of 2B-Alert versus standard caffeine dosing at mitigating physiological and emotional side effects; 3) Determine the effectiveness of 2B-Alert versus standard caffeine dosing at minimizing disruptions in recovery sleep. This will be accomplished by collecting data from 150 healthy participants who will live in a sleep laboratory for four nights, including a 62-hour period of total sleep deprivation. In a double-blind design, participants will be randomly assigned to one of five conditions (n = 30 each), including either 1) 2B-Alert caffeine optimization on both nights (Night 1 and 2), 2) 2B-Alert caffeine optimization on the second night only (Night 2), 3) standard caffeine dosing (i.e., 200 mg every 4 hours) on both nights, 4) standard caffeine dosing (i.e., 200 mg every 4 hours) on the second night only, and 5) placebo only on both nights. The general study design is shown in Figure 1 and individual participant activities are shown hour-by-hour in Figure 2. The primary outcome variables will be psychomotor vigilance test (PVT) performance, focusing on the mean response time (RT), as well as subjective measures of mood, anxiety, physiological side-effects, and subjective sleepiness.

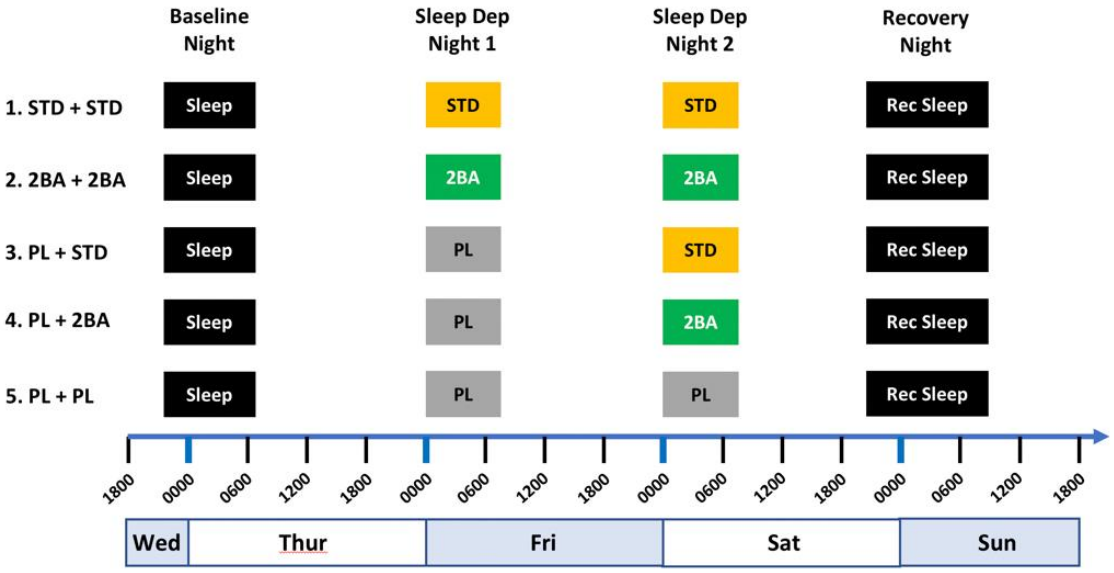

Figure 1. Design of the in-lab sleep deprivation portion of the study. After 13 days of actigraphy and psychomotor vigilance test monitoring at home using the 2B-Alert App, participants will arrive at the sleep lab at 1800. They will obtain 8 hours of time in bed for baseline sleep. Upon awakening at 0700, they will remain awake for the next 62 hours. Participants will then be randomly assigned to one of 5 experimental conditions that differ only in the form of caffeine administration. Condition 1: will involve administering the standard caffeine protocol (STD) of 200 mg every 4 hours from 0100 to 0700 on both nights. Condition 2: will involve dosing individuals with caffeine according to the recommendation of the 2B-Alert App (2BA) on each night. Condition 3: will involve the standard STD regimen but will only provide placebo on the first night and active caffeine on the second. Condition 4: will provide placebo at times suggested by the 2BA App on the first night, and active caffeine on the second. Condition 5: participants will receive placebo on both nights. After 62 hours, all participants will be given a 12-hour recovery sleep period. Participants are released at 1200 the next day.

TIME	Day 14 – BASELINE DAY	Day 15 – DEPRIVATION 1	Day 16 –DEPRIVATION 2	Day 17 – RECOVERY DAY
0000	Subjects arrive night before Sleep from 2300 to 0700 PSG	*0030: PVT TASKS, 0000: VITALS	*0030: PVT TASKS, 0000: VITALS	9pm - 9am Recovery Sleep 12 hours TIB
0100		*0130: PVT TASKS	*0130: PVT TASKS	
0200		*0230: PVT TASKS	*0230: PVT TASKS	
0300		*0330: PVT TASKS	*0330: PVT TASKS	
0400		*0430: PVT TASKS PEAK ALERTNESS	*0430: PVT TASKS PEAK ALERTNESS	
0500		*0530: PVT TASKS	*0530: PVT TASKS	
0600		*0630: PVT TASKS	*0630: PVT TASKS	
0700	0700: Wake up	*0730: PVT TASKS	*0730: PVT TASKS	
0800	VITALS	*0800: VITALS/ 0830: PVT TASKS	*0800: VITALS/ 0830: PVT TASKS	
0900	0930: PVT TASKS	0930: PVT TASKS	0930: PVT TASKS	0930: PVT TASKS/VITALS
1000			1030: PVT TASKS	
1100				
1200	1230: PVT TASKS	1230: PVT TASKS	1230: PVT TASKS	1230: PVT TASKS
1300				
1400				
1500	1530: PVT TASKS	1530: PVT TASKS	1530: PVT TASKS	1530: PVT TASKS
1600	VITALS	VITALS	VITALS	VITALS
1700				
1800	1830: PVT TASKS	1830: PVT TASKS	1830: PVT TASKS	1800: Depart
1900	OPTIMIZE #1	OPTIMIZE #2		
2000			Apply PSG	
2100	2130: PVT TASKS	*2130: PVT TASKS	9pm - 9am Recovery Sleep	
2200				
2300				

Figure 2. Schedule for primary tasks during the Phase 2 (in-lab) sleep deprivation study. Participants will arrive at 1900 on Day 13 and will sleep from 2300 to 0700 the next morning on Day 14 (gray box). Upon awakening, participants will remain awake for 62 hours followed by a period of recovery sleep from 2100 on Day 16 to 0900 on Day 17 (green boxes). Optimization of the caffeine dose will be carried out at 1900 on Day 14 and Day 15 using the 2B-Alert Caffeine Optimization app. Dosing will occur between 2200 and 0800 the next morning. The red shaded areas represent the times of predicted peak alertness that will be the target of the study (0300 to 0900).

2. KEYWORDS:

Sleep, Caffeine, Total Sleep Deprivation, Performance

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim 1: Determine the effectiveness of 2B-Alert versus standard caffeine dosing on (1) psychomotor vigilance and cognition, (2) mitigating physiological and emotional side effects, (3) minimizing disruptions in recovery sleep on single and multiple nights of sleep deprivation.

- **Major Task 1:** Complete IRB/OHRO Approval, Procure Equipment, and Coordinate Study Staff.
    - **Subtask 1:** Prepare Regulatory Documents and Research Protocol
        - Refine eligibility criteria, exclusion criteria, and screening protocol **(completed 8/29/22)**
        - Finalize consent form and human subjects' protocol **(completed 9/26/22)**
        - Submit protocol for local UA IRB Review **(completed 12/16/22)**
        - Submit protocol for Military 2nd level IRB review (ORP/OHRO) **(completed 01/26/23)**
        - Clinicaltrials.gov registration **(complete 10/19/22)**
        - Submit amendments, adverse events, and protocol deviations as needed **(On Going)**
        - Coordinate with sites for annual IRB report for continuing review

*Milestone Achieved: Local IRB approval at University of Arizona **(completed 01/11/23)***

*Milestone Achieved: HRPO approval for all protocols **(completed 01/31/23)***

- **Subtask 2**: Hire Staff and Acquire Testing Materials
    - Hire research staff to administer all tasks and carry out study procedures **(completed 9/06/22)**
    - Train research staff on study-related protocols **(100% complete)**
    - Acquire the assessment tests, instruments, and equipment **(100% complete)**

*Milestone Achieved: All materials and tasks ready for data collection **(completed 03/20/23)***

*Milestone Achieved: Research staff hired and trained **(completed 05/01/2023)***

- **Major Task 2**: Participant Recruitment and initial enrollment efforts
    - **Subtask 1**: Begin recruitment and initial data collection
        - Place advertisements for participant recruitment (***completed* 05/11/23**)
        - Begin to enroll *n* = 150 participants **(*In Progress;* 3% complete)**
        - Conduct initial preprocessing and quality control of PVT, PSG, and cognition data to ensure proper data acquisition and implementation of study procedures **(*completed* 5/19/2023)**

  *Milestone Achieved: Subject recruitment initiated **(completed 05/11/23)***

- **Major Task 3:** Sleep Deprivation data collection

    - **Subtask 1**: Collect data for 2B-Alert vs. STD study
        - Train research staff on sleep deprivation and caffeine administration protocols **(completed 5/19/23)**
        - Obtain materials and set up sleep lab facilities **(completed 06/09/2023)**
        - Participants complete assigned condition over a 17-day period: STD (n=30); 2BA (n=30); PL + STD (n=30); PL + 2BA (n=30); PL (n=30) ***(In Progress)***
        - Conduct initial preprocessing and quality control of data ***(In Progress)***

  *Milestone Achieved: Sleep deprivation phase initiated **(06/21/23)***

- **Major Task 4:** Analyze data and disseminate results

    - **Subtask 1**: Process and analyze all study data
        - Conduct statistical analyses of data

    - **Subtask 2**: Submit publications, final report and prepare transition plans
        - Submit abstracts and manuscripts for publication
        - Prepare final report describing study findings

What was accomplished under these goals?

During the first annual reporting period, this study has executed planning and regulatory activities and moved into the data collection phase with emphasis on recruitment and enrollment efforts. All regulatory processes, including IRB and OHRO approval, were completed in Y1Q2. We have trained four (4) full-time research technicians and fifteen (15) undergraduate research assistants on recruitment, enrollment, and data collection activities. We have acquired all study materials and

equipment for data collection activities and thoroughly pilot tested all of the materials prior to beginning recruitment. As the recruitment, participant monitoring, and data collection aspects of the study are staffed primarily by trained university students who assist the full-time technicians, the study team is currently growing to increase the enrollment effort. This has involved training new staff on study procedures, which will continue on into Y2Q1 and periodically for the remainder of the data collection period for the study.

Recruitment started in Y1Q3 (05/11/2023) and we enrolled our first participant in Y1Q4 (06/09/2023). The milestone for Major Task 3, Subtask 1 was completed when the first sleep deprivation phase was initiated on 2B2_001's 13th day of participation (06/21/2023).

Our primary method of recruitment has been through distributing flyers around the Tucson metropolitan area with a large focus on the University of Arizona campus as college students were returning to the area for the start of the semester. However, a number of other methods have been effective in recruiting participants such as spread information through word of mouth and in-person presentations to a variety college lecture hall classes.

Our sources of study recruitment and overall progress are described below:

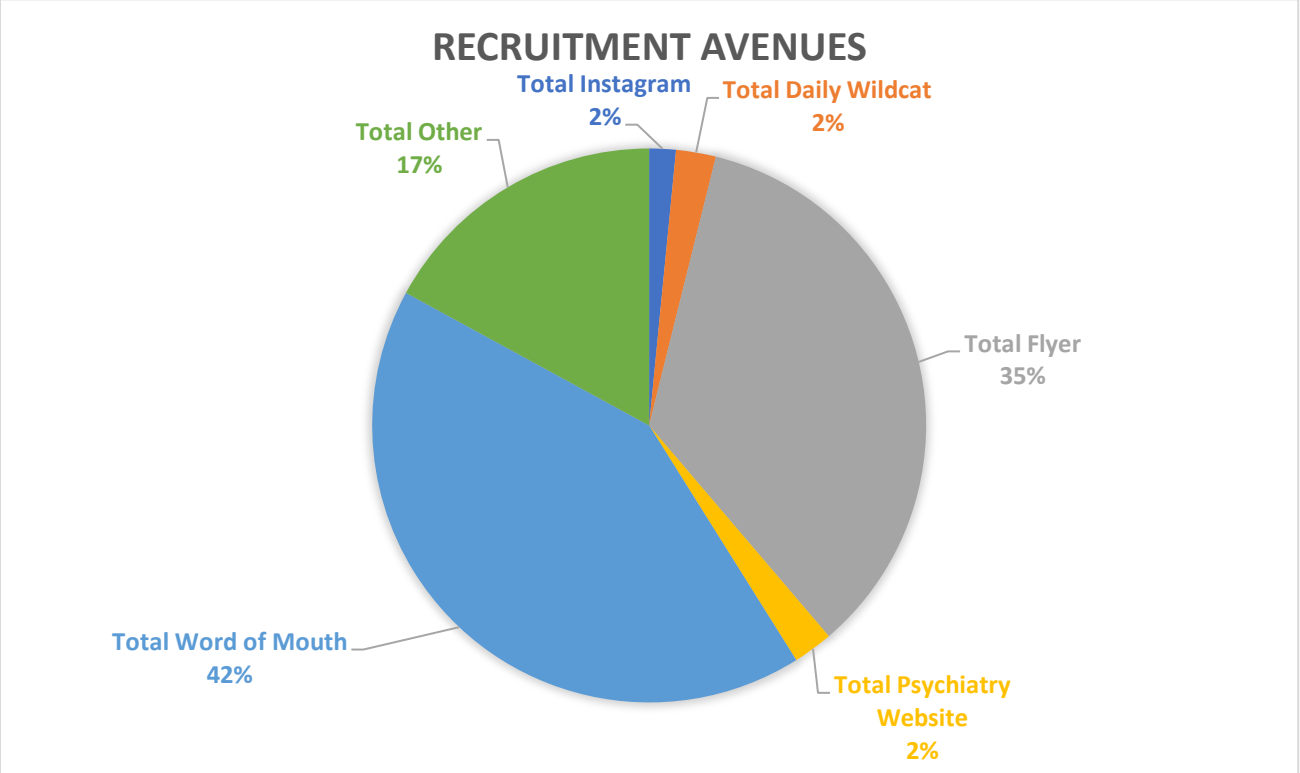

Figure 1: Breakdown of Recruitment Methods

By the end of Y1Q4 our most successful recruitment method was word of mouth (*n*=54) and flyers (*n*=45). Of the other avenues' individuals reported were Instagram (*n*=2), the college newspaper the Daily Wildcat (*n*=3), the University of Arizona Psychiatry website (*n*=3), and through other avenues (*n*=22).

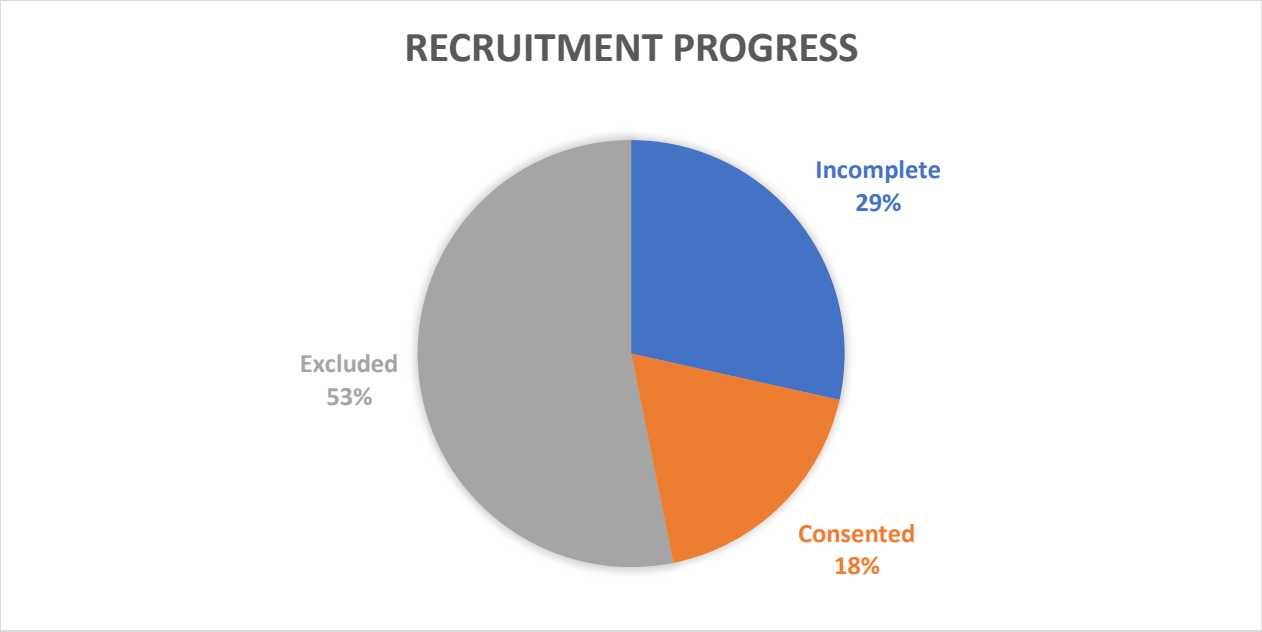

Figure 2: Breakdown of recruitment progress as of the end of this reporting period.

During the annual reporting period a total of 158 individuals showed interest in this study by filling out our online REDCap survey for preliminary screening. Of the 158 entries, 84 individuals were excluded (see Figure 3), 45 individuals never completed the screener and were lost upon re-contact, and 29 individuals were consented and contacted about scheduling their in-person screening appointment.

Below is a figure illustrating the reasons for exclusion from the REDCap preliminary screening.

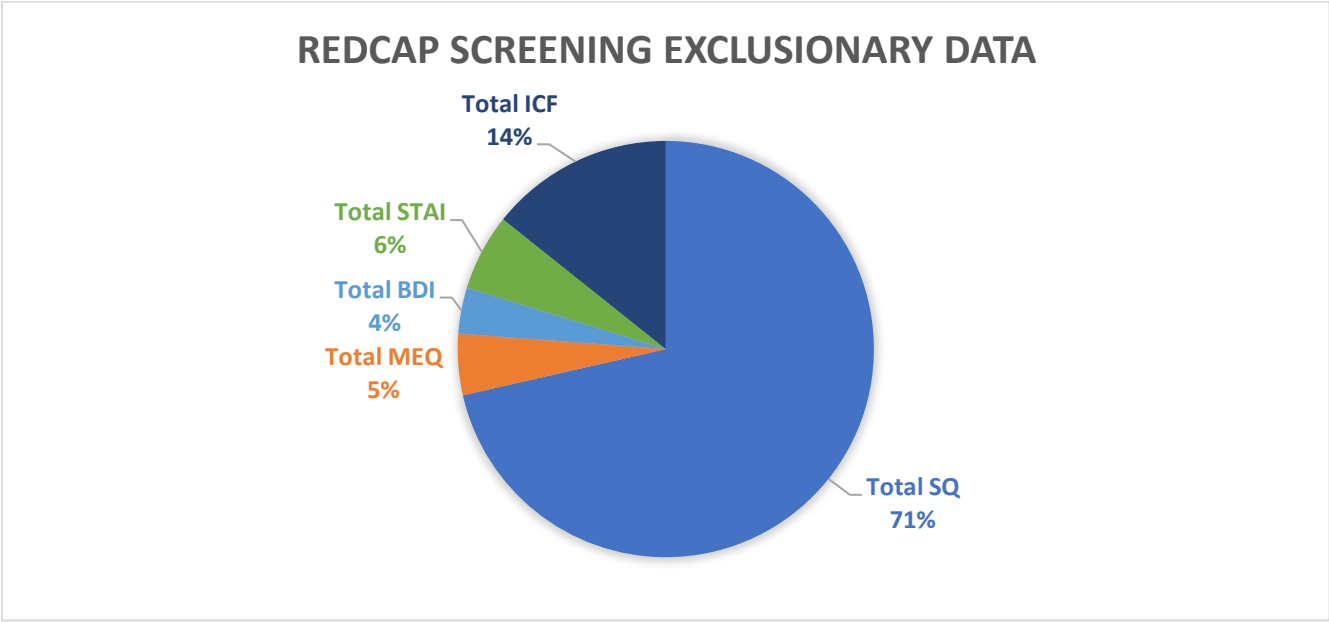

Figure 3: Exclusion factors for the 84 excluded individuals as of 08/31/2023. BDI=Beck Depression Inventory 2nd edition, ICF=Informed Consent Form, MEQ=Morningness Eveningness Questionnaire, SQ=Screening Questionnaire, STAI=State Trait Anxiety Inventory.

As Figure 3 illustrates, the primary exclusion factor for ineligible participants has been due to our general Screening Questionnaire (*n*=60) that covers a variety of health-related topics, followed by individuals who began the screening process but decided to not consent to the study (*n*=12). Besides individuals were also excluded based on high STAI scores (*n*=5), high BDI scores (*n*=3), and extreme MEQ scores (*n*=4).

Below is a breakdown of the topics covered in the Screening Questionnaire (SQ) that excluded participants.

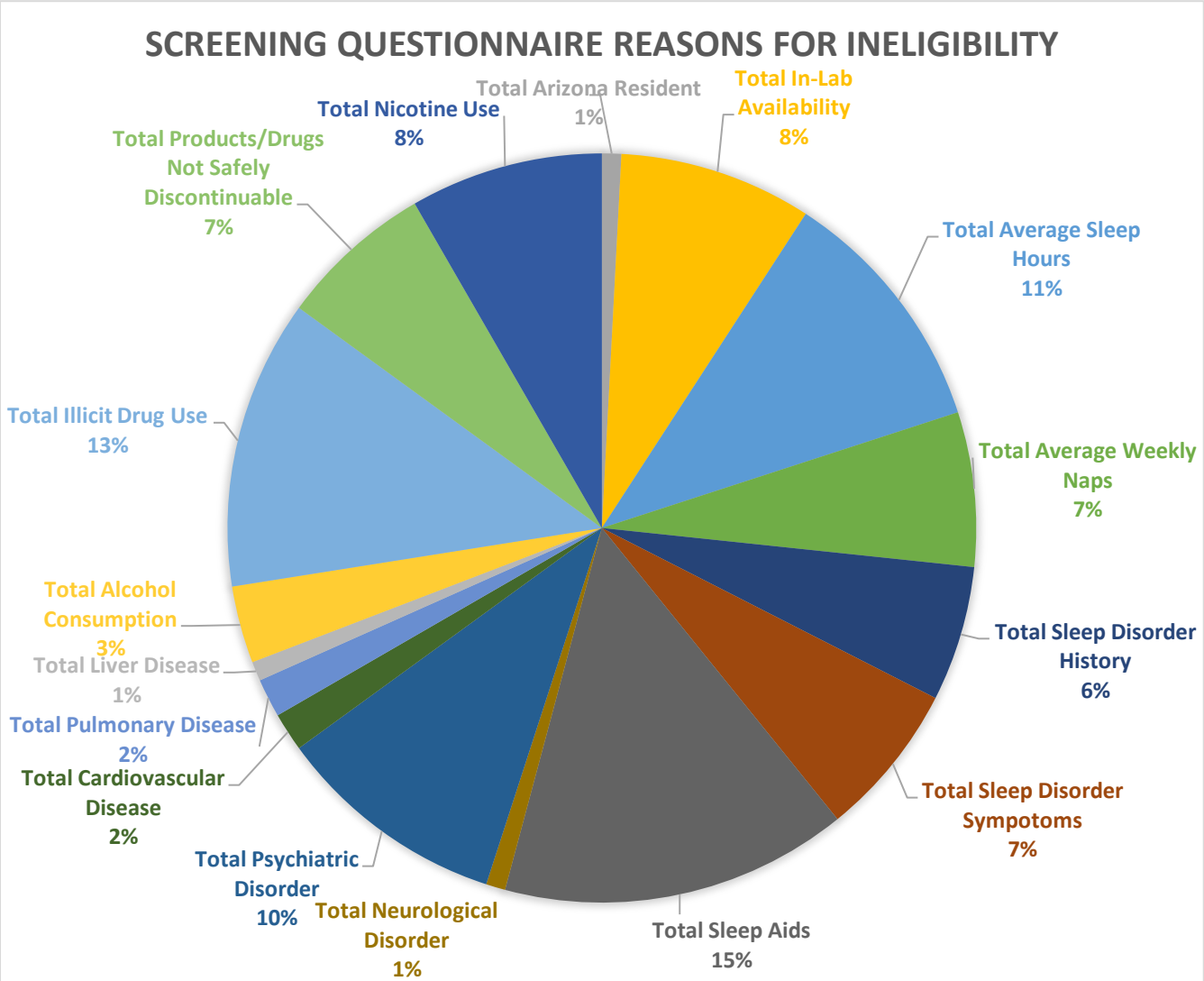

Figure 4: Exclusion factors for the 60 individuals excluded due to the SQ=Screening Questionnaire

As the Screening Questionnaire is the first survey individuals complete during the preliminary screening on REDCap, it contains a large variety of exclusionary items. Figure 4 shows the array of reasons individuals were excluded from continuing with the rest of the online screening and consent process. The primary causes for ineligibility were the use of Sleep Aids (*n*=18), use of Illicit drugs (*n*=15), Average Sleep Hours falling outside of 6-9 hours nightly (n=13), and psychiatric disorders resulting in hospitalization or use of psychiatric medication (*n*=12). Other large causes of ineligibility were due to the use of Nicotine (*n*=10), individuals not being available for the 4-day in-laboratory portion of the study (*n*=10), on average taking too many naps during the week (*n*=8), taking products/drugs/medications that cannot be safely discontinued for the in-laboratory portion of the study (*n*=8), and either having symptoms indicative of a sleep disorder (*n*=8) or a history of a sleep disorder (*n*=7). The all remaining exclusion criteria accounted for less than 5% total screened individuals. Many individuals had more than 1 reason for exclusion (*M*=2.03).

Participants in the study are required to live continuously within the sleep laboratory for 4 days. The sleep facility, known as the University of Arizona Center for Sleep and Circadian Neuroscience Research (CSCNR). The CSCNR is a brand new facility that was undergoing construction for over a year and was only recently opened in May of 2023. Construction delays prevented us from actively running participants during part of the year, which resulted in fewer completed participants for the first year than proposed in the Statement of Work. However, now that the center is completed and open, in conjunction with the start of a new semester at the University, recruitment numbers and staffing availability have improved. During the past few months, we have begun to increase the number of participants in each study run projecting into Y2Q1 and anticipate that with current enrollment projections that we will catch up to enrollment quotas by the end of Y2Q2.

What opportunities for training and professional development has the project provided?

All team members on this study have been trained on all aspects relating to this study. Members include four (4) full time research technicians and a team of fifteen (15) undergraduate research assistants. All members have trained with the Center for Sleep and Circadian Neuroscience Research lead sleep technologist to ensure they are qualified to conduct complete PSG electrode application and utilize the Natus monitoring software. In addition, all members have been trained in proper drug testing procedures, ECG application, and monitoring of subjects undergoing total sleep deprivation during the in-laboratory portions of the study.

How were the results disseminated to communities of interest?

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period we will continue to focus on increasing recruitment efforts and completing subject participation. Currently there are thirteen (13) scheduled screening/ enrollment visits during the next quarterly reporting period and we project to schedule an additional ten (10), making the total projected number of completed participants by the end of Y2Q1 twenty-seven (27), assuming everything stays on target. Additionally, we plan to clean the initial data and conduct initial quality control checks during the next quarter.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Item	Type of amendment	UA IRB Submission	UA IRB Approval Date	UA IRB Approval Submitted to HRPO	Approved by HRPO
New Project Initial Approval	New project	10/06/2022	01/10/2023	01/12/2023	01/31/2023
Amendment #1: Study personnel update	Minor	02/28/2023	02/28/2023	N/A	N/A
Amendment #2: Discarded	Minor	02/28/2023	N/A	N/A	N/A
Amendment #3: A QR code has been added to the recruitment flyers for easy access to the screening project on REDCap. The formatting on Facebook Ad #3 was adjusted to have the study email address be listed on one line.	Minor	02/28/2023	03/22/2023	N/A	N/A

The recruitment email script has been edited to refer to the "UAHS Center for Sleep and Circadian Sciences in the basement of 1501 N. Campbell AVE" for all study activities. It was also updated to list the preliminary screening on REDCap and then list out the rest of the study portions to match the Informed Consent Script. The study phone number was inserted at the bottom. The Screening and Enrollment reminder/confirmation emails were updated to list the "UAHS Center for Sleep and Circadian Sciences in the basement of 1501 N. Campbell AVE" as the location for the screening and enrollment visit. The exit physical document has been uploaded that will be used by the study staff and study physician during the medical release at the end of the study. An additional document describing the mental status assessment task has been uploaded as an Other Attachment.					
Amendment #4: The study protocol is updated to: 1. Remove all mentions of the Oura Ring (hand actigraph). 2. Relocation of the demographic's questionnaire to the enrollment portion of the research procedures 3. The timing of events was updated to include a	Minor	03/22/2023	04/11/2023	N/A	N/A

delayed start date for individuals who get screened and enrolled but cannot come in for the in-lab portion exactly 13 days following their in-person appointment. 4. Clarification that the medical evaluation performed for release from the study consists of two parts, an exit physical performed by a study staff member and a mental evaluation performed via HIPAA Zoom with our study physician. 5. Addition of the video facial recordings during in-lab phase and their purpose. 6. Addition of using BoxHealth as a data repository/sharing platform for the video facial recordings. Removal of the "safesite dropbox" indication for where data will be stored in 14.7 7. Addition of exclusion criteria for females actively trying to conceive. 8. Addition of the explanation of the 2B-Alert app and that it collects PVT data, caffeine logs, and sleep duration logs. 9. Clarified the use of the two informed consent scripts and how they apply to their two scenarios (Online vs. Screening) 10. Clarified what data will be being shared with collaborators 11. According to new standards for caffeine dosing, the caffeine distribution has been modified. In section 1.0 the new standard dosing is					

stated and the source we are basing it off of, changing "200mg every two hours" to "200mg every four hours" and removing the citation for "Kamimori et at., 2005). In 2.0 it has been changed to say "200mg of caffeine every four hours". Then in section 10.2 the dosing schedule has been changed to accommodate two windows of caffeine distribution "Between the windows of 12 and 25 hours of sleep deprivation (Day 14-15) and 37 and 49 hours of sleep deprivation (Day 15-16), either caffeine gum or placebo gum will be administered." Additionally, the conditions were updated to reflect the standard changing to "200mg/4hr.) The informed consent form was updated to: 1. Remove all mentions of the Oura Ring (hand actigraph). 2. The timeline of events was updated to include a delayed start date for individuals who get screened and enrolled but cannot come in for the in-lab portion exactly 13 days following their in-person appointment. 3. Addition of the video facial recordings during in-lab phase. 4. Updated what data we will be sharing with our collaborators at BHSAI to be consistent with protocol. 5. Addition of using BoxHealth as a data repository/sharing platform for the video facial recordings.					

6. Clarification of what is collected on the smartphone through the 2B-Alert app (PVT, caffeine and sleep duration logs) 7. Clarification that the medical evaluation performed for release from the study consists of two parts, an exit physical performed by a study staff member and a mental evaluation performed via HIPAA Zoom with our study physician. 8. Statement of the demographic's questionnaire now in the enrollment portion of the research procedures 9. The dosing schedule has been changed to accommodate two windows of caffeine distribution, "Between the windows of 12 and 25 hours of sleep deprivation (Day 14-15) and 37 and 49 hours of sleep deprivation (Day 15-16)" The recruitment email script has been edited to include information about the potential delayed start after enrollment depending on sleep center availability. The Informed Consent Script for the Online Screening has been modified to: 1. Remove all language of the Oura 2. The statement about the delayed start after enrollment was added. 3. It has also been updated to list the "UAHS Center for Sleep and Circadian Sciences in the basement of 1501 N. Campbell AVE" as					

the location for the screening and enrollment visit. 4. Addition of the video facial recordings during in-lab phase. A new Informed Consent Script has been created to reflect all of the previous changes and the relevant information to the participant once they are at the in-person screening visit. (Screening Informed Consent Script). Due to the addition of the potential delayed start date after enrollment a reminder and confirmation email to begin the at-home portion has been created. The Enrollment Briefing script has been updated to include language about the delayed start of the at-home portion of the study.					
Amendment #5: Study personnel update	Minor	03/22/2023	04/04/2023	N/A	N/A
Amendment #6: The study protocol was updated: 1. In section 10.2 the two windows of caffeine distribution have been changed to comply with BHSAI developments. It now states, "Between the windows of 19 and 25 hours of sleep deprivation (Day 15) and 43 and 49 hours of sleep deprivation (Day 16), either caffeine gum or placebo gum will be administered." The informed consent form was updated: 1. Item 6 under “IN-LABORATORY PHASE”	Minor	04/12/2023	04/26/2023	N/A	N/A

has been edited to be consistent with the timing of ECG collection every 6 hours. It now states, “Full 12-lead Electrocardiogram (ECG) assessments will be conducted every 6 hours, beginning at approximately 2pm the afternoon of your first day in the lab (following your initial night of sleep). There will be 10 total assessments: 2pm from day 1-4, 8pm from day 1-4, 2am during night 1 and 2, and 8am during night 1 and 2.” 2. Item 3 under the things that they should understand to participate in this study has been updated. The two windows of caffeine distribution have been changed to comply with BHSAI development. It now states, "Between the windows of 19 and 25 hours of sleep deprivation (Day 15) and 43 and 49 hours of sleep deprivation (Day 16)" 3. Minor adjusted to formatting and correcting language have been made. The menu options form was updated: 1. The choices for each meal have been added too for a more diverse selection of food. 2. Allergen/Dietary labels have been added to options that comply with specific diets (peanut free – PT, tree nut free – TNF, lactose free – LF, gluten free – GF, and vegetarian – V). 3. An additional specialty menu section has been created with name-brand foods that pertain to the specific diets listed above.					

Amendment #7: Study personnel update	Minor	04/19/2023	04/26/2023	N/A	N/A
Amendment #8: Study personnel update	Minor	06/05/2023	06/16/2023	N/A	N/A
Amendment #9: Exclusion criteria of STAI-T updated to include more individuals, Addition of scripts to contact participants about the online screening, scheduling in-person appointments, and reminder emails.	Minor	06/12/2023	06/15/2023	N/A	N/A
Amendment #10: Update to screening questionnaire to remove ancillary and/or sensitive information from the survey. Updated study protocol and REDCap project to collect contact information first to aid re-contacting efforts. Addition of a script to re-contact participants that started but did not complete the screening survey.	Minor	06/15/2023	06/30/2023	N/A	N/A
Reportable New Information #1: The screening questionnaire on record was out of date and did not match the screening questionnaire that was distributed during initial recruitment efforts. The questionnaire that was distributed had not been IRB approved, however items had only been removed or altered, no new items were added.	RNI	06/29/2023	07/03/2023	N/A	N/A
Amendment #11: Study personnel update	Minor	07/06/2023	07/17/2023	N/A	N/A
Amendment #12: Update to the Enrollment Briefing Script changing the method of communication from phone calls to emails because it was out of date.	Minor	07/17/2023	08/22/2023	N/A	N/A
Reportable New Information #2: Participants had been contacted solely through	RNI	08/16/2023	08/24/2023	N/A	N/A

email during recruitment/enrollment/study participation. This did not match the IRB approved document indicating that the method of communication would be phone calls.					
Amendment #13: Discarded	Minor	07/24/2023	N/A	N/A	N/A
Amendment #14: Study personnel update	Minor	08/27/2023	TBD	N/A	N/A
Amendment #15: Addition of new surveys: MAIA, Reysen Likeability Scale, Reysen Expertise Scale	Minor	08/27/2023	TBD	N/A	N/A

Actual or anticipated problems or delays and actions or plans to resolve them

During this annual reporting period the Center for Sleep and Circadian Neuroscience Research did not open when originally expected. This was due to delayed construction issues that started during the COVID-19 pandemic shutdowns and put the entire construction behind schedule. The Center was finally completed and opened for data collection in May of 2023. Due to this uncontrollable circumstance, we had to delay recruitment efforts and experienced a loss in staffing due to students leaving the university during the summer break. The Center eventually opened scheduling of sleep suite rooms in Y1Q3 (06/01/2023) and we began recruitment efforts. However, since our primary recruitment population was decreased during the summer, local recruitment efforts were slow until the Fall semester approached. Additionally, once the CSCSN opened, there are a number of other research studies that has also been delayed, which created a bottleneck of multiple labs competing for space in the new center. In consideration of the needs of the larger research community at the University, we had to limit our use of the facility to accommodate other researchers. This early bottleneck situation prevented us from being able to run at maximum capacity (4 participants per study run). Thus, initial study runs started with only 1 participants at a time but have recently ramped up to 2 participants per study run in the past month. In order to mitigate the initial issues with recruitment we have increased flyering efforts and have begun advertising around the University of Arizona campus to students as they returned for the fall semester. These efforts are showing signs of success and recruitment has increased for Y2Q1.

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS:

- **Publications, conference papers, and presentations** Nothing to Report
  Journal publications. Nothing to Report
  Books or other non-periodical, one-time publications. Nothing to Report

Other publications, conference papers and presentations. Nothing to Report

- **Website(s) or other Internet site(s)** Nothing to Report
- **Technologies or techniques** Nothing to Report
- **Inventions, patent applications, and/or licenses** Nothing to Report
- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Dr. William “Scott” Killgore
Project Role: Principal investigator
Researcher Identifier:
Nearest person month worked: 4.616
Contribution to project: Dr. Killgore assisted with project development and oversight with the present study.

Name: Alisa Huskey
Project Role: Postdoctoral Fellow
Researcher Identifier:
Nearest person month worked: 1.730
Contribution to project: Dr. Huskey assisted with training of lab staff and development/maintenance of the REDCap study projects.

Name: David Negelspach
Project Role: Postdoctoral Fellow
Researcher Identifier:
Nearest person month worked: 2.040
Contribution to project: Dr. Negelspach assisted with project modeling.

Name: Lindsey Hildebrand
Project Role: Research Operations Manager
Researcher Identifier:
Nearest person month worked: 5.464
Contribution to project: Ms. Hildebrand assisted in procurement of materials, hiring and training of staff, and coordination with outside organizations involved in the project.

Name: Gabriela Franca
Project Role: Research Technician
Researcher Identifier:
Nearest person month worked: 6.120
Contribution to project: Ms. Franca assisted with recruitment efforts, data management, and conducting study data collection.

Name: Kymberly Henderson

Project Role: Research Technician
Researcher Identifier:
Nearest person month worked: 3.390
Contribution to project: Ms. Henderson assisted with recruitment efforts, screening participants, and conducting study data collection.

Name: Melissa Reich-Fuehrer
Project Role: Research Technician
Researcher Identifier:
Nearest person month worked: 10.273
Contribution to project: Mrs. Reich-Fuehrer assisted with recruitment efforts, screening participants, and management of study subjects

Name: Camryn Wellman
Project Role: Research Technician
Researcher Identifier:
Nearest person month worked: 9.840
Contribution to project: Ms. Wellman assisted with recruitment efforts, screening participants, and conducting study data collection.

Name: Palmer Grabner
Project Role: Research Assistant
Researcher Identifier:
Nearest person month worked: 1.320
Contribution to project: Mr. Grabner assisted with recruitment efforts, screening participants, and conducting study data collection.

Name: Darby Wolocko
Project Role: Research Assistant
Researcher Identifier:
Nearest person month worked: 1.320
Contribution to project: Ms. Wolocko assisted with recruitment efforts, screening participants, and conducting study data collection.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Organization Name: University of Arizona Center for Sleep and Circadian Sciences
Location of Organization: University of Arizona, Tucson, AZ
Partner's Contribution to the project: Facilities for the in-laboratory total sleep deprivation, testing rooms for screening/enrollment, biohazard facilities.

Organization Name: Biotechnology HPC Software Applications Institute (BHSAI)
Location of Organization: Frederick, MD
Partner's Contribution to the project: Software development

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: