A Study to Evaluate the Effects of Relaxium in Subjects with Sleep Disorders

Protocol Number:	ABRI-002
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Study Schedule	Initiation:	Screening/Week 1 and Baseline	July 21, 2020
	Completion:	Week 2	January 18, 2020

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Study Summary	
Title	A Study to Evaluate the Effects of Relaxium in Subjects with Sleep Disorders
Protocol Number	ABRI-002
Sponsor	American Behavioral Research Institute
Methodology	Double-blind, randomized, placebo-controlled, parallel group
Objective	To evaluate the efficacy of a nutritional supplement to improve sleep patterns and related sequelae.
Number of Subjects	40 (planned to complete); 37 were randomized and 35 completed the study. Two subjects left the study and could not be reached for follow-up.
Population	Male and Female subjects
Duration	2 Weeks (Screening/ Baseline Week 1; Blinded Week 2)
Study Drug/Frequency/Reference	• Relaxium Sleep, 2 capsules at bedtime x 1 week • Placebo, 2 capsules at bedtime x 1 or 2 weeks
Study Design	This was a randomized, double blind, placebo controlled, parallel group study in subjects with insomnia. After qualifying for the study, subjects had a 1-week lead-in period with placebo, and subjects completed daily sleep diaries [each morning for the quality of their sleep for the previous night (QoN), each evening the overall quality of day (QoD), including levels of daytime energy and concentration] and completed the Leeds Sleep Evaluation Questionnaire (LSEQ) which was a visual analog scale (VAS on an 80 mm line) to indicate their quality of sleep (QoS), getting to sleep (GTS), behavior following awakening (BFW), awake following sleep (AFS) on the last 3 days of the treatment period. Subjects were then randomized 1:1 to placebo or Relaxium in a double-blind manner for another week (Week 2). The daily diaries and LSEQ evaluations were repeated as in the Lead-in period (Week 1). As an exploratory endpoint subjects had wrist actigraphy (Fitbit Inspire) daily during sleep to assess quality and sleep duration over each period.
Statistical Methodology	Descriptive statistics reported for diary responses, LSEQ and sleep time [total, time in bed, time awake, light, deep and rapid eye movement (REM)] for subjects with data in both treatment periods for diary responses and LSEQ, analysis of variance was done to evaluate the statistically differences between placebo and Relaxium. Fisher's exact time was used to evaluate the number of days with no difficulty in concentration during blinded medication. Statistical significance was declared at $p \leq 0.05$.

Results

Based on the LSEQ, a validated test for sleep, Relaxium treatment resulted in improved sleep, compared to placebo treatment. The mean differences the treatments expressed as changes from baseline are shown in the following table. Higher scores represent better quality of sleep (calmer, less wakeful periods), easier time getting to sleep, easier to awake, and more alert following wakening.

Changes in LSEQ

Parameter	Mean Treatment Difference (mm) From Baseline (Lead -in Period Week 1) to Blinded Treatment (Week 2) Between Relaxium and Placebo Groups	P value
QoS	12.3	0.002
GTS	12.2	0.006
BFW	10.2	0.028
AFS	10.4	0.034

The significantly higher scores indicate better sleep and easier awakening with Relaxium compared to placebo.

The daily diary responses on a 5-point severity for level of daytime energy and ability to concentrate were also improved with Relaxium compared to placebo, but only the difference in daytime concentration was statistically significant.

The changes in quality of sleep or mood were not statistically different between the two treatments.

Changes in Daily Diary Responses

Parameter	Mean Treatment Differences From Baseline in Diary Scores Between Relaxium and Placebo Groups	P value
QoN	-0.36	0.162
QoD Q1	0.1621	0.089
QoD Q2	-0.53	0.058
QoD Q3	0.79	0.002

QoD Q1 = level of daytime energy today; QoD Q2 = mood level;
QoD Q3 = level of difficulty in concentration; QoN= quality of sleep last night

The number of days that subjects reported no difficulty in concentration was 21% for placebo and 38% on Relaxium treatment during blinded treatment. The difference between the 2 groups was statistically significant ($p = 0.013$). Thus, there was about an 80% increase in the number of days the subjects reported no difficulty in concentration, compared to placebo.

For the wearable technology (Fitbit Inspire) there were no changes from baseline in time in bed, time asleep, time awake, light sleep, deep sleep, and REM sleep) for placebo and Relaxium treatments.

Summary

In subjects with insomnia, Relaxium treatment improved various parameter related to sleep, compared to subjects treated with placebo. The improvements included:

- easier time to fall asleep
- sleep was calmer with less wakeful periods
- awakening following sleep, was easier

	• improved alertness after awakening Furthermore, subjects had less difficulty in concentration during the day. All of these changes were statistically significant. No adverse events were reported in this study.

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List of Abbreviations

Abbreviation	Definition
AE	Adverse Event
AFS	Awake Following Sleep
BFW	Behavior Following Awakening
BMI	Body Mass Index
BP	Blood Pressure
Ci	Confidence Interval
CRF	Case Report Form
ET	Early Termination
FDA	Food and Drug Administration
GABA	Gamma-Aminobutyric Acid
GCP	Good Clinical Practice
GTS	Getting to Sleep
ICF	Informed Consent Form
ICH	International Council for Harmonization
IP	Investigational Product
IRB	Institutional Review Board
LSEQ	Leeds Sleep Evaluation Questionnaire
OTC	Over the Counter
QoD	Overall Quality of Day
QoN	Quality of Sleep for the Previous Night
QoS	Quality of Sleep
REM	Rapid Eye Movement
SAE	Serious Adverse Event
VAS	Visual Analog Scale

1.0 ETHICS

1.1 Institutional Review Board

The study protocol, amendments (if any), the informed consent form(ICF), and information sheets were approved by the appropriate and applicable Institutional Review Boards (IRBs).

The complete protocol is provided in Appendix 1.

1.2 Ethical Conduct of the Study

This study was conducted in accordance with Good Clinical Practice (GCP) and applicable regulatory requirements and ethical principles.

1.3 Subject Information and Consent

Written informed consent from each subject was obtained at screening, prior to the performance of any study-specific procedures on that subject. The IRB approved ICF is shown in Appendix I.

2.0 Introduction

Insufficient rest or sleep is a prevalent problem for US adults, with more than 50 million suffering from chronic sleep and wakefulness disorders and approximately 29% reporting less than 7 hours of sleep per night which is below the recommended 7 to 9 hours of sleep by the National Sleep Foundation.[1, 2] Insufficient rest or sleep may be associated with chronic diseases, mental disorders, health-risk behaviors, limitations of daily functioning, injury and mortality.[2] In a CDC report analyzing responses via the Behavioral Risk Factor Surveillance System more than 35% of respondents reported unintentionally falling asleep during the day and nodding off and falling asleep while driving was reported in 4.7% of respondents further indicating the dangerous impact of insufficient sleep.[2]

A novel formulation of various herbs and known sleep inducers has been developed and sold in the US under the tradename Relaxium. Key ingredients include melatonin, L-tryptophan, gamma-aminobutyric acid (GABA) and several herbal extracts (e.g. Sensoril® ashwagandha, Valerest™, a blend of hops and valerian, Chamomile Passionflower).

2.1 Melatonin

Melatonin is a hormone produced by the pineal gland and it helps to control sleep and wake cycles. Very small amounts of it are found in foods such as meats, grains, fruits, and vegetables. The body has its own internal clock that modulates one's natural cycle of sleeping and waking hours. The pineal gland controls the endogenous production of melatonin. Normally, melatonin levels begin to rise in the mid- to late evening, remain high for most of the night, and then drop in the early morning hours. Because melatonin levels slowly decline with age, very small amounts of melatonin or none at all are produced, in some subjects and therefore supplementation is required to promote and maintain sleep. These supplements which have been on the market for over two decades may be designed to release melatonin quickly or slowly.

Extensive studies have been conducted on immediate release and sustained release melatonin products. A recent meta-analysis of 19 studies involving 1683 subjects, demonstrated that melatonin significantly improves sleep in subjects with primary sleep disorders compared to placebo. Melatonin reduces sleep-onset latency, increases total sleep time and improves overall

sleep quality compared to placebo to a statistically significant degree. Higher melatonin doses and longer duration trials were related to significant greater effect sizes on sleep latency and total sleep time. There was no evidence of the development of tolerance with melatonin use. No greater effects in sleep quality were observed with melatonin dose or trial duration.[3]

2.2 Other Herbals and Natural Products

Many herbs have a long history of use as mild sedatives and hypnotics. Valeriana officinalis (valerian) for example, was recognized by the ancient Greeks more than 2000 years ago as an effective treatment for nervous unrest, stress and sleep disorders4. In a literature review by Salter and Brownie[5], 12 clinical trials (six of which were randomized, double blind, placebo-controlled trials) studied the effects of valerian on sleep parameters: total sleep time, sleep latency (i.e. time to fall asleep), slow wave sleep, nocturnal awakenings, and sleep quality. Nine of these studies found valerian to be effective in improving at least one of the sleep parameters measured. However, it is important to note that five of these studies had significant methodological flaws, which limits the reliability of their findings, and therefore the extent to which they can be applied to clinical practice. In addition, in most studies, valerian was administered for 1 day only, sample sizes ranged from 8 to 405 subjects and doses ranged from 300 to 950 mg/day. A large scale, double blind, randomized, placebo-controlled trial found that 5.5% [95% confidence interval (CI) 0.2–10.8] more participants in the valerian group perceived their sleep as better or much better (p=0.04) compared to the control (placebo) group6. Evidence supports valerian as a safe herb. Valerian is listed on the FDA Generally Recognized as Safe (GRAS) list, indicating that it is considered safe for use as food (http://vm.cfsan.fda.gov/~dms/eafus.html). In a series of 11 clinical trials involving a total of 633 persons on valerian reported 42 adverse events, which included gastrointestinal discomfort, headache, slight dizziness, residual sedation, heavy sleep, depression, daytime drowsiness, and feeling dazed in the morning.[7-11]. In several trials, adverse events were milder and less common in the valerian group compared to comparison groups treated with hypnotics.[12,13]

Valerian has been demonstrated to be a moderate inhibitor of CYP3A4 and a mild inhibitor of CYP2C19 and 2D6, which could increase plasma levels of the drugs metabolized by these enzymes. CYP3A4 is the P450 subtype most widely involved in drug metabolism and 2C19 and 2D6 subtypes are also involved in metabolism of several common medications.

A clinical trial showed that treatment with Sensoril® ashwagandha extract for 60 days resulted in significant reduction in stress, anxiety, irritability, inability to concentrate, forgetfulness, sleeplessness, fatigue, and other subjective indicators of stress at all doses.[14]

Gamma-amino butyric acid is an amino acid contained in various foods and is known as an inhibitory transmitter of the central nervous system. It is produced by natural fermentation as an ingredient of functional foods and oral administration has effects on the autonomic nervous system which includes reducing anxiety[15] and stress[16] by increasing parasympathetic nerve activity.[17]

Based on electroencephalograms, Yamatsu et al.[18] demonstrated oral GABA (100 mg) administered for 1 week, 30 minutes before bedtime decreased sleep latency by 5.3 minutes in subjects with insomnia.

A randomized double-blind, placebo-controlled pilot trial in 34 patients with primary insomnia for ≥ 6-months was conducted. Patients were randomized to 270 mg of chamomile twice daily or

placebo for 28-days. Chamomile provided modest benefits of daytime functioning and mixed benefits on sleep diary measures relative to placebo in adults with chronic primary insomnia.[19]

As reported by Baek et al.[20] passionflower shown efficacy in at least one randomized clinical trial in healthy subjects.

Regarding L-tryptophan, doses of 1g or more produces an increase in rated subjective sleepiness and a decrease in sleep latency (time to sleep). There are less firm data suggesting that L-tryptophan may have additional effects such as decrease in total wakefulness and/or increase in sleep time. Best results (in terms of positive effects on sleep or sleepiness) have been found in subjects with mild insomnia, or in normal subjects reporting a longer-than-average sleep latency.[21]

2.3 Relaxium

The combination of melatonin, L-tryptophan, Sensoril® ashwagandha extract, Valerest™, a blend of hops and valerian extracts, Chamomile extract, and Passionflower extract administered just prior to bedtime may assist in helping subjects fall asleep faster and to promote a more restful sleep.

A safety study involving 30 subjects with self-reported difficulty falling and staying asleep on a regular basis ≥4 times per week were randomized to Relaxium and placebo in a crossover manner. Each treatment was administered for 4 weeks. There appeared to be modest improvement in the number of nights with shorter sleep latency with Relaxium compared to placebo. On the other hand, the number of days when sleep hours were greater favored placebo over Relaxium. (Clinical Study Report, An Eight-Week Double-Blind, Randomized, Placebo-Controlled, Cross-Over Study Evaluating the Efficacy of a Natural Sleep Aid. May 19, 2016).

Adverse events reported for Relaxium were drowsiness/sleepiness, headache, uneasy stomach, and waking up during normal sleep patterns. Treatment with placebo included mild stomach discomfort and cramping, tummy ache, gas/rumbling stomach, loose stool and diarrhea, headache, and waking up during normal sleep patterns.

3.0 Objectives

3.1 Primary Objective

- To investigate the effect of Relaxium administered prior to bedtime on sleep parameters, compared to placebo, in subjects with insomnia.

3.2 Secondary Objective

- To assess the safety and tolerability of Relaxium

4.0 Investigational Plan

4.1 Study Design

This was a double blind, repeated dose study in subjects with insomnia. After agreeing to participate in the study, subjects had a 1-week lead-in period with placebo capsules and the subjects were to complete daily sleep diaries [each morning for the quality of their sleep for the previous night (QoN), each evening the overall quality of day (QoD), including levels of daytime energy and concentration] and wear wrist actigraphy (Fitbit Inspire) during sleep to assess quality and sleep duration over this period. If subjects were compliant with these tasks, they were randomized

to Relaxium or placebo once daily at bedtime for 1 week. During this Treatment Phase, daily sleep diaries were to be completed, and wrist actigraphy were to be worn daily. The Pittsburgh Sleep Quality Index was assessed at Screening, and the LSEQ was to be completed on Day 5, 6 and 7 (end of the Lead-In period) and on Days 8, 12, 13, 14 and 15 in the Treatment Phase.

Subjects were screened up to 21 days prior to inclusion into the study. Subjects had a clinic visit on Day 1 to receive instruction on how to complete the sleep diary and the LSEQ and use wrist actigraphy. Other clinic visits were scheduled for Days 8 and 15.

Adverse events and will be monitored throughout the study

The schedule of events is shown in Table 1. The protocol and sample case report form (CRF) are provided in Appendix I.

4.2 Rationale for the Study Design, Including the Choice of Control Groups

A randomized, double blind study was conducted to compare Relaxium with placebo in a scientifically valid manner. Subjects with insomnia, not related to other medical conditions, were selected to rule out subjects with labile sleep disturbances and who are capable to complete daily diaries and complete questionnaires about their sleep. In addition, with the advent of wearable technology it was of interest to explore whether this technology could detect changes in sleep pattern that would corroborate how the subjects felt about their sleep. In addition, all subjects had a 1-week lead in period, to minimize the drop-out rate, following assignment to Relaxium or placebo in the blinded portion of the study.

4.3 Selection of Study Population

4.3.1 Inclusion Criteria

1. Non-smoking, males and females between 20 and 80 years of age.
2. Good general health as determined by the medical history or have stable medical conditions (for at least 30 days prior to screening).
3. Subject must have met DSM-IV criteria for primary insomnia for at least one month (e.g. difficulty falling asleep, waking up frequently during the night with difficulty returning to sleep, waking up too early in the morning, or unrefreshed sleep).
4. Pittsburgh Sleep Quantity Index (PSQI) questionnaire score of 5 or higher. The PSQI, a valid measure of sleep quality, differentiates “poor” from “good” sleep by measuring 7 areas: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.
5. Ability to complete written questionnaires.
6. Subject had to own a smart phone and have daily access to Wi-Fi for synchronization.
7. Subject had to be able to download and operate a basic smart phone App after instruction.
8. Subject must have engaged in a regular sleep routine with similar bedtime and awakening times.
9. Consumption of no more than one alcoholic beverage per day.

4.3.2 Exclusion Criteria

1. Clinically unstable medical abnormality, chronic disease or history or presence of significant neurological disorders (including cognitive disorders), depression,

schizophrenia, anxiety disorder, dementia, chronic pain, or frequent nightly urination (>2 times per night), seizure disorder, and restless leg syndrome.
2. Diagnosis of sleep apnea or risk factors for undiagnosed sleep apnea (witnessed apneic episodes).
3. Use of psychotropic medication or beta blockers.
4. Use of any prescription medications/products, hormonal therapy/replacement medications, and any medications known to induce or inhibit drug metabolizing enzymes activity within 28 days prior to Day 1 and during the study.
5. Use of over the counter, non-prescription preparations that are known to affect sleep within 14 days prior to Day 1.
6. History of alcoholism or drug addiction within the past year.
7. Received an investigational agent or medical device within 30 days of study drug administration.
8. Any other reason, in the opinion of the Investigator, which precludes subject participation in the study (e.g. major life stressors).

4.3.3 Removal of Subjects from Therapy or Assessment

Any subject who discontinued from the study for any reason was to have the reason for discontinuation recorded.

Subjects were free to withdraw from the study after signing informed consent for the following reasons:

- Adverse event
- Lost to follow-up
- Withdrawal of consent by subject
- Physician decision
- Study terminated by sponsor
- Other

If a subject withdrew from the study, the Investigator was to complete and report the observations as thoroughly as possible up to the date of withdrawal including the date of treatment and the reason for withdrawal.

If the subject was withdrawn due to an AE, the Investigator followed the subject until the AE has resolved or stabilized.

All subjects who withdrew from the study were to have completed protocol specified withdrawal procedures.

4.3.4 Withdrawal Procedures

Subjects who withdrew from the study were required to undergo Check-out/Early Termination (ET) procedures (Table 1).

If the subject was withdrawn due to an AE, the Investigator or designee attempted to follow the subject until the AE had resolved or stabilized. Whenever possible, withdrawn subjects had End of Study (EoS) procedures after withdrawal and Follow up. Additional safety assessments than those prescribed in this protocol may have been ordered at the Investigator's or designee's

discretion in subjects who were withdrawn due to an AE, but non-protocol assessments were not necessarily included in the clinical database.

4.3.5 Subject Replacement

Subjects who discontinued were not replaced unless approved by the Sponsor.

5.0 Treatments Administered

5.1 Investigational Product

The Investigator ensured that the investigational products (IP) will be used only in accordance with the protocol. Although Relaxium is a marketed product, for the purposes of this study, it is called an IP. Each capsule of Relaxium contained melatonin (5 mg), L-tryptophan (500 mg), Sensoril® ashwagandha extract (125 mg), Valerest™, (a blend of hops and valerian extracts) (228.9 mg), magnesium citrate, glycinate, oxide (100 mg), chamomile extract (75 mg and Passionflower extract (75 mg). The lot number of the Relaxium capsules was 7636. The lot number of the placebo capsules was 083RD0000021468.

5.2 Method of Assigning Subjects to Treatments and Blinding

Following a lead in period, subjects entered the double-blind portion of the study. For the first week, placebo was administered (Lead-in Period) and if the subject remained eligible, based on LSEQ (VAS ≥40 mm) on Days 5-7 and wrist actigraphy, to continue in the study, blinded medication was administered for the Treatment Period on Day 8.

5.3 Method of Assessing Treatment Compliance

To ensure treatment compliance, each bottle of unused medication was returned to the clinic at each clinic visit. The time of medication dosing was recorded in the diary.

5.4 Labeling and Packaging

An unblinded pharmacist prepared individual bottles of study medication for each period for each subject using a randomization schedule prepared by an independent statistician. The label contained the directions for use, subject number, randomization number, protocol number and name of the Sponsor. The bottles used in Lead in Period were labeled as LIP and those for the double-blind treatment Period were labeled as TP. One bottle per subject was provided on Days 1 and 8. Each bottle contained 20 capsules.

5.5 Preparation

The study product was administered in accordance with the protocol and administered only to subjects participating in the clinical study. It is a violation of the regulations to use an IP for purposes other than stated in the protocol.

The site completed the required documentation as provided by the Sponsor or its representatives to document dispensing of the product. All information was to be recorded immediately on a drug dispensing form each time the study drug was dispensed to a subject.

5.6 Storage Conditions

All clinical supplies were to have been stored in a secure, limited access storage area under the recommended storage conditions.

All test products were to be stored at 20°C to 25°C (68°F to 77°F) in the subject's home.

In the event that storage conditions exceeded the permissible temperatures, the Sponsor should have been contacted within 24 hours of becoming aware of the incident.

5.7 Drug Accountability

When the drug shipment was received, the Investigator or designee checked the amount and condition of the drug, check for appropriate local language in the label, drug expiration date and sign the Receipt of Shipment Form provided. The Receipt of Shipment Form may have faxed as instructed on the form. The original was retained at the site. In addition, the Investigator or designee shall contact the Sponsor as soon as possible if there is a problem with the shipment.

A Drug Accountability Record was provided for the IP. The record must have been kept current and should have contained the dates and quantities of drug received, subject's (identification number and/or initials or supply number as applicable), for whom the IP was dispensed, the date and quantity of IP dispensed and remaining, if from individual subject drug units as well as the initials of the dispenser.

At EoS, or as directed, all unused, partially used, or empty containers, was to be returned to a designee as instructed by Sponsor. IP was returned only after the study monitor had completed a final inventory to verify the quantity to be returned. The return of IP must have been documented. At EoS, a final IP reconciliation statement was to have made by the Investigator or designee and provided to the Sponsor. Unused drug supplies may have been destroyed by the Investigator when approved in writing by Sponsor and Sponsor has received copies of the site's drug handling and disposition Standard Operating Procedures.

All IP inventory forms must have been made available for inspection by a Sponsor-authorized representative or designee and regulatory agency inspectors. The Investigator was responsible for the accountability of all used and unused study supplies at the site.

5.8 Concomitant Medications

Medications used within 30 days prior to Screening was to have been recorded.

Use of any prescription or OTC medications was recorded at Screening. Medications needed for chronic medical conditions (hypertension, diabetes, anti-inflammatory agents) were continued as long as the dose had been stable for at least 30 days and it did not have effects on sleep. Use of any medication (narcotic analgesics, anti-depressants, sedating antihistamines, appetite suppressants, decongestants, L-tryptophan, sedative/hypnotics, anxiolytics) known to interfere with sleep were not permitted.

Any new medication (other than study drug) taken by subjects during the course of the study was to have been recorded. If drug therapy other than that specified by the protocol was taken, a joint decision was to have been made by the Investigator or designee and Sponsor as to whether to continue or discontinue the subject.

5.9 Lifestyle Guidelines

At Screening, subjects were informed that if accepted for the study, they agreed to abstain from alcohol- and caffeine-containing products within 48 hours prior to Day 1 and during the entire study.

Subjects were to have refrained from use of tobacco- or nicotine-containing products, including but not limited to cigarettes, e-cigarettes, pipes, cigars, chewing tobacco, nicotine patches, nicotine lozenges, or nicotine gum within 6 months prior to Day 1.

All subjects agreed not to donate blood, plasma, platelets, or any other blood components from Screening through 4 weeks post dose.

6.0 Study Assessments

6.1 Assessments and Assessment Schedule

A schedule of study assessments and procedures is described in Table 1 below.

Table 1 Schedule of Assessments

Assessment	Screening	Lead in Period (Day)			Double Blind Treatment Phase (Day)			
		1	2-4	5-7	8	9-11	12-14	15
Informed Consent	X							
Inclusion/exclusion Criteria	X							
Demography (height, weight)	X							
Medical/Surgical History	X	X						
Pittsburgh Sleep Quality Index	X							
Drugs of abuse/Alcohol	X							
Vital Signs (BP, HR, RR, temp)	X							
AE Reporting		X	X	X	X	X	X	X
Prior and Concomitant	X	X	X	X	X	X	X	X
Administer Placebo		X	X	X				
Assess subject's eligibility for Treatment Phase					X			
Randomize to Double Blind Medication					X			
Administer Double Blind					X	X	X	
Complete LSEQ				X	X		X	X
Clinic visit	X	X			X			X
Wrist actigraphy		X	X	X	X	X	X	X
Daily sleep diary (am and pm)		X	X	X	X	X	X	X
Collect daily sleep diaries					X			X

BP= blood pressure; HR=heart rate; LSEQ = Leeds Sleep Evaluation Questionnaire; RR= respiratory rate; temp=temperature, LSEQ=Leeds Sleep Evaluation Questionnaire

6.2 Efficacy Variables

The efficacy variables were as follows and are listed in Appendix I.

- Leeds Sleep Evaluation Questionnaire: 10 VAS scores that measure four domains of sleep and morning behavior: ease of getting to sleep (GTS), quality of sleep (QoS), hangover on awakening from sleep (AFS), and alertness and behavioral integrity the following morning (BFW).

- Pittsburgh Sleep Quality Index, a valid measure of sleep quality, differentiates "poor" from "good" sleep by measuring 7 areas: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.

- Daily diary: Subjects were instructed to rate each morning, the quality of their sleep (QoN) the last night and each evening, the overall quality of day (QoD), which included

- QoD Q1 level of daytime energy today on a 5-point severity rating scale: 1 = very poor, 5 = very good
- QoD Q2 mood level on a 5-point severity rating scale: 1 = very poor, 5 = very good
- QoD Q3 level of difficulty in concentration on a 5-point severity rating scale: 0 = not present 1 =mild, 2= moderate, 3 = severe, 4= very severe
- QoN: quality of sleep last night on a 5-point severity rating scale: 1 = very poor, 5 = very good

- Wrist actigraphy was used while sleeping to record motion which can be described as total sleep time (time spent asleep after sleep onset), sleep efficiency (total sleep time divided by time in bed multiplied by 100%), wake after sleep onset (sum of mid sleep arousal times after sleep onset), number of awakenings (between sleep onset and offset), and sleep latency (the lag period between entering bed and sleep onset).

6.3 Safety Variables

- Adverse events

6.3.1 Adverse Events

The protocol defined an AE as: Any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product (ICH E2A Guideline: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. Oct 1994).

Note: A procedure is not an AE or SAE, but the reason for the procedure may be an AE or SAE.

Adverse events were collected and reported from the time of signing the ICF to the end of study assessment and follow-up period. Investigators followed subjects with AEs until the event resolved or the condition stabilized. In case of unresolved AEs, these events were followed up until resolution or until they became clinically not relevant.

6.3.2 Assessment of Severity

The following definitions were to have been used to assess intensity of AEs:

Mild: Awareness of sign or symptom, but easily tolerated, i.e., does not interfere with subject's usual function

Moderate: Discomfort enough to cause interference with usual activity

Severe: Incapacitating with inability to work or do usual activity, i.e., interferes significantly with subject's usual function

6.3.3 Causality Assessment

The investigator assessed causal relationship between an adverse event and the study drug on the basis of his/her clinical judgment and the following definitions. The causality assessment must have been made based on the available information and could have been updated as new information became available.

- Related:

The AE follows a reasonable temporal sequence from study drug administration, and cannot be reasonably explained by the subject's clinical state or other factors (e.g., disease under study, concurrent diseases, and concomitant medications).

The AE follows a reasonable temporal sequence from study drug administration, and is a known reaction to the drug under study or its chemical group, or is predicted by known pharmacology.

- Not Related:

The AE does not follow a reasonable sequence from study product administration or can be reasonably explained by the subject's clinical state or other factors (e.g., disease under study, concurrent diseases, and concomitant medications).:

6.3.4 Event Outcome

Adverse event outcomes were defined as follows:

- Recovered/Resolved
  - The subject fully recovered from the AE with no residual effect observed.
- Recovering/Resolving
  - The AE improved but did not fully resolved.
- Not Recovered/Not Resolved
  - The AE itself was still present and observable.
- Recovered/Resolved with Sequelae
  - The residual effects of the AE were still present and observable.
  - Included sequelae/residual effects.
- Fatal
  - The word fatal was used when death was a direct outcome of the AE.
- Unknown

6.3.5 Treatment Required for the Event

Treatment, if any, required for an AE was recorded as one of the following:

- None: No treatment was required.
- Medication Required: Prescription and/or over-the-counter medication was required to treat the AE.

- Other: to be specified in the eCRF.

6.3.6 Serious Adverse Events

The investigator or other study personnel was to immediately (within 24 hours) inform the Sponsor of all SAEs that occurred in study subjects regardless of causal relationship. An SAE was an AE that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Is a congenital anomaly/birth defect, or
- Is an important medical event.

Note: The term "life-threatening" in the definition of "serious" refers to an adverse event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe (ICH E2A Guideline. Clinical Safety Data Management: Definitions and Standards or Expedited Reporting. Oct 1994).

Medical and scientific judgment was exercised in deciding whether expedited reporting was appropriate in other situation, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above. Examples include allergic bronchospasm, convulsions, and blood dyscrasias or development of drug dependency or drug abuse.

6.4 Urine Drug Screen

A urine screen for alcohol, cotinine and drugs of abuse (opiates, benzodiazepines, amphetamines, cannabinoids, cocaine, barbiturates, and phencyclidine) was performed for all subjects at Screening. A breath test was also acceptable for alcohol screening. A positive test result disqualified a subject.

6.5 Vital Signs

Vital signs were to be recorded at Screening. Vital signs were to have been recorded after at least 5 minutes in the sitting position and consisted of pulse, DBP, SBP, oral temperature, and respiratory rate.

Body height and weight were to have been measured for all subjects at Screening to determine body mass index (BMI).

6.6 Data Quality Assurance

The investigational site permitted study-related monitoring, audits, IRB review, and regulatory inspections by providing direct access to source data/documents. Direct access included

permission to examine, analyze, verify, and reproduce records and reports that were important to the evaluation of a clinical study.

All data collected during the study were recorded in individual, subject-specific paper-based CRFs, diaries, or on questionnaires. Instructions were provided for the completion of the diaries and questionnaires.

All information and other material used by subjects and investigative staff used vocabulary and language that are clearly understood. The CRF was completed, reviewed, and signed off signed by the investigator. These signatures indicated that the investigator inspected or reviewed the data on the CRF and agreed with the content.

6.7 Statistical Methods Planned in the Protocol and Determination of Sample Size

6.7.1 Statistical/Analytical Issues

6.7.1.1 Stratification and Adjustments for Covariates

Subjects were not stratified, and no adjustments were covariates were made for this study.

6.7.2 Handling of Dropouts or Missing Data

For the data analysis, missing data were not imputed except medications start and stop dates and AE start dates, AE severity and AE relationship to study drug.

Subjects who dropped out or were discontinued were not replaced.

6.7.2.1 Interim Analyses and Data Monitoring

Not applicable.

6.7.2.2 Multicenter Studies

Not applicable.

6.7.2.3 Multiple Comparisons/Multiplicity

There was no adjustment for multiple comparisons/multiplicity.

6.7.2.4 Use of Efficacy Subset or Per-Protocol Analyses

Not applicable.

6.7.2.5 Active-Control Studies Intended to Show Equivalence

Not applicable.

6.7.2.6 Examination of Subgroups

Not applicable.

6.7.3 Statistical Issues in Efficacy Analyses

All data collected in the study were included in tabular summaries. For statistical analysis using repeated measures, only those subjects who had a minimum number of observations were included.

6.7.4 Statistical and Analytical Plans

6.7.4.1 Study Population Data

Demographic characteristics of the analysis sets will be summarized. Continuous demographic variables (age [calculated from date of birth to Screening visit], weight, height, and BMI) for all subjects will be summarized with descriptive statistics

6.7.4.2 Efficacy Analyses

The sleep quality from the diary and LSEQ data and wrist actigraphy that were collected during the run-in period (Week 1) served as the baseline. Data collected from Days 8 to 15 (Week 2 double blind period) were used to evaluate treatment effect. Individual values for each variable (4 diary questions) were tabulated for each day and then were averaged so that there was one value for each day.

For LSEQ, the subject drew a vertical mark on the line for each response. The distance was measured from left to right for each of the 10 queries and lower values indicated poor sleep and higher numbers represented better sleep. The numbers of questions for getting to sleep domain, quality of sleep domain, awake following sleep domain, and behavior following sleep domain were 3, 2, 2, and 3, respectively. Within each domain, the average of the 2 or 3 scores was generated, and that value was used in the analysis.

For wrist actigraphy, data from the lead-in period were averaged as a baseline and compared to the data from Days 8-14. Variables measured were to include: minutes in bed, total sleep time (total minutes in light sleep, deep sleep and rapid eye movement (REM) sleep while in bed), sleep efficiency (total sleep time divided by time in bed multiplied by 100%), number of minutes and percent of time awake while in bed, number of awakenings between sleep onset and offset, sleep onset latency (the lag period between entering bed and sleep onset), as well as the number of episodes of, duration of, and percentage (number of minutes in the specific stage of sleep, divided by the total time in bed), specific stages of sleep (light sleep, deep sleep and REM sleep).

For those subjects who had data for the changes in each parameter from baseline, the treatment differences between the groups were to be compared.

Descriptive statistics were calculated for all variables (one value for the entire treatment period) and included group means and standard deviations (SD). Individual data from daily diary (4 questions regarding quality of sleep and daytime functioning),

The sleep quality from the diary and LSEQ data collected during the run-in period will be used to evaluate the baseline severity and data collected on from Days 8 to 15 will be used to evaluate treatment effect.

To assess within subject changes in sleep, for each of the LSEQ domains, a repeated measures analysis of variance test was performed to evaluate the change from baseline for the placebo and Relaxium treatment. In addition, treatment differences between placebo and Relaxium from baseline (end of Week 1) to the end of Week 2 (end of the double-blind period) were compared. For this analysis subjects needed to have 3 measurements for each of the domains. Using daily diary data, similar analyses were each of the questions related to level of daytime energy, mood, level of difficulty in concentration, and the quality of sleep was performed. For these analyses, subjects needed to have 6 responses for each question.

To assess differences in the number of days in which there was no difficulty in concentration was reported, both treatment groups were compared during Week 2 using Fisher's Exact test. For all analyses, statistically significant differences were declared when $p \leq 0.05$.

Change from Screening in PSQI was to be compared within subjects.

6.7.4.3 Safety Analyses

Safety data were summarized by AEs.

AEs were reported verbatim and were listed in the data listing.

6.8 Changes in the Conduct of the Study or Planned Analyses

6.8.1 Changes in the Conduct of the Study

- Vital signs were not assessed at study completion.
- Body weight, height, and BMI were not calculated.
- Changes in PSQI were not determined from Screening to the end of the study.

6.8.2 Changes in the Planned Analyses

For actigraphy, the following variables were not measured,

- sleep efficiency (total sleep time divided by time in bed multiplied by 100%)
- percent of time awake while in bed,
- number of awakenings between sleep onset and offset,
- sleep onset latency (the lag period between entering bed and sleep onset),
- number of episodes of and percentage [number of minutes in the specific stage of sleep (light, deep and REM sleep), divided by the total time in bed), specific stages of sleep].

6.9 Sample Size Determination

A total of 40 subjects was planned for this study. Sample size calculations were based on mean improvement from baseline in sleep quality based on a prolonged release-melatonin group compared with that in the parallel placebo treated group by about 6 mm on the LSEQ with a SD of 6 (J. Sleep Res. (2007) 16, 372–380). This change in sleep quality would require 16 participants in each group (with α=0.05 and power=80%).

7.0 Results

7.1 Study Subjects

The number of subjects who enrolled in the study, completed the lead-in period and were randomized to double blind medication is shown in Table 2. One subject received lead-in medication and did not return for any follow-up and no data were collected. One subject from each treatment group did not complete the study and no data were collected during Week 2.

Table 2 Subject Enrollment and Disposition

Status	N	Comments
Enrolled	38	
Completed Lead In Period	37	
Discontinued	1	No data
Randomized to Relaxium	20	
Randomized to Placebo	17	
Completed Placebo	16	1 discontinued
Completed Relaxium	19	1 discontinued

7.2 Demographic and Other Baseline Characteristics

Table 2 summarizes the demographic and other baseline characteristics. The average ages for each group were similar with a predominately female White population. The mean PSQI scores were similar between the treatment groups.

Table 3 Demographics and Baseline Characteristics

Parameter[i)]	Placebo (N=17)	Relaxium (N=20)	Overall (N=37)
Age (years)			
Mean (SD)	55.6 (29.97)	52.1 (26.02)	53.6 (28.05)
Minimum	30	28	28
Maximum	73	75	75
Gender			
Male	3	7	10
Female	10	12	22
Not Reported	4	1	5
Ethnicity			
Hispanic or Latino	3	4	7
Not Hispanic or Latino	9	12	21
Not Reported	5	4	9
Race			
Black or African American	2	5	7
White	8	11	19
Not Reported	7	4	11
PSQI score			
Mean (SD)	13.8 (3.62)	14.1 (5.68)	14.5(5.95)
Minimum	3	6	3
Maximum	20	20	20

7.3 Prior and Concomitant Medication

One subject was diabetic and took medication for that condition prior to and during the study.

Other medications included lisinopril, L-Synthroid, and an unidentified medication for the treatment of hypertension.

7.4 Measurements of Treatment Compliance

The investigator conducted pill counts of the returned capsules.

7.5 Protocol Deviations

All of the protocol deviations were minor and consisted of not answering all of the questions of the LSEQ and the daily diary. In addition, several technical difficulties occurred with the actigraphy and in some cases on total sleep time and time in bed were recorded. Unfortunately, the subjects did not monitor these findings periodically or attempt to get them corrected during the trial, so data was lost.

8.0 Efficacy Results

8.1 Daily Diary

Individual responses to the diary questions were averaged for each study day. For each subject a mean value was generated. The grand mean (SD) values for each treatment group for the baseline and treatment periods are shown in Table 4. Baseline values were similar between the groups. Most subjects completed 6 to 7 diaries per week.

In the both groups, 1 subject did not complete the diary and 2 subjects in each group did not complete the diary data during the blinded portion of the study.

Table 4 Daily Diary (All Subjects)

Variable	Placebo (N=17)		Relaxium (N=20)	
	Baseline	Blinded	Baseline	Blinded
QoN				
Mean	2.815	3.323	2.981	3.300
SD	0.860	1.197	1.188	1.453
N	17	17	19	16
QoD Q1				
Mean	3.114	3.531	3.176	3.518
SD	0.990	1.393	1.286	1.511
N	17	16	19	16
QoD Q2				
Mean	3.079	3.428	3.184	3.650
SD	0.953	1.367	1.166	1.564
N	17	16	19	17
N				
QoD Q3				
Mean	1.549	1.193	1.354	1.073
SD	0.702	0.805	0.935	0.868
n	17	16	19	17

QoN =the quality of their sleep the previous night was rated in the morning.
In the evening, the overall quality of day (QoD Q1), level of daytime energy (QoD Q2) were rated on a 5-point scale 1 = very poor, 5 = very good, and the level of difficulty in concentration (QoD

Q3) was rated on a 5-point severity rating scale, 0 = not present 1 =mild, 2= moderate, 3 = severe, 4= very severe.

Repeated measures analysis of variance for subjects with complete data showed a statistically significant difference in concentration level (QoD Q3) between the 2 treatment groups as shown in Table 6. There was clearly a trend for improvement in daytime energy with Relaxium, but it did not reach statistical significance.

Table 5 Mean (SD) Daily Diary Scores (Subjects with both Baseline and Blinded Treatment Periods)

Variable	Placebo (N=17)		Relaxium (N=20)	
	Baseline	Blinded	Baseline	Blinded
QON				
Mean	2.895	3.406	2.93	3.29
95% CI	2.500, 3.291	3.011, 3.801	2.567, 3.297.	2.93, 3.65.
N	16	16	18	18
P value		0.072		0.162.
QoD Q1				
Mean	3.125	3.600	3.111	3.528
95% CI	2.718, 3.5321	3.180, 4.021	2.651, 3.571	3.067, 3.988
N	16	16	18	18
P value		0.107		0.202
QoD Q2				
Mean	3.042	3.367	3.472	3.426
95% CI	2.691, 3.517	2.94 ,3.79	3.029, 3.869	2.983, 3.864
N	16	16	18	18
P value		0.3737		0.881
QoD Q3				
Mean	1.625	1.287	1.278	0.981
95% CI	1.305, 1.945	0.958, 1.620	0.8445, 1.712	0.547, 1.416
N	16	16	18	18
P value		0.1464		0.333

P value based on the within group differences between Baseline and Blinded periods.

Table 6 Daily Diary Scores Differences Between Relaxium and Placebo

Difference between Relaxium and Placebo Groups	QoN	QoD Q1	QoD Q2	QoD Q3
	-0.36	-0.44	-0.53	0.79
P-value	0.1621	0.0889	0.0584	0.0021

As a follow-up to the statistical difference in QoD Q3, which relates to difficulty in concentration while taking blinded treatment, the number of days that subjects reported no difficulty in concentration was 19 of 90 days for placebo (21%) and 41 of 108 days) for Relaxium treatment (38%). The difference between the 2 groups was highly statistically significant at p = 0.013. Thus, there was about an 80% increase in the number of days the subjects reported no difficulty in concentration, compared to placebo.

8.2 Leeds Sleep Evaluation Questionnaire

Subjects completed LSEQ over the last 3 to 4 days of each treatment period. The individual values were averaged for each domain and the mean (SD) values are shown in Table 7. Higher values indicate improved sleep and better outcomes after awakening. The Relaxium treatment group had values for GTS and QoS that were lower than for the placebo indicating that those subjects had more difficulty getting to sleep and a lower quality of sleep. Most subjects completed the evaluations during Weeks 1 and 2.

Table 7 Mean (SD) VAS Scores (mm) for LSEQ (All Subjects)

Variable	Placebo (N=17)		Relaxium (N=20)	
	Baseline	Blinded	Baseline	Blinded
GTS				
Mean	36.37	44.65	29.04	47.76
SD	18.341	20.931	16.644	21.072
N	15	15	16	15
QoS				
Mean	36.51	38.52	22.19	52.99
SD	20.591	22.986	19.980	25.244
N	15	15	16	15
AFS				
Mean	34.50	48.77	32.44	57.96
SD	22.844	21.297	22.886	23.607
N	15	15	16	15
BFW				
Mean	39.14	50.29	37.14	55.89
SD	21.493	23.094	21.270	23.844
N	15	15	16	16

AFS = awakening following sleep (compared to usual), BFW = behavior following awakening (how you feel when you wake up), GTS = getting to sleep (compared to usual), QoS = quality of sleep (compared to normal sleep)

For the repeated measures analysis of variance, only subjects with complete data for both treatment periods were included (Table 8). Relaxium treatment resulted in improved parameters such as getting to sleep (easier time to fall asleep, less time to fall asleep and more sleepy than normal) and quality of sleep (calmer sleep with fewer wakeful periods). For behavior following wakening, subjects in both groups felt they were more alert after awakening, but the effect was greater in the Relaxium group (Tables 8 and 9). For the domain AFS (awakening was easier than usual and took less time), Relaxium treatment had a statistically greater effect from the lead-in period and was statistically different from placebo treatment.

Table 8 Mean (SD) VAS Scores (mm) for LSEQ (Subjects with both Baseline and Blinded Treatment Periods)

Variable	Placebo (N=15)		Relaxium (N=14)	
	Baseline	Blinded	Baseline	Blinded
GTS				
Mean	35.80	44.17	27.92	48.01
95% CI	27.92, 43.66	36.291, 52.043	20.69, 35.15	40.778, 55.25
N	15	15	14	14
P value		0.13		0.0004
QoS				
Mean	35.84	44.21	22.56	53.214
95% CI	26.40, 45.28	34.77, 53.65	12.18, 32.94	43.39, 63.05
N	15	15	14	14
P value		0.21		0.002
AFS				
Mean	34.83	48.11	34.92	58.595
95% CI	25.46, 44.21	38.74, 57.48	25.68, 44.15	49.80, 67.39
N	15	15	14	14
P value		0.05		0.001
BFW				
Mean	35.40	50.24	31.89	56.91
95% CI	26.68, 49.11	41.52, 58.95	23.46, 40.33	48.67, 65.15
n	15	15	14	14
P value		0.02		0.002

AFS = awakening following sleep, BFW = behavior following awakening, GTS = getting to sleep, QoS = quality of sleep

P value based on the within group differences between Baseline and Blinded periods.

For all 4 domains the treatment effect of Relaxium was statistically greater than for placebo. The mean differences the treatments expressed as changes from baseline are shown in Table 9.

Table 9 Change From Baseline: Treatment Differences Between Relaxium and Placebo

	QoS	GTS	BFW	AFS
Difference between Relaxium and Placebo Groups	+12.3	+12.2	+10.2	+10.4
P-value	0.002	0.006	0.028	0.034

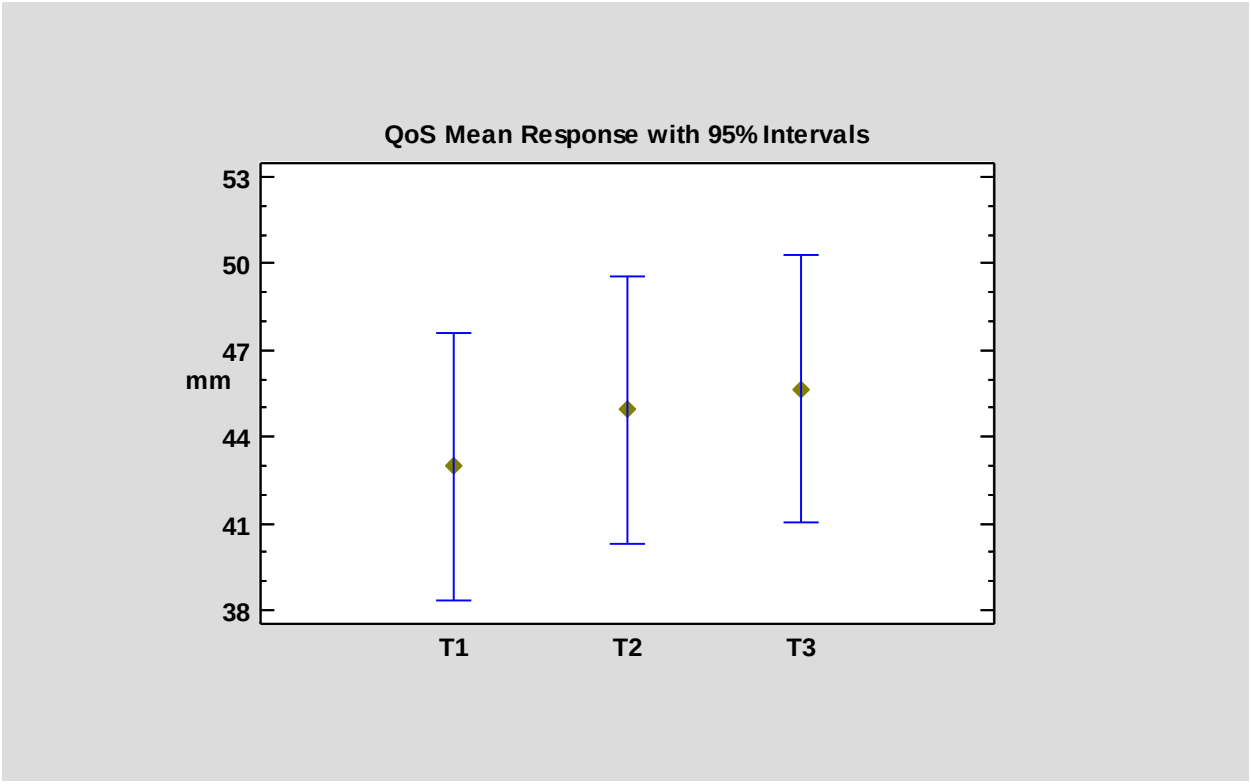
To determine relative effectiveness, the mean changes in LSEQ from Week 2 to Week 1 were compared in subjects who had paired values. The ratios of the mean increase from baseline in VAS scores are shown in the Table 10 and indicate that there was a 2.4 to 3.7-fold more favorable effect in getting to sleep and quality of sleep, compared to baseline. The changes in awakening following sleep (easier time for awakening) and behavior following awakening (more alert) were also greater by 1.7 to 1.8-fold.

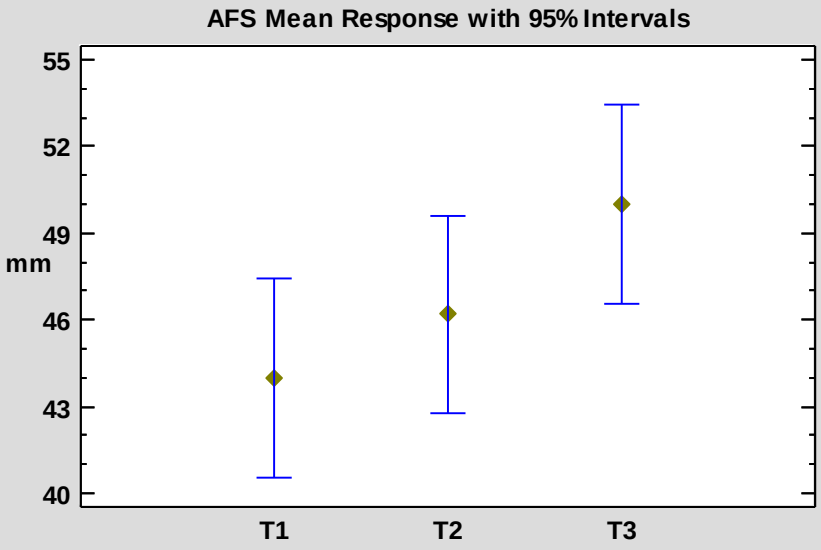
Table 10 Relative Effectiveness of Relaxium to Placebo

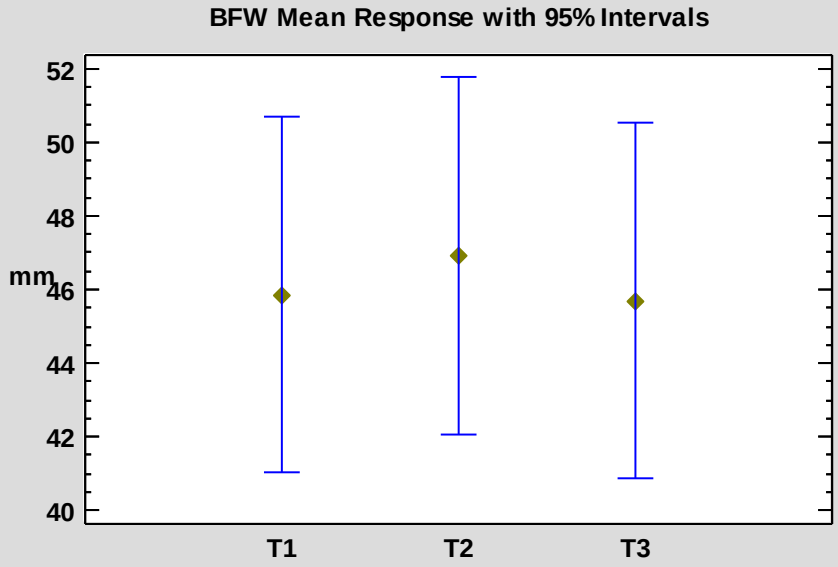
Parameter	Placebo (mm)	Relaxium (mm)	Fold Increase
GTS	8.37	20.09	2.4
QoS	8.37	30.65	3.66
AFS	13.28	23.67	1.78
BFW	14.84	25.02	1.69

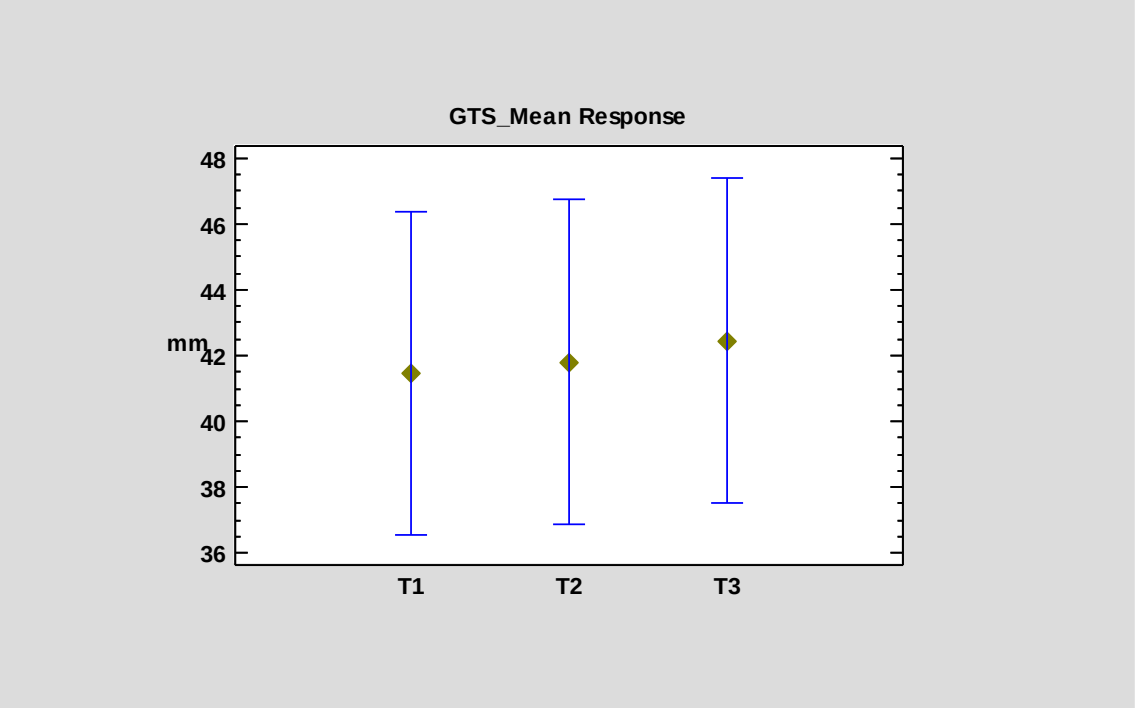
It was also of interest to determine what the variability of the responses in the four domains for Relaxium over 3 consecutive days (T1, T2 and T3) at the end of Week 2. Figure 1 summarizes the response for each domain. For the most part there was no difference between days except for AFS (awakening was easier than usual and took less time) seemed to improve with time.

Figure 1 Mean and 95% CI for Four LSEQ Domains Over 3 Days with Relaxium




AFS Mean Response with 95% Intervals
55
52
49
mm
46
43
40
T1
T2
T3


BFW Mean Response with 95% Intervals
52
50
48
mm
46
44
42
40
T1
T2
T3



8.3 Fitbit Data

Mean (SD) values for various sleep parameters (time in bed, time asleep, time awake, light sleep, deep sleep, and REM sleep) were recorded for most of the subjects (Table 11). For some subjects, not all measurements were taken for each of the days or some of the variables could not be determined. The was likely to either the device not being worn correctly or technical issues with the device.

Table 11 Mean (SD) Sleep Parameters Values with Fitbit Device (All Subjects)

Sleep Parameters	Placebo (N=17)		Relaxium (N=20)	
	Baseline	Blinded	Baseline	Blinded
Asleep				
Mean	370.0	352.8	362.6	355.7
SD	63.5	109.0	99.6	91.4
N	17	16	17	16
In Bed				
Mean	414.9	396.2	413.7	411.7
SD	71.3	124.8	116.6	109.4
N	17	16	17	16
Awake				
Mean	48.7	48.3	54.5	53.7
SD	19.5	23.4	21.3	20.2
N	15	14	15	14

Light Sleep				
Mean	217.6	214.9	219.5	225.7
SD	85.2	98.8	74.4	76.2
N	15	14	15	14
Deep Sleep				
Mean	57.2	60.7	60.3	55.9
SD	24.1	28.1	25.0	24.9
N	15	14	15	14
REM Sleep				
Mean	75.5	74.7	74.7	66.6
SD	31.9	36.1	30.9	28.3
N	15	14	15	14

Overall, it does not appear that there is any difference for these sleep parameters between Relaxium and placebo. As noted in the study objectives, this was an exploratory endpoint, and it is not clear if subjects were diligent in the placement of the device on the wrist since time awake, light sleep, deep sleep, and REM sleep were detected as zero and there were considered missing for the purposes of the calculation.

9.0 Safety Results

There were no adverse events reported in this study.

10.0 Discussion and Conclusion

Based on the findings of this relatively small double-blind randomized placebo-controlled study, using a validated methodology, it was found that sleep was improved on Relaxium treatment. The LSEQ findings showed that subjects had an easier time to fall asleep, the sleep was rated as calmer with less wakeful periods than during the lead-in period. In addition, awakening following sleep was easier and there was improved alertness after awakening.

Placebo treated subjects also reported the improvements in AFS and BFW, but the magnitude of the difference from the respective Lead in Period was significantly greater for Relaxium. The observation that placebo had some effect on AFS and BFW underscores the need to conduct double blind for evaluation of sleep.

Consistent with subjects being more alert, the findings from the daily diary found that concentration improved more significantly with Relaxium than placebo. The number of days that subjects reported no difficulty in concentration was about 80% higher with Relaxium compared to placebo.

In summary, Relaxium treatment over 1 week had a dramatic positive impact on various sleep indices as shown using validated methodology. No adverse events were reported in this study.

11.0 References

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Appendix I

Protocol

CLINICAL%20STUDY
%20PROTOCOL-Rela:

Case Report Form

ABRI%20-002%20CR
F.doc

Leeds Sleep Evaluation Scale

Leeds and
Ptittsburgh Questionr

Daily Diary

ABR-002%20sleep%
20diary%20QOD%20

Informed Consent Form

4-24-19%20final%20
from%20IRB.docx

Appendix II End of Text Tables

Daily Diary

QoD

Q1	How would you rate the quality of your day (QOD)?				
	1	**2**	**3**	**4**	**5**
	Very Poor				Very Good
Q2	How would you rate the level of daytime energy today?				
	1	**2**	**3**	**4**	**5**
	Very Poor				Very Good
Q3	How would you rate the level of difficulty in concentration today?				
	0 = Not present	**1 =Mild**	**2= Moderate**	**3 =Sev**	**4= Very severe**

QoN

Q1	How would you rate the quality of your sleep last night (QON)?				
	1	**2**	**3**	**4**	**5**
	Very Poor				Very Good

Q = question; sev = severe

Placebo

Baseline ubject	QoN	QoD Q1	QoD Q2	QoD Q3
2	4.13	4.50	4.13	1.50
4	2.80	3.43	2.86	1.71
5	3.00	3.17	4.00	0.67
8b	2.70	3.10	2.90	0.10
10	3.00	2.60	2.70	2.30
12	2.75	3.00	3.00	1.86
14	3.60	4.40	4.00	1.00
22	2.10	2.17	2.33	1.33
24	2.43	3.00	3.00	1.71
28	ND	ND	ND	ND
30	2.86	3.00	2.86	2.00
36	2.86	3.00	2.86	1.71
40	2.00	2.57	2.29	1.86
46	2.86	2.71	2.43	1.57
50	3.14	3.86	4.14	1.71
54	2.50	2.57	2.71	2.14
56	3.29	3.71	3.57	0.71
58	1.86	2.14	2.57	2.43
Mean	2.815	3.114	3.079	1.549
SD	0.860	0.990	0.953	0.702

Blinded Subject	QoN	QoD Q1	QoD Q2	QoD Q3
2	4.43	4.57	4.86	0.43
4	4.14	4.14	3.71	2.00
5	3.40	3.50	3.71	0.80
8B	2.40	3.30	3.00	0.00
10	3.30	3.10	3.00	2.30
12	2.88	ND	ND	ND
14	4.86	5.00	4.70	0.40
22	4.30	4.29	4.14	0.71
24	3.17	3.00	3.17	1.17
28	ND	ND	ND	ND
30	3.33	3.17	2.83	2.00
36	2.00	3.00	2.00	2.00
40	1.71	2.00	2.14	2.00
46	4.00	4.14	4.00	0.71
50	4.00	4.14	4.00	0.71
54	2.00	2.29	2.43	1.57
56	3.86	4.14	4.00	0.43
58	2.71	2.71	3.14	1.86
Mean	3.323	3.531	3.428	1.193
SD	1.197	1.393	1.367	0.805

Relaxium

Baseline Subject	QoN	Q1	Q2	Q3
3	3.0	3.0	3.0	1.9
5	3.0	3.2	4.0	0.7
7	1.5	1.3	2.00	0.5
8	2.7	3.1	2.9	0.1
11	4.9	4.9	4.9	0
15	2.7	3.1	2.9	0.1
17	2.7	4.9	4.7	1.3
20	1.7	1.1	2.3	2.6
21	2.7	4.0	3.3	1.2
23	2.3	3.2	3.2	1.0
25	4.3	4.4	4.3	0.0
27	3.0	3.0	2.9	1.9
33	2.9	3.0	3.4	2.0
35	1.9	2.1	1.6	3.1
37	3.9	3.9	3.9	2.6
39	2.9	2.5	2.3	1.5
43	2.1	2.0	2.9	1.1
45	3.4	4.0	3.7	1.3
49	2.9	3.1	3.1	1.0
55	5	3.6	2.1	2
Mean	2.967	3.173	3.167	1.292
SD	0.948	1.031	0.887	0.911

Blinded

Subject	QoN	Q1	Q2	Q3
3	ND	2	2	2.3
5	3.4	3.5	3.7	0.8
7	4.6	4.1	4.4	0.0
8	2.4	3.3	3.0	0.0
11	ND	ND	ND	ND
15	2.5	3.3	2.8	0.0
17	ND	ND	ND	ND
20	3.3	3	4.1	1.9
21	4.0	4.5	4.3	0.3
23	2.3	3.0	3.6	1.0
25	4.3	4.3	4.4	0.4
27	3.0	3.4	3.3	1.9
33	4.0	4.0	4.1	1.0
35	2.7	3.3	2.7	2.3
37	3.8	3.9	3.9	2.1
39	3.2	3.2	3.2	1.2
43	1.4	2.1	3.0	0.0
45	4.1	4.3	4.8	0.7
49	3.3	2.9	2.7	2.3
55	2.9	5	5	0
Mean	3.247	3.507	3.613	1.016
SD	1.416	1.312	1.361	0.909

Leeds

Placebo	**Baseline**	**Baseline**	**Baseline**	**Baseline**
Subject	GTS	QoS	AFS	BFW
2	32.7	29.6	7.6	11.5
4	29.9	23.5	41.7	36.2
8	55.3	54.7	55.3	56.0
10	56.0	47.3	48.0	41.5
12	ND	ND	ND	ND
14	34.8	15.0	15.3	18.3
22	26.2	30.8	2.8	73.3
24	26.0	76.7	76.0	66.0
28	ND	ND	ND	ND
30	28.7	23.7	32.3	24.7
36	6.0	20.7	13.0	35.0
40	42.0	26.7	22.0	49.3
46	22.3	19.3	24.0	20.0
50	45.3	45.8	47.8	38.7
54	51.0	50.7	47.3	32.0
56	58.7	57.7	59.0	58.7
58	30.7	25.7	25.3	26.0
Mean	36.37	36.51	34.50	39.14
SD	18.341	20.591	22.844	21.493
Placebo	**Blinded**	**Blinded**	**Blinded**	**Blinded**
Subject	GTS	QoS	AFS	BFW
2	68.8	69.8	70.4	72.7
4	57	55.5	58.8	63.5
8	27.5	33.0	50.0	58.5
10	30.0	11.7	35.0	24.7
12	ND	ND	ND	ND
14	35.3	28.8	27.5	34.5
22	69.1	6.3	67.0	67.3
24	43.8	61.8	56.5	56.8
28	ND	ND	ND	ND
30	21.7	21.7	47.0	19.3
36	44.0	40.7	42.0	52.7
40	22.7	8.0	18.3	47.3
46	64.3	64.3	65.0	69.3
50	54.0	49.0	59.7	64.0
54	38.0	35.3	40.0	27.0
56	50.3	49.3	50.0	51.3
58	43.3	42.7	44.3	45.3
Mean	44.65	38.52	48.77	50.29
SD	20.931	22.986	21.297	23.094

FitBit

Placebo Baseline Week 1 (minutes)

Subject	Asleep	In Bed	Awake	Light	Deep	REM
2	363.2	394.3	34.8	193.3	58.8	97.3
8B	364.8	420.6	55.3	246.3	68.1	37.3
10	445.3	493.7	48.3	306.8	64.2	74.3
12	459.2	459.2	nd	nd	nd	nd
14	390.3	439.3	49.0	210.3	62.7	117.3
22	336.2	384.4	46.2	190.0	59.2	61.0
24	387.0	432.3	45.3	215.2	91.3	80.5
28	346.2	394.7	47.8	219.2	31.7	82.0
30	387.3	439.2	51.2	211.4	50.0	92.2
36	313.3	346.5	33.2	193.7	47.0	72.7
39	300.1	331.6	nd	nd	nd	nd
40	459.7	532.8	78.2	307.8	70.2	86.6
46	347.9	392.1	39.6	170.4	54.4	69.3
50	275.3	310.9	40.3	199.0	33.5	34.3
54	503.8	574.4	66.0	282.6	72.4	84.0
56	305.3	347.4	42.0	161.5	38.8	68.2
58	305.6	360.4	53.6	156.2	56.0	75.6
Mean	370.0	414.9	48.7	217.6	57.2	75.5
SD	63.5	71.3	19.5	85.2	24.1	31.9
N	17	17	15	15	15	15

Placebo Blinded Week 2 (minutes)

Subject	Asleep	In Bed	Awake	Light	Deep	REM
2	418.2	453.0	33.6	216.4	61.8	120.0
8B	404.9	469.9	64.6	269.9	73.7	42.1
10	469.1	528.1	59.0	327.1	67.0	75.0
12	369.5	369.5	ND	ND	ND	ND
14	348.6	391.3	41.1	180.4	56.0	89.1
22	285.3	316.8	31.5	161.5	56.7	67.2
24	362.0	400.0	33.8	164.8	85.7	68.7
28	350.0	406.0	56.0	241.5	38.5	70.0
30	324.5	369.0	51.0	198.3	75.7	99.0
36	258.2	280.8	36.0	175.3	40.3	68.0
39	273.0	300.8	ND	ND	ND	ND
40	445.8	532.2	86.3	309.2	67.8	68.8
46	ND	ND	ND	ND	ND	ND
50	272.6	310.6	44.0	198.5	53.5	50.3
54	452.0	507.8	55.8	249.8	86.7	115.5
56	273.0	312.9	36.1	144.9	35.9	51.3
58	337.4	390.9	47.7	170.6	50.3	60.6
Mean	352.1	396.2	48.3	214.9	60.7	74.7
SD	109.0	124.8	23.4	98.8	28.1	36.1
	16	16	14	14	14	14

Relaxium Baseline Week 1 (minutes)

Subject	Asleep	In Bed	Awake	Light	Deep	REM
3	356.1	410.0	50.7	214.6	41.6	53.3
5	310.1	342.9	34.7	195.0	43.7	86.2
7	431.4	514.3	81.9	280.7	63.6	64.7
11	273.1	310	43.0	212.8	54.5	39.8
15	364.8	420.6	55.3	246.3	68.1	37.3
17	367.2	415.5	48.0	203.7	72.7	73.5
20	ND	ND	ND	ND	ND	ND
21	358.1	414.4	63.8	208.4	60.4	76.8
23	379.5	439.8	58.5	207.2	73.3	78.7
25	334.0	373.3	39.3	214.0	46.0	74.0
27	386.8	443.7	56.8	191.2	83.8	111.8
33	397.2	442.4	46.3	199.8	85.3	70.0
35	318.9	381.0	64.2	248.5	23.7	54.0
37	352.4	395.4	42.0	190.3	41.3	91.4
39	300.1	331.6	ND	ND	ND	ND
43	390.7	445.4	53.9	215.6	82.7	72.3
45	497.4	585.3	83.3	252.0	70.7	109.1
49	279.4	319.4	50.0	181.8	54.6	79.8
55	425.1	480.6	55.4	269.4	58.7	97.0
57	366.8	395.3	ND	ND	ND	ND
Mean	362.6	413.7	54.5	219.5	60.3	74.7
SD	99.6	116.6	21.3	74.4	25.0	30.9
N	18	17	15	15	15	15

Relaxium Blinded Week 2 (minutes)

Subject	Asleep	In Bed	Awake	Light	Deep	REM
3	317.0	363.8	44.2	185.4	38.0	50.6
5	356.0	400.8	44.8	232.8	31.8	91.3
7	378.4	443.1	64.7	267.9	51.9	58.7
11	317.2	360.0	41.8	228.6	33.6	32.0
15	404.9	469.9	64.6	269.9	73.7	42.1
17	421.6	468.3	45.7	237.3	78.1	84.1
20	ND	ND	ND	ND	ND	ND
21	344.0	403.3	59.3	240.0	43.8	67.5
23	365.0	410.7	45.2	196.3	83.7	69.5
25	356.3	403.7	47.3	232.2	47.2	77.0
27	377.0	434.5	57.5	199.2	79.2	98.7
33	387.8	436.8	49.0	242.5	65.5	79.8
35	303.0	356.3	60.8	229.6	35.0	45.6
37	341.4	386.9	45.4	191.4	60.1	78.7
39	273.0	300.8	ND	ND	ND	ND
43	318.9	367.0	60.0	230.0	77.6	60.0
45	425.0	514.9	86.9	254.3	61.3	89.1
49	322.2	373.2	44.5	166.2	28.5	35.2
55	394.8	516.0	52.0	234.0	62.0	72.0
57	ND	ND	ND	ND	ND	ND
Mean	355.7	411.7	53.7	225.7	55.9	66.6
SD	91.4	109.4	20.2	76.2	24.9	28.3
N	16	16`	15	15	15	15

Appendix III: Data Listing

Subject 2

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	16-Sep	2	5	4	4
	17-Sep	3	4	4	3
	18-Sep	4	4	3	2
	19-Sep	4	4	3	1
	20-Sep	5	5	5	0
	21-Sep	5	5	5	0
	22-Sep	5	5	5	0
	23-Sep	5	4	4	2
	24-Sep	4	4	4	1
Wk 2	25-Sep	3	4	5	1
	26-Sep	4	4	5	0
	27-Sep	5	5	5	1
	28-Sep	5	5	5	0
	29-Sep	5	5	5	0
	30-Sep	5	5	5	0

Leeds

	Week 1				Week 2			
GTS	6.53	0.2	2.53	3.8	6.47	6.87	6.63	7.53
QoS	4.05	3.75	0.05	4	6.1	7.7	6.75	7.35
AFS	0	0.05	0.2	2.8	7	6.7	7.05	7.40
BFW	2	0	0.13	1.33	7.57	7	7.13	7.36
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
9/18/19	239	251	0	0	0	0
9/19/19	217	235	18	110	48	59
9/20/19	253	284	31	169	24	60
9/21/19	543	579	0	0	0	0
9/22/19	618	682	64	320	102	196
9/23/19	309	335	26	174	61	74
9/24/19	491	534	43	220	101	170
9/25/19	398	431	27	173	57	68
9/26/19	304	341	37	158	43	103
9/27/19	552	596	44	336	44	172

9/30/19	346	363	17	195	64	87

Subject 3

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	21-Jul	3	3	3	2
	22- Jul	nd	3	3	2
	23- Jul	3	3	3	1
	24- Jul	3	3	3	1
	25- Jul	3	3	3	2
	26- Jul	3	3	3	3
	27- Jul	3	3	3	2
Wk 2	28- Jul	2	3	2	2
	29- Jul	2	2	2	2
	30- Jul	nd	nd	nd	nd
	31- Jul	2	2	2	2
	1- Aug	2	2	2	2

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
7/21/19	303	357	54	195	51	57
7/22/19	250	286	30	158	7	6
7/23/19	488	545	57	332	43	113
7/24/19	292	342	50	193	59	40
7/25/19	287	342	55	191	40	56
7/26/19	415	475	53	195	49	34
7/27/19	458	523	56	238	42	67
7/28/19	279	321	32	111	17	24
7/29/19	228	271	43	144	24	60
7/30/19	428	484	53	229	56	55
7/31/19	292	329	37	198	47	47
8/1/19	358	414	56	245	46	67

Subject 4

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	26-Jan	3	4	2	2
	27-Jan	3	4	3	2
	28-Jan	2	3	2	2
	29-Jan	3	3	2	2
	30-Jan	nd	4	3	3

	31-Jan	nd	3	5	0
	1-Feb	3	3	3	1
Wk 2	5-Feb	4	4	4	3
	6-Feb	4	4	3	3
	7-Feb	4	3	4	2
	8-Feb	4	4	4	2
	9-Feb	4	4	3	3
	10-Feb	4	5	4	1
	11-Feb1	5	5	4	0

Leeds

	Week 1				Week 2			
GTS	2.37	3.1	3.5		4.83	5.93	6.33	
QoS	2.65	2.4	2		4.55	6.3	5.8	
AFS	4.35	3.25	4.9		4.65	6.85	6.15	
BFW	2.47	4.03	4.37		6.6	6.43	6.03	
Values in 0.1 mm								

NO FITBIT

Subject 5

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	12-Jan	3	3	4	0
	13-Jan	3	3	4	1
	14-Jan	3	3	4	0
	15-Jan	3	4	4	1
	16-Jan	3	3	4	1
	17-Jan	3	3	4	1
	18-Jan	nd	3	4	2
Wk 2	18-Jan	Nd	4	4	1
	19-Jan	3	3	4	1
	20-Jan	Nd	4	4	1
	21-Jan	3	4	4	1
	22-Jan	5	4	4	0
	23-Jan	3	3	3	1
	24-Jan	3	3	3	1

Leeds

	Week 1				Week 2			
GTS	0.9	1.6	0.9		1.8	6.1	6.8	

QoS	1.5	1.1	1.5		1.2	5.9	6.6	
AFS	2.3	4	2.3		6.6	6.1	6.9	
BFW	5	6.1	5		6.9	6.8	7.4	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/12/20	278	308	30	136	34	108
1/13/20	445	487	42	272	61	112
1/14/20	211	234	23	163	30	18
1/15/20	368	402	34	232	51	85
1/16/20	302	346	44	170	35	97
1/17/20	222	243	nd	nd	nd	nd
1/18/20	345	380	35	197	51	97
1/19/20	490	542	52	298	66	126
1/20/20	276	315	39	212	0	64
1/21/20	288	328	40	185	26	77
1/22/20	449	500	51	289	42	118
1/23/20	341	394	53	210	51	80
1/24/20	292	326	34	203	6	83

Subject 7

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	1-Aug	2	2	2	0
	2-Aug	1	1	2	1
	3-Aug	2	1	2	0
	4-Aug	1	1	3	1
	5-Aug	1	1	1	0
	6-Aug	2	2	2	1
Wk 2	18-Sep	5	4	4	0
	19-Sep	4	4	4	0
	20-Sep	4	4	4	0
	21-Sep	5	4	5	0
	22-Sep	5	4	5	0
	23-Sep	4	4	4	0
	24-Sep	5	5	5	0

Leeds

	Week 1	Week 2

GTS	0.75	1	0.8		7.2	6.9	7.2	
QoS	1.05	1.15	0.85		7.2	6.8	6.85	
AFS	1.1	0.8	1		7	6.85	6.9	
BFW	0.67	0.9	1.03		6.9	6.7	6.77	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
7/31/19	341	387	39	95	28	61
8/1/19	411	502	91	294	58	59
8/2/19	428	522	94	314	60	54
8/3/19	460	538	78	274	102	84
8/4/19	468	537	69	364	59	45
8/5/19	428	515	87	315	56	57
8/6/19	484	599	115	309	82	93
9/17/19	426	507	81	251	58	117
9/18/19	431	502	71	364	33	34
9/19/19	333	385	52	282	30	21
9/20/19	266	325	59	157	42	67
9/21/19	435	505	70	319	55	61
9/22/19	287	321	34	207	46	34
9/23/19	471	557	86	295	99	77

Subject 8A

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	27-Aug	3	3	3	4
	28-Aug	2	2	3	3
	29-Aug	3	3	4	3
	30-Aug	nd	nd	3	2
	1-Sep	3	3	4	3
	2-Sep	3	3	2	2
	3-Sep	2	2	3	3
Wk 2	4-Sep	3	3	3	3
	5-Sep	3	3	4	4
	6-Sep	0	0	nd	nd
	7-Sep	3	3	3	2
	8-Sep	3	3	3	2
	9-Sep	3	3	4	4
	10-Sep	2	2	3	3

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
8/27/19	422	485	63	264	98	60
8/28/19	400	453	53	292	77	31
8/29/19	304	339	35	234	59	11
8/30/19	432	521	89	280	101	51
8/31/19	255	287	32	197	41	17
9/1/19	383	447	64	249	61	73
9/2/19	351	399	nd	nd	nd	nd
9/3/19	371	434	51	208	40	18
9/4/19	461	535	74	294	103	64
9/5/19	406	462	56	327	75	4
9/6/19	372	405	30	188	39	11
9/7/19	430	504	74	284	73	73
9/8/19	393	460	67	299	68	26
9/9/19	356	419	63	237	73	46
9/10/19	416	504	88	260	85	71

Subject 8B

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	26-Jan	2	3	3	2
	27-Jan	2	3	3	2
	28-Jan	3	3	3	1
	29-Jan	3	3	3	1
	30-Jan	3	3	4	2
	31-Jan	3	4	4	2
	1-Feb	4	4	4	2
Wk 2	5-Feb	3	3	3	2
	6-Feb	3	3	4	2
	7-Feb	4	4	4	2
	8-Feb	3	4	4	2
	9-Feb	4	4	4	2
	10-Feb	4	4	4	2
	11-Feb	3	4	4	2

Leeds

	Week 1				Week 2			
GTS	4.7	5.8	6.1		2.8	2.7		
QoS	5.7	5.2	5.5		2.8	3.8		
AFS	4.7	5.8	6.1		4.1	5.9		

BFW	5.8	5.4	5.6		5.3	6.4		
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/26/20	357	417	60	211	71	75
1/27/20	219	256	37	152	23	44
1/28/20	526	606	80	358	53	115
1/29/20	332	388	56	200	53	79
1/30/20	315	358	31	155	34	4
1/31/20	201	230	29	183	8	10
2/1/20	291	319	28	191	44	56
2/5/20	334	380	46	255	43	36
2/6/20	262	305	43	179	32	51
2/9/20	331	368	0	0	0	0

Subject 10

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	26-Sep	3	3	2	3
	27-Sep	3	2	3	2
	28-Sep	2	2	2	2
	29-Sep	4	2	2	2
	30-Sep	3	3	4	2
	1-Oct	3	3	2	3
	2-Oct	3	3	4	2
Wk 2	4-Oct	4	3	2	2
	5-Oct	3	3	4	1
	6-Oct	3	3	2	2
	7-Oct	3	3	2	2
	8-Oct	4	4	4	3
	9-Oct	3	3	3	3
	10-Oct	3	3	4	3

Leeds

	Week 1				Week 2			
GTS	2.8	5.1	6.8	7.7	2.8	3.1	3.1	Nd
QoS	2.1	6.1	4.9	5.8	0.8	1.2	1.5	Nd
AFS	2.1	3.1	6.5	7.5	3.4	3.4	3.7	Nd
BFW	4.1	4.2	1	7.3	2.6	1.9	2.9	Nd
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
9/27/19	478	526	48	315	77	86
9/28/19	496	580	84	378	91	27
9/29/19	433	465	32	314	58	61
9/30/19	414	441	27	252	70	92
10/1/19	415	465	50	272	39	104
10/2/19	436	485	49	310	50	76
10/4/19	532	601	69	366	83	83
10/5/19	421	490	69	305	60	56
10/6/19	435	494	59	269	62	104
10/7/19	519	567	48	384	46	89
10/8/19	399	462	63	274	42	83
10/9/19	475	534	59	334	94	47
10/10/19	503	549	46	358	82	63

Subject 11

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	11-Oct	5	5	5	0
	12-Oct	5	5	5	0
	13-Oct	5	5	5	0
	14-Oct	5	5	5	0
	15-Oct	5	5	5	0
	16-Oct	5	5	5	0
	17-Oct	4	4	4	0

Leeds

	Week 1				Week 2			
GTS	3.1	2.87	3.73		4.93	4.93	5.3	
QoS	1.2	1.35	1.4		7.3	7.2	7.5	
AFS	1.15	2.05	0.75		7.4	7.2	7.2	
BFW	1.37	1.3	0.87		7.36	7.4	7.43	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/10/19	295	343	48	209	48	38
10/12/19	261	289	28	167	55	39
10/13/19	69	69	nd	nd	nd	nd
10/14/19	388	436	48	241	86	61

10/15/19	271	320	49	196	30	45
10/16/19	398	446	48	285	68	45
10/17/19	230	267	37	179	40	11
10/19/19	240	273	33	202	26	12
10/20/19	282	340	58	205	73	4
10/21/19	431	472	41	345	12	74
10/22/19	362	412	50	268	29	65
10/23/19	271	303	27	123	43	5

Subject 12

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	9-Sep	2	3	3	2
	10-Sep	3	3	3	2
	11-Sep	3	3	3	1
	12-Sep	2	3	3	1
	13-Sep	3	3	3	2
	14-Sep	4	3	3	3
	15-Sep	2	3	3	2
	16-Sep	3	nd	nd	nd
Wk 2	17-Sep	2	nd	nd	nd
	18-Sep	3	nd	nd	nd
	19-Sep	3	nd	nd	nd
	20-Sep	3	nd	nd	nd
	21-Sep	4	nd	nd	nd
	22-Sep	2	nd	nd	nd
	23-Sep	3	nd	nd	nd
	24-Sep	3	nd	nd	nd

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
9/11/19	596	596	0	0	0	0
9/12/19	594	594	0	0	0	0
9/13/19	366	366	0	0	0	0
9/14/19	432	432	0	0	0	0
9/15/19	477	477	0	0	0	0
9/16/19	290	290	0	0	0	0
9/17/19	393	393	0	0	0	0
9/18/19	352	352	0	0	0	0

9/19/19	313	313	0	0	0	0
9/20/19	262	262	0	0	0	0
9/21/19	352	352	0	0	0	0
9/22/19	662	662	0	0	0	0
9/23/19	284	284	0	0	0	0
9/24/19	338	338	0	0	0	0

Subject 14

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	12-Oct	4	5	4	1
	13-Oct	3	3	2	2
	14-Oct	3	5	4	1
	15-Oct	4	5	5	0
	16-Oct	1	3	3	2
	17-Oct	5	5	5	0
	18-Oct	5	5	5	1
Wk 2	19-Oct	5	5	5	1
	20-Oct	5	5	5	0
	21-Oct	5	5	5	1
	22-Oct	5	5	3	1
	23-Oct	5	5	5	0
	24-Oct	4	5	5	0
	25-Oct	5	5	5	0

Leeds

	Week 1				Week 2			
GTS	3.7	4.3	2.5	3.4	3.5	3.4	3.5	3.7
QoS	1.2	1	1.4	2.4	2.8	2.9	3.3	2.5
AFS	0.6	1	1.7	2.8	2.4	2.4	3.6	2.6
BFW	0.7	2.5	1.5	2.6	2.8	3.2	4.6	3.2
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/12/19	464	526	62	263	67	134
10/13/19	371	413	42	181	74	116
10/14/19	414	451	37	196	82	136
10/15/19	411	452	41	207	40	164
10/16/19	252	292	40	148	44	60
10/17/19	476	538	62	250	105	121
10/18/19	344	403	59	227	27	90

10/19/19	382	425	43	179	66	137
10/20/19	424	468	44	240	49	135
10/21/19	400	441	41	220	74	106
10/22/19	420	498	78	240	91	89
10/23/19	329	362	33	162	69	98
10/24/19	161	172	0	0	0	0
10/25/19	324	373	49	222	43	59

Subject 15

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	27-Aug	3	3	4	1
	28-Aug	2	3	3	0
	29-Aug	3	4	3	0
	30-Aug	nd	3	2	0
	1-Sep	3	4	3	0
	2-Sep	3	2	2	0
	3-Sep	2	3	3	0
Wk 2	4-Sep	3	3	3	0
	5-Sep	3	4	4	0
	6-Sep	1	3	2	0
	7-Sep	3	3	2	0
	8-Sep	3	3	2	0
	9-Sep	3	4	4	0
	10-Sep	2	3	3	0

Leeds

	Week 1				Week 2			
GTS	5.9	2.6	4.1					
QoS	3	1.4	3.6					
AFS	2	1.5	3.1					
BFW	8.6	1.3	4.9		4.7	3.5	6.4	6.00
Values in 0.1 mm								

NO FITBIT

Subject 17

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	23-Jan	5	5	5	0
	24-Jan	4	5	5	0
	25-Jan	5	5	5	0
	26-Jan	2	5	5	4

27-Jan	1	4	4	1
28-Jan	1	5	5	4
29-Jan	1	5	4	0

Leeds

	Week 1				Week 2			
GTS	1.5	2.2	3.6		4.7	3.5	3.6	
QoS	2.4	2.1	2.5		4.2	4.8	6.6	
AFS	3.6	3.4	4.8		4.2	5.9	6.8	
BFW	2.4	2.4	3.1		5.5	7.5	7.8	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/23/20	462	521	59	257	101	104
1/24/20	420	459	39	223	88	109
1/26/20	201	223	22	116	48	37
1/27/20	321	382	61	191	69	61
1/28/20	473	548	75	279	89	105
1/29/20	326	360	32	156	41	25
1/30/20	463	533	70	299	78	86
1/31/20	402	439	37	226	101	75
2/1/20	466	503	37	228	94	144
2/2/20	249	280	29	124	23	43
2/4/20	492	553	61	342	64	86
2/6/20	362	408	46	225	84	53
2/7/20	517	562	40	217	103	102

Subject 20

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	12-Oct	2	2	2	2
	13-Oct	2	1	2	3
	14-Oct	1	1	2	3
	15-Oct	2	1	2	2
	16-Oct	2	1	3	3
	17-Oct	1	1	3	3
	18-Oct	2	1	2	2
Wk 2	19-Oct	3	3	3	2
	20-Oct	3	3	4	2

21-Oct	3	3	4	2
22-Oct	4	2	4	2
23-Oct	3	3	4	1
24-Oct	3	4	5	2
25-Oct	4	3	5	2

Leeds

	Week 1				Week 2			
GTS	2.7	2.6	2.8	2.6	4.5	4.8	5.1	5.00
QoS	0.3	0	0.1	0.3	4.9	5.1	4.7	5.70
AFS	0.2	0	0.1	0.2	4.2	4.8	5.5	5.80
BFW	2.8	0.2	0.1	1.3	4.3	4.5	4.6	5.50
Values in 0.1 mm								

NO FITBIT

Subject 21

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	20-Oct	2	4	3	2
	21-Oct	2	4	3	1
	22-Oct	3	4	4	1
	23-Oct	2	4	3	1
	24-Oct	4	4	3	1
	26-Oct	3	4	4	1
Wk 2	27-Oct	2	3	3	1
	28-Oct	4	4	4	0
	29-Oct	4	5	4	0
	30-Oct	4	5	5	0
	2-Nov	5	5	5	0
	3-Nov	5	5	5	1

Leeds

	Week 1				Week 2			
GTS	4.5	3.8	3.4	2.6	5.2	5.1	4.8	5.20
QoS	1.9	5.8	4.9	0.3	7	7.1	7.2	7.20
AFS	4.7	6.5	3.1	0.2	7	7	7	6.10
BFW	2.3	6.4	4.7	2.6	7.4	7.2	7.2	5.90

Values in 0.1 mm

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/20/19	340	418	78	267	52	21
10/21/19	345	394	49	174	91	80
10/22/19	341	397	56	187	57	97
10/23/19	365	416	nd	nd	nd	nd
10/24/19	360	444	84	207	71	82
10/25/19	342	394	52	207	31	104
10/26/19	414	438	nd	nd	nd	nd
10/28/19	369	433	64	252	50	67
10/29/19	359	397	38	249	34	76
10/30/19	322	362	40	193	51	78
10/31/19	353	408	55	217	45	91
11/2/19	362	428	66	287	39	36
11/3/19	299	392	93	242	nd	57

Subject 22

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	5-Feb	2	2	2	2
	6-Feb	2	2	2	1
	7-Feb	2	3	3	1
	8-Feb	2	2	2	1
	9-Feb	2	nd	nd	nd
	10-Feb	3	2	3	2
	11-Feb	2	2	2	1
Wk 2	18-Feb	4	4	4	1
	18-Feb	4	4	4	1
	20-Feb	4	5	4	0
	21-Feb	5	4	5	1
	22-Feb	4	4	4	1
	23-Feb	5	4	4	1
	24-Feb	4	5	4	0

Leeds

	Week 1				Week 2			
GTS	2.93	3.47	1.47		6.63	6.2	7.9	
QoS	3.25	3.75	2.25		5.65	6.2	7	
AFS	2.8	3.5	2.05		6.7	6.5	6.9	

BFW	2.67	3.67	2.87		7.33	6.47	6.4	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
2/5/20	236	262	26	173	33	30
2/6/20	235	252	17	117	68	50
2/7/20	340	420	80	180	76	84
2/9/20	402	452	50	227	88	87
2/11/20	468	536	58	253	31	54
2/18/20	274	309	35	168	37	69
2/19/20	283	311	28	122	81	80
2/20/20	351	397	46	190	64	97
2/21/20	201	221	20	115	57	29
2/22/20	285	302	17	174	63	48
2/24/20	318	361	43	200	38	80

Subject 23

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	13-Oct	3	nd	nd	nd
	14-Oct	2	3	2	1
	15-Oct	3	3	4	1
	16-Oct	2	4	4	1
	17-Oct	2	3	3	1
	18-Oct	2	3	3	1
	19-Oct	2	3	3	1
Wk 2	20-Oct	2	3	3	1
	21-Oct	3	3	4	1
	22-Oct	2	3	4	1
	23-Oct	4	2	2	1
	24-Oct	2	4	4	1
	25-Oct	2	3	4	1
	26-Oct	1	3	4	1

Leeds

	Week 1				Week 2			
GTS	0.7	2.8	1.8	1.6	1.3	1.9	2.7	2.4
QoS	0.25	0.5	1	0.5	0.9	0.7	2.3	1.8

AFS	7.5	4.5	3.3	5.9	5.3	3.8	4.9	5.3
BFW	4.4	3.5	2.8	4.1	2.5	3.3	4.2	4
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/13/19	532	666	134	333	114	85
10/14/19	293	351	58	197	47	49
10/15/19	293	324	31	158	57	78
10/16/19	372	424	52	200	68	104
10/18/19	354	414	60	177	101	76
10/19/19	433	460	16	178	53	80
10/20/19	471	515	44	254	82	135
10/21/19	408	447	39	233	81	94
10/22/19	440	533	90	209	87	51
10/23/19	345	377	32	156	105	84
10/24/19	241	277	36	169	65	7
10/25/19	285	315	30	157	82	46

Subject 24

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	12-Oct	2	2	2	3
	13-Oct	2	2	2	3
	14-Oct	3	4	4	1
	15-Oct	3	3	3	1
	16-Oct	3	3	3	2
	17-Oct	3	4	4	0
	18-Oct	1	3	3	2
Wk 2	19-Oct	4	4	4	1
	20-Oct	3	3	3	1
	21-Oct	3	3	3	1
	22-Oct	3	2	3	1
	23-Oct	3	3	3	1
	24-Oct	3	3	3	2
	25-Oct	nd	nd	nd	nd

Leeds

	Week 1	Week 2

GTS	1.9	4	1.9	Nd	3.2	4.9	4.1	5.30
QoS	7.8	7.4	7.8	Nd	8.1	6.6	5.5	4.50
AFS	7.7	7.4	7.7	Nd	5.9	5.3	6.1	5.30
BFW	6.6	6.6	6.6	Nd	5.3	5.2	6.2	6.00
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/13/19	327	355	28	178	82	67
10/14/19	336	380	44	160	91	85
10/15/19	479	532	53	262	126	91
10/16/19	403	458	55	207	100	96
10/17/19	350	387	37	233	64	53
10/18/19	427	482	55	251	85	91
10/19/19	257	282	0	0	0	0
10/20/19	424	471	47	263	82	79
10/21/19	316	336	20	175	86	55
10/22/19	400	441	41	189	120	91
10/23/19	424	462	38	206	142	76
10/24/19	351	408	57	156	84	111

Subject 25

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	12-Oct	4	4	4	0
	13-Oct	4	4	4	0
	14-Oct	4	4	4	0
	15-Oct	4	5	4	0
	16-Oct	5	4	4	0
	17-Oct	4	5	5	0
	18-Oct	5	5	5	0
Wk 2	21-Oct	3	3	4	1
	22-Oct	3	4	4	1
	23-Oct	5	4	5	1
	24-Oct	5	4	5	0
	25-Oct	4	5	5	0
	26-Oct	5	5	4	0
	27-Oct	5	5	4	0

Leeds

	Week 1				Week 2			
GTS	5.3	5.1	6.8	7	5.2	5.1	5.1	5.00
QoS	7.1	7.3	5.5	7.5	7.6	7.5	7.8	5.70
AFS	5.4	7.6	4.4	7.5	7.8	6.4	7.6	5.80
BFW	5.4	6.9	5	7.8	7.7	6	6.4	5.50
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/13/19	302	326	24	187	50	65
10/14/19	368	406	38	177	75	116
10/15/19	304	352	48	211	28	65
10/16/19	384	442	58	255	67	62
10/17/19	304	329	25	199	37	68
10/18/19	342	385	43	255	19	68
10/21/19	447	501	54	236	80	131
10/22/19	181	213	32	166	5	10
10/23/19	362	443	81	291	27	44
10/24/19	261	280	19	150	46	65
10/25/19	373	410	37	251	49	73
10/26/19	514	575	61	299	76	139

Subject 27

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	13-Oct	3	4	3	2
	14-Oct	3	3	2	2
	15-Oct	3	3	4	2
	16-Oct	4	3	3	2
	17-Oct	2	2	2	2
	18-Oct	3	3	3	2
	19-Oct	3	3	3	1
Wk 2	20-Oct	2	3	3	2
	21-Oct	3	3	3	2
	22-Oct	4	4	4	2
	23-Oct	3	4	4	2
	24-Oct	2	3	2	1
	25-Oct	4	4	4	2
	26-Oct	3	3	3	2

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/20/19	380	444	64	206	77	97
10/22/19	394	458	64	202	77	115
10/23/19	382	446	64	206	75	101
10/24/19	240	293	53	145	50	45
10/25/19	462	509	47	207	125	130
10/26/19	404	457	53	229	71	104
10/27/19	365	413	48	202	51	112
10/28/19	275	317	42	162	65	48
10/29/19	379	423	44	153	109	117
11/2/19	427	498	71	210	98	119
11/3/19	418	464	46	227	75	116
11/4/19	418	491	73	166	126	126

Subject 28

NO DIARY

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
10/21/19	334	389	55	212	32	90
10/22/19	290	324	34	137	66	87
10/24/19	311	360	49	243	21	47
10/25/19	404	463	59	293	18	93
10/26/19	383	416	29	178	30	95
10/28/19	355	416	61	252	23	80
10/29/19	330	377	47	209	34	87
10/30/19	370	435	65	274	43	53

Subject 30

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	8-Dec	2	3	3	2
	9-Dec	3	3	3	2
	10-Dec	3	3	3	2
	11-Dec	3	3	3	2

	12-Dec	3	3	2	2
	13-Dec	3	3	3	2
	14-Dec	3	3	3	2
Wk 2	15-Dec	4	4	3	2
	16-Dec	3	3	2	2
	17-Dec	3	3	3	2
	18-Dec	3	3	3	2
	19-Dec	4	3	3	2
	20-Dec	3	3	3	2

Leeds

	Week 1				Week 2			
GTS	3.7	3.2	1.7	nd	2.4	1.5	2.6	nd
QoS	2.7	2.8	1.6	nd	2.5	1.7	2.3	nd
AFS	5.1	2.5	2.1	nd	6.2	2.2	5.7	nd
BFW	2.9	2.9	1.6	nd	2.5	1.2	2.1	nd
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/8/19	322	358	23	108	26	51
12/9/19	632	743	95	356	39	76
12/11/19	150	163	nd	nd	nd	nd
12/12/19	425	469	44	220	82	123
12/13/19	526	597	58	236	46	136
12/14/19	269	305	36	137	57	75
12/15/19	518	603	85	322	90	106
12/16/19	221	244	23	94	60	67
12/18/19	380	425	45	179	77	124
12/20/19	179	204	nd	nd	nd	nd

Subject 33

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	8-Dec	3	3	3	2
	9-Dec	3	3	4	2
	10-Dec	2	3	3	2
	11-Dec	3	3	3	2
	12-Dec	3	3	4	2

	13-Dec	3	3	4	2
	14-Dec	3	3	3	2
Wk 2	6-Feb	4	4	5	1
	7-Feb	4	4	4	1
	8-Feb	4	4	4	1
	9-Feb	4	4	4	1
	10-Feb	4	4	4	1
	11-Feb	4	4	4	1
	12-Feb	4	4	4	1

Leeds

	Week 1				Week 2			
GTS	5.33	4.87	4.25	nd	4.73	4.13	5.33	nd
QoS	5.05	5.55	5.4	nd	5.6	5.75	5.8	nd
AFS	6.25	5.6	5.65	nd	5	5.55	5.5	nd
BFW	4.1	4.13	4.07	nd	5.1	5.83	5.63	nd
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/8/19	502	538	nd	nd	nd	nd
12/9/19	491	563	72	291	93	107
12/12/19	343	369	26	161	105	77
12/13/19	449	526	72	224	96	65
12/14/19	201	216	15	123	47	31
2/6/20	387	430	43	269	40	78
2/8/20	272	294	22	174	51	47
2/11/20	504	578	74	306	92	106
2/12/20	388	445	57	221	79	88

Subject 35

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	8-Dec	2	3	2	3
	9-Dec	2	2	1	4
	10-Dec	1	2	1	4
	11-Dec	1	2	2	4
	12-Dec	1	1	2	4
	13-Dec	3	2	1	2

Wk 2	14-Dec	3	3	2	1
	15-Dec	4	3	3	2
	16-Dec	4	4	3	2
	17-Dec	2	3	2	2
	18-Dec	2	3	3	3
	19-Dec	3	3	3	2
	20-Dec	2	4	3	2
	21-Dec	2	3	2	3

Leeds

	Week 1				Week 2			
GTS	1.6	1.9	2.7		6.5	6.2	1.9	
QoS	1.5	2	2		6.7	5.9	1.7	
AFS	1.4	2.4	2.3		6.1	6.4	4.3	
BFW	3.1	3	2.6		5.9	6.7	2.2	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/8/19	369	456	87	319	32	18
12/9/19	379	472	93	216	45	118
12/10/19	275	325	nd	nd	nd	nd
12/11/19	362	414	52	308	14	40
12/12/19	216	240	24	184	5	27
12/13/19	345	421	76	259	5	81
12/14/19	286	339	53	205	41	40
12/15/19	212	242	30	167	40	5
12/16/19	388	478	90	219	70	99
12/17/19	331	378	39	183	6	30
12/18/19	237	265	nd	nd	nd	Nd
12/19/19	221	254	Nd	nd	nd	nd
12/20/19	352	443	91	264	34	54
12/21/19	380	434	54	315	25	40

Subject 36

Date	QoN	QoD Q1	QoD Q2	QoD Q3

Wk 1	8-Dec	3	3	2	2
	9-Dec	2	3	3	2
	10-Dec	3	4	4	1
	11-Dec	2	3	3	2
	12-Dec	3	3	3	2
	13-Dec	4	2	2	1
	14-Dec	3	3	3	2
Wk 2	15-Dec	1	3	2	2
	16-Dec	2	3	2	2
	17-Dec	2	3	2	2
	18-Dec	3	3	2	2
	19-Dec	2	3	2	2
	20-Dec	2	3	2	2
	21-Dec	2	3	2	2

Leeds

	Week 1				Week 2			
GTS	0.4	0.6	0.8		3.1	4.8	5.3	
QoS	0.7	3.1	2.4		1.4	6.6	4.2	
AFS	0.4	0.8	2.7		3.8	4.5	4.3	
BFW	4.1	3.3	3.1		5.3	6	4.5	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/8/19	319	381	62	184	70	65
12/9/19	279	301	22	148	35	96
12/10/19	329	364	35	221	16	92
12/11/19	311	337	26	184	70	57
12/12/19	312	343	31	180	47	85
12/14/19	330	353	23	245	44	41
12/15/19	239	244	Nd	nd	nd	nd
12/17/19	201	201	nd	nd	nd	nd
12/18/19	236	263	27	140	37	59
12/20/19	305	347	42	194	51	60
12/21/19	310	349	39	192	33	85

Subject 37

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	8-Dec	4	4	4	4
	9-Dec	4	4	4	2
	10-Dec	4	3	3	3
	11-Dec	4	4	4	2
	12-Dec	3	4	4	3
	13-Dec	4	3	3	2
	14-Dec	4	5	5	2
Wk 2	15-Dec	4	4	4	3
	16-Dec	4	3	4	2
	17-Dec	3	4	4	2
	18-Dec	4	4	4	2
	19-Dec	nd	4	4	2
	20-Dec	4	4	3	2
	21-Dec	4	4	4	2

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/8/19	276	310	34	158	29	89
12/9/19	291	328	37	191	26	74
12/10/19	412	455	43	194	67	151
12/11/19	338	390	52	207	50	81
12/12/19	423	470	47	229	44	81
12/13/19	399	439	33	149	36	77
12/14/19	328	376	48	204	37	87
12/15/19	298	322	24	102	44	74
12/16/19	413	466	53	240	63	110
12/17/19	336	387	51	243	43	50
12/18/19	319	371	52	187	72	60
12/19/19	353	426	73	219	67	67
12/20/19	304	332	28	155	62	87
12/21/19	367	404	37	194	70	103

Subject 39

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	8-Dec	2	3	2	2
	9-Dec	3	2	3	2
	10-Dec	4	3	3	1

	11-Dec	4	2	2	1
	12-Dec	2	3	2	2
	13-Dec	3	2	2	1
	14-Dec	2	nd	nd	nd
Wk 2	15-Dec	3	3	4	1
	16-Dec	nd	3	3	1
	17-Dec	4	4	3	1
	18-Dec	4	4	4	1
	19-Dec	2	2	2	1
	20-Dec	2	3	3	2
	21-Dec	4	nd	nd	nd

Leeds

	Week 1				Week 2			
GTS	0.8	1.9	1.7		6.8	6.7	5.4	
QoS	0.6	1.1	0.9		7.1	6.7	6.5	
AFS	0.9	1.6	1.2		4.5	7	5.7	
BFW	2.1	1.9	1.4		2.3	5.6	7	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/8/19	238	274	nd	nd	nd	nd
12/9/19	355	392	nd	nd	nd	nd
12/10/19	341	381	nd	nd	nd	nd
12/11/19	474	516	nd	nd	nd	nd
12/12/19	361	386	nd	nd	nd	nd
12/13/19	221	245	nd	nd	nd	nd
12/14/19	111	127	nd	nd	nd	nd
12/15/19	324	346	nd	nd	nd	nd
12/17/19	243	281	nd	nd	nd	nd
12/18/19	194	215	nd	nd	nd	nd
12/19/19	131	137	nd	nd	nd	nd
12/20/19	386	417	nd	nd	nd	nd
12/21/19	360	409	nd	nd	nd	nd

Subject 40

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	15-Dec	1	2	2	2

	16-Dec	3	2	2	2
	17-Dec	2	3	3	2
	18-Dec	2	2	2	2
	19-Dec	2	3	2	2
	20-Dec	2	4	3	1
	21-Dec	2	2	2	2
Wk 2	22-Dec	4	2	2	2
	23-Dec	1	nd	2	2
	24-Dec	1	1	1	3
	25-Dec	2	2	3	2
	26-Dec	2	2	2	2
	27-Dec	1	3	3	2
	28-Dec	1	2	2	1

Leeds

	Week 1				Week 2			
GTS	5.9	2.6	4.1		2.4	1.1	3.3	
QoS	3	1.4	3.6		0.7	0	1.7	
AFS	2	1.5	3.1		0	1.9	3.6	
BFW	8.6	1.3	4.9		4.7	3.5	6	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/15/19	435	483	nd	nd	nd	nd
12/16/19	444	508	64	292	66	86
12/17/19	461	548	87	309	54	98
12/18/19	496	572	76	340	83	73
12/19/19	458	536	78	282	64	112
12/21/19	464	550	86	316	84	64
12/22/19	401	484	83	289	78	34
12/23/19	407	480	73	248	56	103
12/25/19	465	579	114	358	62	45
12/26/19	371	438	67	201	100	70
12/27/19	435	501	66	292	51	92
12/28/19	596	711	115	467	60	69

Subject 43

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	15-Dec	5	3	3	1
	16-Dec	3	3	4	1
	17-Dec	1	1	3	2
	18-Dec	1	1	2	2
	19-Dec	1	1	1	2
	20-Dec	1	1	2	0
	21-Dec	3	4	5	0
Wk 2	5-Jan	1	1	2	0
	6-Jan	2	2	3	0
	7-Jan	1	2	3	0
	8-Jan	1	2	2	0
	9-Jan	1	1	3	0
	10-Jan	3	3	3	0
	11-Jan	1	4	5	0

Leeds

	Week 1				Week 2			
GTS	2.5	2.6	2.5		4.4	6.8	5.1	
QoS	0.2	0.2	0.2		4.6	2.2	2.8	
AFS	6.9	6.7	7		3.9	5.2	4.4	
BFW	2.4	2.5	3.9		4.4	3	4.3	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/15/19	326	358	32	161	81	84
12/16/19	384	434	50	234	82	68
12/17/19	417	489	72	274	67	76
12/18/19	463	528	65	260	102	101
12/19/19	462	513	45	195	85	41
12/20/19	346	416	70	187	92	67
12/21/19	337	380	43	198	70	69
1/5/20	123	140	nd	nd	nd	nd
1/6/20	405	457	52	221	91	93
1/7/20	451	501	41	203	50	49

1/8/20	122	133	nd	nd	nd	nd
1/9/20	453	543	90	269	109	75
1/10/20	332	402	70	250	50	32
1/11/20	346	393	47	207	88	51

Subject 45

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	15-Dec	3	5	3	1
	16-Dec	2	4	3	2
	17-Dec	4	4	5	2
	18-Dec	4	4	3	1
	19-Dec	4	3	4	1
	20-Dec	3	4	3	1
	21-Dec	4	4	5	1
Wk 2	22-Dec	3	4	5	1
	23-Dec	4	nd	nd	1
	24-Dec	3	5	5	1
	25-Dec	5	4	5	0
	26-Dec	5	5	4	1
	27-Dec	4	4	5	1
	28-Dec	5	4	5	0

Leeds

	Week 1				Week 2			
GTS	3.1	5.2	3.3		3.7	3	4	
QoS	4.2	5	5.2		4.5	2.1	5.2	
AFS	5.7	5.1	5.4		5.1	3.9	5.9	
BFW	5.5	5.1	5.8		5.4	4.9	2.1	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/15/19	438	508	70	233	87	118
12/16/19	407	473	60	182	54	67
12/17/19	512	617	105	313	90	109
12/18/19	609	740	123	311	82	103
12/19/19	564	643	61	189	44	89
12/20/19	510	592	82	260	86	164
12/21/19	442	524	82	276	52	114

12/22/19	448	527	79	243	75	130
12/23/19	453	538	85	296	78	79
12/24/19	475	608	133	309	78	88
12/25/19	403	495	92	272	39	92
12/26/19	472	580	108	282	83	107
12/27/19	357	417	60	207	47	103
12/28/19	367	439	51	171	29	25

Subject 46

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	15-Dec	2	3	3	1
	16-Dec	3	2	3	1
	17-Dec	3	3	2	2
	18-Dec	3	3	2	2
	19-Dec	3	2	2	2
	20-Dec	3	3	2	1
	21-Dec	3	3	3	2
Wk 2	5-Jan	5	4	4	0
	6-Jan	4	4	4	1
	7-Jan	3	4	3	1
	8-Jan	2	4	4	2
	9-Jan	4	4	4	1
	10-Jan	5	4	4	0
	11-Jan	5	5	5	0

Leeds

	Week 1				Week 2			
GTS	2.2	2.1	2.4		6.8	6.8	5.7	
QoS	2.6	1.6	1.6		6.1	7	6.2	
AFS	2.8	2.3	2.1		5.9	7	6.6	
BFW	2.2	1.9	1.9		6.9	7	6.9	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/15/19	202	231	29	105	45	52
12/16/19	328	367	39	164	76	88
12/17/19	308	353	45	180	67	61

12/18/19	346	387	41	172	61	113
12/19/19	455	502	43	179	64	52
12/20/19	379	441	48	243	21	36
12/21/19	417	464	32	150	47	83

Subject 49

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	22-Dec	3	3	4	1
	23-Dec	3	3	2	1
	24-Dec	3	3	3	1
	25-Dec	2	3	3	1
	26-Dec	3	3	3	1
	27-Dec	3	3	3	1
	28-Dec	3	4	4	1
Wk 2	5-Jan	2	4	4	1
	6-Jan	4	4	4	3
	7-Jan	4	3	2	1
	8-Jan	4	2	2	1
	9-Jan	3	2	2	4
	10-Jan	3	2	2	4
	11-Jan	3	3	3	2

Leeds

	Week 1				Week 2			
GTS	3.5	3.3	2.4		3.2	3.3	6.7	
QoS	3.1	3	2.2		3	5.6	6.8	
AFS	2.6	3.1	2.3		3.5	6.6	7.2	
BFW	2.5	2.4	2.8		6.3	6.2	6.4	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/22/19	317	403	86	200	47	70
12/23/19	338	391	53	177	66	95
12/24/19	339	394	55	179	48	112
12/25/19	135	144	nd	nd	nd	nd
12/26/19	266	294	26	108	42	27
12/27/19	151	170	nd	nd	nd	nd
12/28/19	410	440	30	245	70	95
1/5/20	336	410	52	132	23	41

1/6/20	329	394	61	149	54	30
1/7/20	318	331	nd	nd	nd	nd
1/8/20	271	290	19	156	46	69
1/9/20	365	425	60	304	19	42
1/11/20	314	389	75	256	29	29

Subject 50

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	22-Dec	3	4	4	2
	23-Dec	3	4	5	2
	24-Dec	5	5	5	1
	25-Dec	3	4	4	2
	26-Dec	2	3	4	2
	27-Dec	2	3	3	2
	28-Dec	4	4	4	1
Wk 2	5-Jan	5	4	4	0
	6-Jan	4	4	4	1
	7-Jan	3	4	3	1
	8-Jan	2	4	4	2
	9-Jan	4	4	4	1
	10-Jan	5	4	4	0
	11-Jan	5	5	5	0

Leeds

	Week 1				Week 2			
GTS	4.9	3.7	5		5.1	5.5	5.6	
QoS	4.4	3.95	5.4		4.3	6.6	3.8	
AFS	4.5	4.65	5.2		6.6	6	5.3	
BFW	2.2	5.4	4		7.6	4.4	7.2	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
12/22/19	429	474	23	116	33	25
12/23/19	339	392	53	246	36	57
12/24/19	300	331	25	200	16	25
12/25/19	184	216	nd	nd	nd	nd
12/26/19	178	192	nd	nd	nd	nd
12/27/19	313	373	60	234	49	30
12/28/19	184	198	nd	nd	nd	nd

1/5/20	244	285	41	138	57	49
1/6/20	223	265	42	131	40	52
1/7/20	403	455	52	292	52	59
1/8/20	154	168	nd	nd	nd	nd
1/9/20	339	380	41	233	65	41

Subject 54

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	5-Jan	3	2	3	2
	6-Jan	3	3	3	2
	7-Jan	2	3	2	2
	8-Jan	2	2	3	2
	9-Jan	3	2	2	2
	10-Jan	nd	3	3	2
	11-Jan	2	3	3	3
Wk 2	12-Jan	2	2	3	2
	13-Jan	2	3	3	2
	14-Jan	2	2	2	1
	15-Jan	2	2	2	1
	16-Jan	2	2	2	2
	17-Jan	2	2	2	1
	18-Jan	2	3	3	2

Leeds

	Week 1				Week 2			
GTS	3.8	6.1	5.4		3.5	3.3	4.6	
QoS	3.5	5.8	5.9		3.9	3.2	3.5	
AFS	3.5	5.7	5		3.8	3.6	4.6	
BFW	1.1	3.8	4.7		3.1	2.4	2.6	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/5/20	508	580	67	228	93	113
1/6/20	477	532	50	210	100	91
1/7/20	622	702	67	325	50	73
1/8/20	443	513	70	290	66	87
1/9/20	469	545	76	360	53	56
	599	666	67	362	88	149

1/13/20						
1/14/20	394	441	47	195	82	117
1/15/20	570	632	62	326	95	149
1/16/20	472	538	66	253	106	113
1/17/20	307	345	38	209	55	43
1/18/20	370	425	55	154	94	122

Subject 55

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	5-Jan	5	4	2	1
	6-Jan	5	4	2	0
	7-Jan	5	4	2	2
	8-Jan	5	3	2	3
	9-Jan	5	3	2	3
	10-Jan	5	5	3	4
	11-Jan	5	2	2	1
Wk 2	12-Jan	3	5	5	0
	13-Jan	3	5	5	0
	14-Jan	2	5	5	0
	15-Jan	3	5	5	0
	16-Jan	3	5	5	0
	17-Jan	4	5	5	0
	18-Jan	2	nd	nd	nd

NO LEEDS DATA

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/5/20	519	587	68	371	36	112
1/6/20	338	400	62	202	33	103
1/7/20	328	372	44	239	44	45
1/8/20	417	462	45	229	83	105
1/9/20	440	496	56	306	45	89
1/10/20	461	522	61	265	72	124
1/11/20	473	525	52	274	98	101
1/12/20	359	673	42	230	56	73
1/16/20	374	423	44	194	52	21
1/17/20	427	499	72	252	81	94
1/18/20	419	469	50	260	59	100

Subject 56

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	5-Jan	3	3	3	1
	6-Jan	3	3	3	1
	7-Jan	2	4	4	1
	8-Jan	4	4	4	1
	9-Jan	3	4	3	1
	10-Jan	4	4	4	0
	11-Jan	4	4	4	0
Wk 2	12-Jan	4	4	4	1
	13-Jan	4	4	4	0
	14-Jan	3	4	4	0
	15-Jan	4	5	4	0
	16-Jan	5	4	4	0
	17-Jan	3	4	4	1
	18-Jan	4	4	4	1

Leeds

	Week 1				Week 2			
GTS	5.5	6	6.1		4.5	5.1	5.5	
QoS	5.4	5.7	6.2		4.5	5.1	5.2	
AFS	5.4	6	6.3		4.5	5.1	5.4	
BFW	5.5	5.9	6.2		4.9	5	5.5	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/5/20	328	361	29	127	33	52
1/6/20	297	338	41	199	30	68
1/7/20	257	280	nd	nd	nd	nd
1/8/20	242	287	45	104	32	106
1/9/20	364	431	67	238	59	67
1/10/20	305	345	40	189	50	66
1/11/20	344	390	30	112	29	50
1/12/20	354	405	40	106	35	70
1/13/20	292	348	56	191	72	29
1/14/20	359	396	22	165	19	31
1/15/20	166	189	23	119	20	27
1/16/20	304	366	62	215	31	58
1/17/20	187	207	20	107	36	44
1/18/20	249	279	30	111	38	100

Subject 58

	Date	QoN	QoD Q1	QoD Q2	QoD Q3
Wk 1	5-Jan	2	2	3	2
	6-Jan	2	3	3	2
	7-Jan	2	2	2	3
	8-Jan	2	2	2	3
	9-Jan	2	3	3	2
	10-Jan	1	1	2	3
	11-Jan	2	2	3	2
Wk 2	12-Jan	1	2	3	2
	13-Jan	2	2	3	2
	14-Jan	3	3	3	2
	15-Jan	2	2	3	2
	16-Jan	3	3	3	2
	17-Jan	4	4	4	1
	18-Jan	4	3	3	2

Leeds

	Week 1				Week 2			
GTS	4.3	1.8	3.1		4	4.6	4.4	
QoS	3	2.3	2.4		4.2	4.7	3.9	
AFS	2.8	2.4	2.4		4.4	4.5	4.4	
BFW	3.1	2.4	2.3		4.6	4.8	4.2	
Values in 0.1 mm								

Wrist Actigraphy (minutes)

Sleep Day	Asleep	In Bed	Awake	Light	Deep	REM
1/7/20	299	337	32	124	36	50
1/8/20	188	252	64	119	40	29
1/9/20	402	466	64	186	99	117
1/10/20	211	253	42	128	36	47
1/11/20	428	494	66	224	69	135
1/12/20	392	432	nd	nd	nd	nd
1/13/20	272	311	39	179	34	59
1/14/20	306	358	52	171	60	75
1/15/20	231	259	28	162	27	42
1/16/20	408	490	82	253	68	87
1/17/20	426	480	54	212	109	105
1/18/20	327	406	79	217	54	56