The effects of a personalized sleep improvement App from SleepScore Labs: a single-blinded randomized waitlist controlled trial

Title	The effects of a personalized sleep improvement App from SleepScore Labs: a single-blinded randomized waitlist controlled trial
Protocol version identifier	Apr 28, 2023 (replaces previous version from Jan 26, 2023)
Product	SleepScore Labs App commercially distributed for measuring sleep and providing sleep advice based on a dynamic and personalized advice engine.
Sponsor	ResMed Germany Inc., Fraunhoferstr. 16, 82152 Martinsried, Germany
Research question and objectives	Primary objective: - To assess changes in subjective sleep quality measured using validated questionnaires (SF-B) between active sleep-improvement condition through the Dein Schlaf. Dein Tag. App and waitlist condition after 6 weeks and 12 weeks Secondary objectives: - To assess changes in further metrics between app condition and waitlist condition comparing baseline with 6 weeks and 12 weeks follow-up including feeling of being refreshed in the morning, overall sleep complaints, and health measures using validated questionnaires (PSQI, PSS, SF-12, SF-B). Within the app condition, six objective sleep parameters (sleep onset latency, wake after sleep onset, total sleep time, sleep efficiency, sleep staging, nighttime awakenings) will be assessed by comparing baseline with 6 weeks and 12 weeks follow-up.
Country of study	Germany
Author	• Christoph Schöbel (Principal Investigator) • Elie Gottlieb (Primary SSL) • Daniela Ehrsam-Tosi (Primary ResMed) • Susanne Fischer (Secondary ResMed)

Marketing authorisation holder(s)

Marketing authorisation holder(s)	Legal representative in Europe: ResMed Germany Inc., Fraunhoferstr. 16, 82152 Martinsried, Germany Phone: +49 (0) 89 99 01-001 Fax: +49 (0) 89 99 01-10 08

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2. List of abbreviations

Abbreviation	Definition
GCP	Good Clinical Practice
GDPR	The General Data Protection Regulation
ICH-GCP	International Conference on Harmonisation on Good Clinical Practice
IEC	Independent Ethics Committee
IRB	Institutional Review Board
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
SF-12	Short Form 12 Health Survey Questionnaire
SF-B	Schlaffragebogen B
SOP	Standard Operating Procedure

2.1 Declaration of Helsinki and Signatures

The undersigned have read this protocol and agreed to conduct this study in accordance with all stipulations of the protocol and in accordance with the Declaration of Helsinki.

Date	Name and Signature
_____	DocuSigned by: Elie Gottlieb A71C9A2AE3DD47E... _____ Elie Gottlieb (Applied Sleep Scientist, SleepScore Labs)
_____	DocuSigned by: Daniela Ehrsam-Tosi 04FB054265AE4BF... _____ Daniela Ehrsam-Tosi (Director Medical Affairs CRS, ResMed)
_____	DocuSigned by: Susanne Fischer B6337AFF84D74C4... _____ Susanne Fischer (Senior Manager Medical Affairs CRS, ResMed)
_____	_____ Christoph Schöbel (Univ.-Prof. Dr. med., Principal Investigator)

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The undersigned have read this protocol and agreed to conduct this study in accordance with all stipulations of the protocol and in accordance with the Declaration of Helsinki.

Date	**Name and Signature**
_____	_____ Elie Gottlieb (Applied Sleep Scientist, SleepScore Labs)
_____	_____ Daniela Ehrsam-Tosi (Director Medical Affairs CRS, ResMed)
_____	_____ Susanne Fischer (Senior Manager Medical Affairs CRS, ResMed)
09.05.2023	_____ Christoph Schöbel (Univ.-Prof. Dr. med., Principal Investigator)

3. Abstract

Title	The effects of a personalized sleep improvement App from SleepScore Labs: a single-blinded randomized waitlist controlled trial
Rationale and Background	The Dein Schlaf. Dein Tag. sleep improvement App powered by SleepScore has not yet been empirically validated in the long-term assessment and management of people in the general population suffering from sleep complaints but did not yet fulfill the clinical criteria of an insomnia disorder.
Research objectives	Primary objective: Assessed at baseline, 6 weeks and 12 weeks, improvements in self-reported sleep quality while using a dynamic and personalized sleep advice engine app will be compared to a waitlist control group. Secondary objectives: Assessed at baseline, 6 weeks and 12 weeks, improvements in mental health, sleep problems, and stress will be compared to a waitlist control group. In the intervention (app) group, changes in objectively measured sleep parameters (sleep onset latency, wake after sleep onset, total sleep time, sleep staging, nighttime awakenings) over 6 and 12 weeks will be studied .
Study design	Single-blinded randomized waitlist controlled trial
Population	Inclusion criteria: ▪ iOS user, or user of one of the following: Samsung Galaxy S7 Edge and S7, S8, S8+, S9, S9+, S20, S20 FE, S20+, S21 Ultra Samsung Galaxy Note 8 and 9 ▪ Regensburg Insomnia Scale (subclinical insomnia: Score 13-24) ▪ ≥ 18 years old. ▪ Naive to the SleepScore Labs App ▪ Able to fully understand information on data protection and provide written informed consent ▪ Not included in other treatments targeting sleep Exclusion criteria: ▪ Clinically significant sleep disorders (e.g. Restless legs disorders, sleep-related breathing disorders, parasomnias) ▪ Bedtime less than 6 hours ▪ Any of the following medical problems:

	○ Current mental disorder affecting sleep (e.g., depression, anxiety disorders, bipolar disorder, schizophrenia) ○ Current severe medical conditions (e.g. chronic pain, cancer) ▪ Any of the following medications/substance use: ○ Prescription of sleep medication or over-the-counter sleep medication (e.g., melatonin, "Hoggar night") ○ Medication for other conditions (e.g., anxiety, ADHD) that affect sleep, e.g., antidepressants, antipsychotics. ○ Consumption of 3+ units of alcohol on 4 or more nights per week ○ Recreational drug use ▪ Pregnant or nursing mothers ▪ Infant or child under age 1 at home ▪ Shift work ▪ Current use of other Sleep Tracking App's
Variables	Questionnaire data will be collected at baseline, after 6 and 12 weeks. Objective sleep data will be collected using the SleepScore App, and stored within the Microsoft Azure cloud system, an ISO 27001 certified and SOC 1 and SOC 2 compliant cloud service provider. Self-reported questionnaire data will be captured using an EU data center of Forsta/Decipher which is GDPR compliant, ISO 27001 certified, with SOC2 accredited data centers.
Data sources	<u>Data obtained from users:</u> Baseline, 6-weeks, and 12-weeks measurements derived from validated questionnaires <u>Data imported from the Dein Schlaf. Dein Tag. App:</u> Objective sleep data, daily logging, and usage monitoring data recorded by the Dein Schlaf. Dein Tag. App
Study size	Overall, 600 users (300 app condition, 300 waitlist control group) will be included in Germany.
Data analysis	The questionnaire date will be analyzed by an ANOVA, with one factor (app condition vs. waiting list control group) and time (Baseline, 6-weeks, 12-weeks). To handle missing values, a mixed-model approach with the same factors will be applied. The

	critical statistical test would be the interaction term between app condition and the waiting-list control group. Objectively measured data will be analyzed using multi-level modeling (MLM) in a nested way (nights within participants), allowing for analyzing changes within the intervention (app) group. To evaluate changes in primary and secondary outcome measures assessed by validated scales at baseline, 6-weeks, and 12-weeks, we will compare within-group differences for each time-point using a t-test if normally distributed, or the Mann Whitney-U test for non-normally distributed continuous data. In addition, effect sizes for the changes within both groups (questionnaire data) and app group (objective sleep parameters) will be computed.

4. Amendments and updates

Amendment No. 1, Jan 26 2023
Amendment No. 2, Apr 28 2023

Section	Amendment or update detail	Reason
5 Milestones	Dates changed	Adapted according to preparation of study
9.4 Design	Deleted “written”, added “A participant information document with consent form will be provided with page-turning function. Participant has to agree that his/her data will be used in this study by clicking “yes, I agree” or “no I don`t agree and do not want to participate”.”	Electronic consent ensures a that participants can follow a defined workflow and pathway and will be guided smoothly through the recruitment portal. This avoids that too many potential participants are being lost during the course of recruitment.
9.4.1	Adapted flowchart: Informed Consent – then baseline assessment – then randomization	Now follows the routine in study practice. Before the randomization should have occurred before the baseline assessment. Since randomization means access to the app for the “app group”, the timepoint of filling out the baseline questionnaire could have been after first app usage. This will be avoided when doing baseline before randomization and app download.
9.5.1 Data	Deleted Munich Chronotype Questionnaire	Conversion into electronic format problematic; would have compromised the outcomes

9.5.1 Data	Deleted Landecker Inventar zur Erfassung von Schlafstörungen (LISST)	Study flow and assessment of participants for eligibility in the e-portal required a combination of in-/exclusion criteria with the LISST to ensure all screening criteria could be met. LISST is not required to be applied as a separate questionnaire.
9.7.1 Data management	Deleted […]„forwarded to SleepScore, there combined with objectively measured sleep data, and then securely shared with ResMed where it will be stored for 10 years." Added: "Objective sleep data from the app as collected and controlled by SleepScore Labs and self-reported questionnaire data as collected by a vendor on behalf of ResMed Objective sleep data from the Dein Schlaf. Dein Tag. App as specified in this protocol, and without personal identifiers will be send to vendor, combined with self-reported questionnaire data by vendor and equipped with new identifiers to result in a de-identified set of study data. […]shared with Sleepscore Labs for joint analysis." Added: "De-identified study data will be stored at ResMed for 10 years."	Changes were necessary to be compliant with EU-GDPR. Processes had to be restructured to prevent ResMed from potentially getting access to personal data of study participants.
Annex 1	Deleted LISST	Not required as separate questionnaire. Accurate recruitment of participants through automated electronic assessment made a fusion of eligibility criteria necessary.
Annex 1	Deleted Munich Chrontype Questionnaire	Conversion into electronic format problematic; would have compromised the outcomes
Inclusion criteria	Added "Samsung Galaxy S7 Edge and S7, S8, S8+, S9, S9+, S20, S20 FE, S20+, S21 Ultra Samsung Galaxy Note 8 and 9"	Increasing the number of active users of the application by also allowing other devices which have been validated to deliver a similar performance in running the app.

5. Milestones

Milestone	Planned date
Start of enrolment	January 2023 (actual)
End of enrolment	May 2023 (anticipated)
Final results	July/August 2023 (anticipated)

6. Rationale and background

Sleep disturbances have a documented impact on general mental and physical well-being across many domains (e.g., Cappuccio et al., 2010; Dinges et al., 1997; Knutson et al., 2007). It has been estimated that approximately 20-35% of individuals report moderate symptoms of poor sleep (Hillman and Lack, 2013). Sleep-wake dysfunction contributes to the pathogenesis and evolution of neuropsychiatric conditions including depression, anxiety, and chronic pain, and are associated with an increased risk of chronic neurological health conditions including cerebrovascular disease, cardiovascular disease and neurodegenerative disorders. Those with poor sleep may experience general dissatisfaction with sleep quality or quantity which may be associated with minor to moderate difficulty initiating or maintaining adequate sleep (Benca et al., 2005).

The cause of sleep-wake dysfunction may be attributed to a myriad of environmental (e.g., excessive bright light before sleep), cognitive (e.g., pre-sleep worrying and anxiety), behavioral (e.g., caffeine or alcohol consumption prior to sleep), and physiological factors (e.g., pre-sleep arousal). A variety of sleep improvement options exist for poor sleep including pharmacological interventions, over-the-counter sleep aids, and cognitive and behavioral interventions. While the preferred treatment for those with clinical threshold poor sleep is cognitive behavioral therapy for insomnia (CBT-i) delivered in person, this effective approach is both time-consuming and costly, with implementation limited by an unmet need for trained providers (Espie et al., 2001). Furthermore, studies suggest that many individuals with sleep difficulties do not seek professional help and report a preference for non-pharmacological and personalized, self-help strategies (Vincent and Lionber, 2001, Morin et al., 2006). Despite this, few evidenced-based sleep improvement digital programs exist founded on the principles of behavioral change psychology and sleep hygiene targeting non-clinical populations for primary prevention.

Due to poor sleep's multitude of causes (e.g., environmental, cognitive, behavioral, or physiological) and symptoms (e.g., long sleep onset latency, short sleep duration, elevated wake after sleep onset and nighttime awakenings, poor sleep quality), a personalized and dynamic sleep improvement program tailored to a user's lifestyle and specific needs may be required to help nudge users towards sleep-promoting behaviors and attitudes. Digital and mobile health platforms are also highly scalable and cost-effective, thus allowing for widespread implementation across larger populations.

The purpose of the present study is to conduct a randomized controlled trial to evaluate a digital smartphone application, the Dein Schlaf. Dein Tag. application powered by SleepScore, designed to improve sleep and sleep-permissive behaviors. The Dein Schlaf. Dein Tag smartphone application utilizes a dynamic and personalized sleep advice engine founded in the principles of behavior change psychology and sleep hygiene that offers a novel, non-invasive and non-pharmacological solution designed to improve sleep

outcomes in those with common sleeping difficulties. While the sleep measurement technology behind Dein Schlaf. Dein Tag. has already been previously validated against gold-standard polysomnography (Zaffaroni et al., 2019), its sleep improvement features have not yet been empirically validated in the long-term assessment and management of people in the general population with a broader range of sleep problems.

7. Research question and objectives

The primary objective of the present study is to examine improvement regarding self-reported sleep quality when using the Dein Schlaf. Dein Tag. sleep improvement engine App when compared to a waitlist condition. Validated questionnaires will be administered to assess self-reported sleep quality, health perception, psychosocial factors and sleep-permissive behaviors (i.e., preventative health).

Due to the dynamic and personalized nature of the intervention and its potential impact on various sleep-wake parameters depending on the user's objectively measured sleep (only app condition) and self-assessed goals, we have chosen multiple secondary endpoints: sleep onset latency, wake after sleep onset and total sleep time will be used to determine sleep changes.

Participants will be required to complete the following tasks during the study period:

1. Start the sleep tracking device via a smartphone app before lying down in bed and turning off the lights to go to sleep (only for intervention (app) group).
2. In the morning, turn off the sleep tracking device as soon as they wake up and decide to leave the bed (only for intervention (app) group).
3. Log day and regularly use the different modules addressing different aspects of sleep, including advice for change (only for intervention (app) group).
4. At the three time points shown in 8.4.1 flow diagram, complete a longer questionnaire using an E-Link. These questionnaires will cover demographic information, subjective mental and physical health, subjective sleep, and stress level. (valid for app condition and waitlist control group)

8. Intensity of Use

Although app condition participants will be instructed to track sleep and engage with the app every night, the minimal internal compliance threshold for intensity of use is set at 3 nights of tracking per week. If participants track less than 3 nights per week, they will receive up to 3 reminder follow-up emails. The primary analysis will include all randomized participants. Secondary analyses will be conducted using an adherent to treatment approach, excluding participants who did not sufficiently engage with app throughout the study (<3 tracked nights of sleep per week).

9. Research methods

9.1 Study design

The study is a randomized waitlist controlled trial of a sleep improvement app. The present study design is summarized in Figure 1. We decided to use a between-group design as we want to determine the effect of the sleep improvement app vs. not using anything, as the study app is aiming to improve subjective sleep quality in order to prevent progression to clinical relevant sleep problems (primary prevention). Participants will be randomly assigned to the Sleep Improvement App intervention or the waitlist condition. Online assessments will take place at Baseline (0 weeks), 6 weeks (during the intervention), and 12 weeks (after intervention).

9.2 Randomization and allocation concealment

This study will use simple randomization with an allocation ratio of 1:1, as recommended for large randomized controlled trials. Randomization will be conducted by an automated online system; hence the research team will be unable to influence randomization and have no access to future allocations.

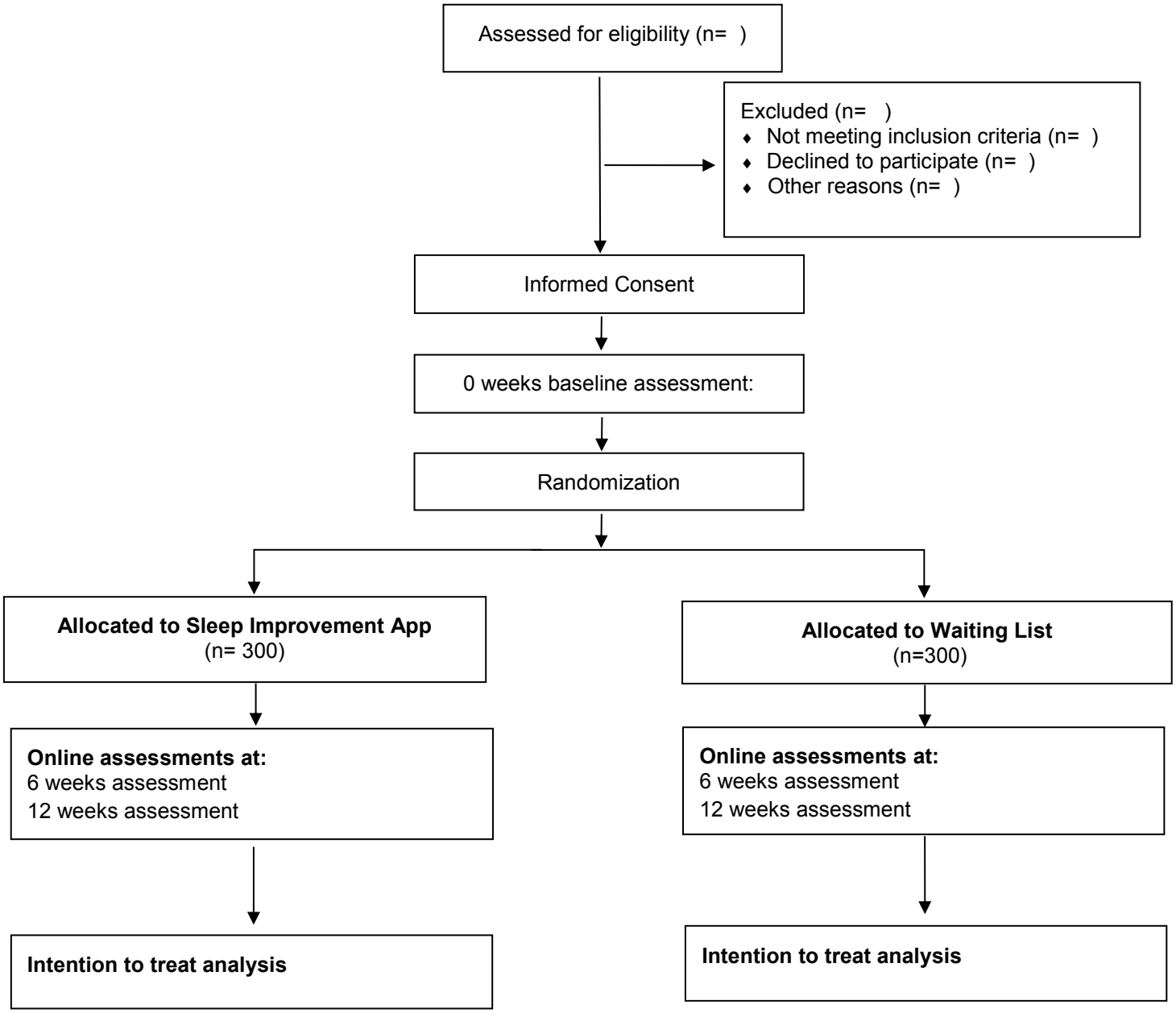
9.3 Blinding

Assessments will be self-reported and carried out online, and the research team will be blinded to outcomes during the trial. Participants will be informed of their randomization outcome by an automatic email, and hence they will not be blinded to treatment allocation. It is notable that the study sponsors will not have any contact with research participants and will therefore be unable to bias the allocation or assessments. If participants do contact the team and reveal the allocation, the absence of assessments carried out by an investigator prevents any biases.

9.4 Type/Design of study

Naïve participants will be consecutively enrolled into the trial and randomized into either the wait-list condition or Sleep Improvement App-condition, provided that all inclusion and exclusion criteria are met and consent is given to use their data according to data privacy regulations. A participant information document with consent form will be provided with page-turning function. Participant has to agree that his/her data will be used in this study by clicking “yes, I agree” or “no I don`t agree and do not want to participate”.
Eligible participants will receive written information about all relevant aspects of the study and that their participation in the study is voluntary and they have the right to refuse or withdraw their consent at any time without negative consequences. The study has been registered with ClinicalTrials.gov (210915DSDT). This paper contains modifications, which will be submitted to the Ethics Committee for approval prior to implementation. The current and further amendments will be documented in detail in the ClinicalTrials.gov registry. On the consent form, participants will be asked if they agree to the use of their data in case of withdrawing from the trial. Participants will also be asked for permission for the research team to share relevant data with people from SleepScoreLabs and ResMed taking part in the research or from regulatory authorities, where relevant. This trial does not involve collecting biological specimens for storage.

9.4.1 CONSORT Study Flow Diagram



9.4.2 Primary Endpoint

Statistically significant improvement in subjective sleep quality measured using a validated questionnaire between active sleep-improvement condition through the Dein Schlaf. Dein Tag. App and the waitlist condition comparing baseline with 6 weeks and 12 weeks measures.

- Self-report sleep parameters: Sleep Quality score (SQ) of the SF-B (9 Items)

9.4.3 Secondary Endpoints

Improvements in sleep metrics between app condition and waitlist condition comparing baseline with 6 weeks and 12 weeks measures

Note, given the dynamic and personalized nature of the intervention and its potential impact on various self-assessed goals, we have chosen multiple secondary endpoints that we expect to see statistically significant sleep improvements in depending on baseline self-reported sleep parameters, including the following:

- Health measures including overall sleep problems, feeling of being refreshed in the morning, mental health stress (PSQI, PSS, SF-12, SF-B)
- Objective sleep parameters (only app condition): Total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency.
- Self-reported app-based items in app condition group.

9.4.4 Study population

This research aims to target a non-clinical population with sublinical sleep disturbances that is interested in improving their sleep. To ensure we recruit a non-clinical sample, we will exclude users who have indicated they have a diagnosed sleep disorder as well as those identified as being at high risk of a sleep disorder based on validated screening tools. This research has no specific recruitment goals with respect to race or ethnicity and will not base participant eligibility on such criteria. However, this information may be recorded as part of the data collected.

Inclusion criteria:

- iOS user, or user of one of the following: Samsung Galaxy S7 Edge and S7, S8, S8+, S9, S9+, S20, S20 FE, S20+, S21 Ultra Samsung Galaxy Note 8 and 9
- Regensburg Insomnia Scale (poor sleep indicated by a score of 13-24, excluding those without sleep problems and those with probable insomnia disorder)
- ≥ 18 years old.
- Naive to the SleepScore Labs App
- Not included in other treatments around sleep
- Able to fully understand information on data protection and provide written informed consent

Exclusion criteria:

- Bedtime less than 6 hours
- Any of the following medical problems:
  - Untreated psychological disorder affecting sleep (e.g., depression , anxiety disorders, bipolar disorder, schizophrenia)
  - Current severe medical conditions (e.g. chronic pain, cancer)
- Any of the following medications/substance use:
  - Prescription sleep medication or regular use of over-the-counter sleep medication
  - Medication for other conditions (e.g., anxiety, ADHD) that affect sleep, e.g. antidepressants, antipsychotics
- Consumption of 3+ units of alcohol on 4 or more nights per week
- Recreational or nightly drug use
- Pregnant or nursing mothers
- Shift work
- Travel across 2 or more time zones during study period
- Sleeping more than 7 nights not at home during study period
- Users who newly received a diagnosis of a sleep disorders
- Users who start sleep or other psychoactive medication during the study period

- Use of other Sleep Tracking App's during the study period

9.4.5 Study duration

Recruitment for the study will be rolling, Baseline Assessment is at week 0. A follow up is scheduled after 6 weeks and 12 weeks of both the app and waitlist group. The end of data collection is planned after 12 weeks from baseline of the last user included. Final intention to treat analysis of study data will subsequently be performed.

9.4.6 Withdrawal from the trial

Participants are free to withdraw from the trial at any time without giving any reasons. They will not have any negative consequences in the relationship to SleepScore Labs or ResMed. In the event that a user withdraws consent, the date and reason for termination – if provided – will be documented. For participants who drop out of the study, assessments that are part of the study design will be conducted only if the participants agree.

9.4.7 Compensation

All enrolled participants will receive 20 euros for completing each follow-up assessment including baseline, 6-weeks, and 12-weeks, paid at the end of the study.
Regular use of the sleep app will be compensated with 50 Euros.

9.4.8 Sleep Measurement

The Dein Schlaf. Dein Tag. application powered by SleepScore includes a polysomnography-validated non-contact sleep monitoring technology employing inaudible sonar to monitor the movements and respiration of a participant in bed. A validation study of the sonar technology against gold-standard polysomnography showed high sensitivity (88%) and specificity (65%), exceeding agreement that is typically reported for actigraphy based devices (Zaffaroni et al., 2019).

Sleep measurement is achieved via a smartphone app, which have become ubiquitous in the last decade, eliminating the initial barrier to adoption represented by the cost and effort associated with purchasing a custom piece of hardware. The average emitted acoustic power is less than 75dB, well within the most stringent guidelines on sound exposure and the frequencies employed are above 18 KHz, above the audibility range of the vast majority of the adult population. The app utilizes a patented sensing technology and custom algorithms. Sleep monitoring can be achieved by placing a smartphone onto the bedside locker and starting the app. The app employs sophisticated algorithms to identify sleep stages: Wake (W), Light Sleep (N1, N2 sleep), Deep Sleep (N3 sleep), REM or Absence. The algorithms for the app technology were developed by using several hundred-night recordings from multiple subjects in their home consisting of concurrent measurements performed via a smartphone equipped with the Drive app and a ResMed S+ device respectively.

9.4.9 Intervention and Control

The Dein Schlaf. Dein Tag. App powered by SleepScore is a personalized and dynamic digital sleep improvement program offered via smartphone. The app begins with a brief

onboarding and registration process that informs the personalized sleep advice, followed by sleep improvement personalization goals including the following potential options: sleep longer, wake up less, fall asleep easier, sharpen my mind, recharge my body, stay asleep until morning, or perfect my sleep (improve SleepScore). Users are then asked to select health-related measures that are most important for them, the regularity of their bedtime, how often they exercise, common sleep disturbances, and overall self-reported sleep quality.

Based on the user's onboarding data and nightly objective sleep tracking data, the Dein Schlaf. Dein Tag. application powered by SleepScore provides personalized evidenced-based sleep advice and sleep education content founded in the principles of sleep hygiene and cognitive behavioural skills. Additional sleep improvement features embedded within the app include weekly sleep challenges, sleep sanctuary bedroom checks, sleep sounds, smart alarm, bedtime reminders, and sleep education blogs.

To increase user engagement and adherence to tracking and sleep improvement features, the application integrates contextual reinforcement strategies through daily and weekly prompts to encourage positive sleep health-related behaviours. These prompts include smartphone push notifications, in-app overlays, and emails providing sleep education content, sleep tips, individual sleep feedback, tracking/daily log reminders.

The app uses several behaviour change techniques to improve sleep-wake functioning, including the following:

Goal setting and planning. Goal setting is a key component to app onboarding and the advice engine. Users can select any of the following goals: sleep longer, wake up less, fall asleep easier, sharpen my mind, recharge my body, stay asleep until morning, or perfect my sleep (improve SleepScore). Users are then asked to select health-related measures that are most important for them, the regularity of their bedtime, how often they exercise, common sleep disturbances, and overall self-reported sleep quality. The app then uses criteria to give feedback to users when they are nearing or meeting sleep improvement criteria based on these goals.

Feedback and monitoring. The sleep history page shows retrospective SleepScore's in order to reduce false beliefs about sleep by providing objective sleep data. In relation to goals and planning, feedback on behaviour is provided based on the measurement of objective sleep and daytime behaviours logged in the log-your-day feature.

Shaping knowledge. We use advice and insights based on the sleep guide and log your day items with instructions on how to remove or reduce aversive stimuli (e.g., excessive caffeine intake, excessive pre-bed light, alcohol consumption, sedentary behavior) and improve stimulus control (e.g., only using bed for sleep and intimacy).

Natural consequences. Information about health consequences and the salience of insufficient or poor quality sleep are provided to users in the sleep guide and research articles summarized as blog posts.

9.4.10 Inclusion of users and baseline parameters

The investigator will inform eligible users about the study and the use of data. If the user is willing to participate, the informed consent form for data use will be handed out for signature. After signing by user and investigator, study relevant data will be reported after the participants has completed relevant questionnaires (see Annex1)

9.4.11 Assessments Table

Assessment	Baseline	6 weeks	12 weeks
Inclusion and exclusion criteria	X		
Demographics	X		
History	X		
Social status	X		
Self-report questionnaires (see Annex 1)	X	X	X
Assessment of objective sleep parameters via Dein Schlaf. Dein Tag App (each night)	X	X	X

9.5 Data sources

9.5.1 Data obtained from users

Baseline and 6-weeks and 12-weeks data regarding sleep, stress, and mental health questionnaires including:

1	Regensburg Insomnia Scale
2	Schlaffragebogen B
3	Short Form 12 Health Survey Questionnaire (SF-12)
4	Pittsburgh Sleepiness Quality Index (PSQI)
5	Perceived Stress Scale (PSS)

9.5.2 Data imported from the Dein Schlaf. Dein Tag. App

Digital data objectively measured using the Dein Schlaf. Dein Tag. App will contain the following parameters,

- Sleep stage and sleep-wake data included by not limited to total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency and usage patterns.

9.6 Study size

An a priori power analysis was performed using GPower version 3.1.9.7. Previous research indicates that effect sizes between 0.20 and 0.50 can be expected using a digital sleep application. A conservative approach (assuming an effect size of 0.20) will require 150 participants in each group (N=150) to detect significant effects between app group and wait-list control group for both primary and secondary outcome measures (alpha: 0.05, power: 0.80, allocation ratio 1:1). As trials with solely online recruitment may have higher drop out rates, we increased the participants in each group to 300 (total: 600 participants).

9.7 Data management

Applicable national and international legal requirements for data handling and data archiving will be met. Participant study materials including recruitment materials, participant informed consent documents (PICF), study withdrawal forms, and study progress will be collected using an EU data center of Forsta/Decipher which is GDPR compliant, ISO 27001 certified, with SOC2 accredited data centers.

Objective sleep data will be collected using the Dein Schlaf. Dein Tag. application, and stored within an EU data center of the Microsoft Azure cloud system, an ISO 27001 certified and SOC 1, SOC 2, and GDPR compliant cloud service provider. Self-reported questionnaire data will be captured using an EU data center of Forsta/Decipher which is GDPR compliant, ISO 27001 certified, with SOC2 accredited data centers. Objective sleep data is encrypted in transit and at rest and additionally, personally identifiable information is hashed before being stored in the database. Access to databases for data analysis which include person identifiable information is limited to approved administration staff and is locked to the corporate IP address in the EU.

Personal information identifiers are separated from measurements so that employees of SleepScore Labs International LTD can work with accordance of least privilege to perform adequate work duties. Authentication controls are also implemented to protect customer data using passwords and usernames – external parties do not have any authentication services. Upon completion of data collection, de-identified objective data from Microsoft Azure cloud system and self-reported Forsta/Decipher data will be merged into a GDPR compliant data repository. Azure Data Factory will be used to combine the data, with processed data being stored in a Microsoft Azure SQL Server hosted in the EU. Access to this repository, which is required for analysis, will be limited to specific EU-based employees.

9.7.1 Personal data and data protection

Data collected in the course of this study are subject to strict data protection measures. Objective data in the system is encrypted and secure while in transit and at rest using the latest security protocols. The data protection notice informs end-users about their data protection rights and how to exercise them (i.e. make data subject rights requests). We will comply with the requirements of Articles 12 to 21 GDPR, as applicable. All study participant data that is recorded will be pseudonymized for storage and analysis: Objective sleep data from the app as collected and controlled by SleepScore Labs and self-reported questionnaire data as collected by a vendor on behalf of ResMed Objective sleep data from the Dein Schlaf. Dein Tag. App as specified in this protocol, and without personal identifiers will be send to vendor, combined with self-reported questionnaire data by vendor and equipped with new identifiers to result in a de-identified set of study data. At the end of the project, the data will be deleted from the vendor's servers, transferred to ResMed and shared with Sleepscore Labs for joint analysis. De-identified study data will be stored at ResMed for 10 years.. Data will be collected and processed to reach the goals of the study and furthermore possible evaluations for sleep research and publications. Participants will be informed about their rights in terms of data usage, data storage, correction of data and deletion of stored data through the data protection notice. This notice sets out the data protection rights of the user and how they can exercise their data protection rights under GDPR.

9.8 Data analysis

Demographic and other key study variables will be compared between intervention group and control group at the baseline using t tests for continuous variables and chi squared for categorical variables to test whether the randomization has worked adequately.
The primary analysis will include all randomized participants. Secondary analyses will be conducted using an adherent to treatment approach, excluding participants who did not sufficiently engage with app throughout the study (<3 tracked nights of sleep per week, respectively used the app modules regularly).

The questionnaire data will be analyzed by an ANOVA, with one factor (app condition vs. waitlist control group) and time (Baseline, 6-weeks, 12-weeks). To handle missing values, a mixed-model approach with the same factors will be applied. The critical statistical test would be the interaction term between app condition and the waitlist control group.

For objectively recorded sleep data, repeated measured data will be analyzed using multi-level modeling (MLM) in a nested way (nights within participants), will be performed allowing for analyzing changes with the intervention (app) group. To evaluate changes in primary and secondary outcome measures assessed by validated scales at baseline, 6-weeks, and 12-weeks, we will compare within-group differences for each time-point using a t-test if normally distributed, or the Mann Whitney-U test for non-normally distributed continuous data. In addition, effect sizes for the changes within both groups (questionnaire data) and app group (objective sleep parameters) will be computed.

9.9 Quality control

Quality control is defined as the operational techniques and activities, such as monitoring, undertaken within the quality assurance system to verify that the requirements for quality of the study related activities have been fulfilled. Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Quality assurance is defined as the planned and systematic actions that are established to ensure that the study is performed, and the data generated, documented (recorded) and reported, in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements.

9.9.1 Access to Source Data/Document

The investigator will permit, and participating subjects will consent for, potential study-related monitoring, audits, Ethics Committee review and regulatory inspections, providing direct access to primary participant's data (i.e. source data) that support data in the Microsoft Azure cloud. Direct access is defined as the permission to examine, analyze, verify and reproduce any records and reports that are important to evaluation of a study. Any party (e.g. domestic and foreign regulatory authorities, the sponsor and/or authorized representatives of the sponsor such as monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirements to maintain the confidentiality of users identities and sponsor proprietary information.

9.9.2 Quality assurance:

Quality assurance is defined as the planned and systematic actions that are established to ensure that the study is performed, and the data are generated, documented (recorded) and reported in compliance with GCP and the applicable regulatory requirements.

9.10 Study monitoring

The sponsor or authorized, qualified representatives of the sponsor will accomplish the monitoring during the study. Source documents will be reviewed for verification of consistency. The investigator agrees that representatives or the designees of the sponsor, and appropriate regulatory bodies will be given direct access to the regular files of the user. It is important that the investigator and their relevant personnel are available during the monitoring visits and possible audits and that an appropriate location and sufficient amount of time is devoted to the process. During the monitoring visit a PC with internet connection should be available to the monitor for direct connection to the internet database of the study and to all the data of the users if stored in the data system.

9.10.1 Audit

An audit is a systematic and independent review of study related activities and documents to determine whether the validated study related activities were conducted and the data were recorded, analyzed and accurately reported according to the protocol, designated Standard Operating Procedure (SOPs), GCP and the applicable regulatory requirements.

9.11 Limitations of the research methods

It is expected that variations in the use of the Dein Schlaf. Dein Tag will occur, i.e., some users will use the app very intensely, others might use it regularly but not so intense. Due to the expected of variations in procedures and in particular in usage times of the sleep advice engine, the magnitude of statistical significance (i.e., effect size) is expected to be smaller but still within the range of 0.20 to 0.50.

9.12 Other aspects

None

10. Protection of human subjects

All sleep advice engine support activities used are decided individually by the user and are not pre-defined by the study protocol. All sleep advice engine support activities are to be used in line with their marketing authorisation. Participation does not pose additional risks and adverse events are not expected given the behavioural nature of the intervention. All Sleep advice engine support activities are performed in accordance with all applicable ethical and regulatory standards. Before initiating the study in a country, approval of the IRB / IEC will be obtained.

11. Management and reporting of Adverse Events/Adverse Reactions

Unanticipated problems or any unexpected adverse events will be promptly reported by the PI to an IRB representative from the Ethik-Kommission der Medizinischen Fakultät der Universität Duisburg-Essen by phone (+49 (0) 201 - 723 3448) or email (ethikkommission@uk-essen.de), as well as any other medium (e.g. faxed form) requested by the 3rd party IRB following email/phone notification.

12. Plans for disseminating and communicating study results

Study results will be pooled for the purpose of publication that will be jointly coordinated by SleepScore Labs and ResMed. Preparation of the comprehensive publication will occur at the completion of the study. Publications arising from this study will be jointly defined, executed, and published or alternately consented by both sides.

Annex 1. Questionnaires

	Items	Recruitment	Baseline	6 Weeks	12 Weeks	Purpose
Regensburg Insomnia Scale	10	X				Eligibility
SF-B	29		X	X	X	Effect on sleep
SF-12	12		X	X	X	Effect on preventative health
Pittsburgh Sleep Quality Index (PSQI)	19		X	X	X	Effect on sleep quality
Perceived Stress Scale	10		X	X	X	Effect on Stress

Annex 2. References

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