STATISTICAL ANALYSIS PLAN (SAP)

Melatonin for Chronic Back Pain (The MOCHA trial): A Randomized, Double-Blind, Placebo-Controlled Trial

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Section 1: Administrative information

1. Title and Trial registration

- 1a: Melatonin for Chronic Back Pain (The MOCHA trial): A Randomized, Double-Blind, Placebo-Controlled Trial
- 1b.1: European Medicens Agency (EMA), Clinical Trial Information System (CTIS): EU CT nr. 2023-503530-41-00 (date 26-08-24)
- 1b.2: ClinicalTrials.gov ID: NCT06476392 (date 20-06-24)

2. SAP version

- Version 1.0; Date: March 13th, 2026 (uploaded March 13th 2026 at https://findresearcher.sdu.dk/ws/portalfiles/portal/305769352/MOCHA_SAP_ver1.0.pdf)

3. Protocol version

- The SAP has been written based on the protocol approved by EMA (EU CT nr. 2023-503530-41-00) and the published study protocol for the MOCHA trial (1). The SAP adheres to the Guidelines for the content of statistical analysis plans in clinical trials (2). The SAP was made publicly available before finishing the data collection of the primary end point of the last patient and before any statistical analyses began.

4. SAP revisions

- 4a: Revision history
- 4b: Justification for revisions
- 4c: Timing of revision

Protocol version	Updated SAP version no.	Section number changed	Reason	Date Changed

5. Roles and responsibility

- Names and roles of SAP contributors:

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6. Signatures of SAP authors

- 6a: SAP author signature (Jonas Bloch Thorlund):

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- 6c.: Study sponsor signature (Karin Due Bruun):

  Date: March 13th 2026

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Section 2: Introduction

7. Background and rationale

- Chronic back pain remains a leading cause of disablity worldwide with high societal and healthcare costs and limited effective treatment options. More than 50% of people with chronic back pain also report insomnia symptoms.

  Melatonin is a hormone excreted by the pineal gland that regulates the circadian rhythm and sleep. Melatonin is also available as a drug, which is well known for its use in people with insomnia and jetlag. It has a favorable safety profile with no reported side-effects of major clinical significance and have a low potential for dependency and rebound effect.

  Some studies involving patients with non-musculoskeletal pain conditions such as migraines, endometriosis and irritable bowel syndrome have shown that melatonin may have an analgesic effect. This effect may be mediated e.g. through direct effect on pain processing or indirect through improved sleep. Further, studies have shown promising effect of melatonin for fibromyalgia pain but there are no large, randomized trials investigating the effect of melatonin on chronic back pain.

8. Objectives

- The primary objective of this trial is to investigate if treatment with melatonin 10 mg (given as two 5mg tablets) compared with identically appearing placebo tablets (lactose monohydrate, Potato starch, Mucilago Gelatinae 4%, Magnesium stearate and talc) once daily before bedtime for 6 weeks is superior in reducing chronic disabling back pain.

  (The null hypothesis is that there is no difference in improvement in pain between melatonin vs placebo groups. The alternative hypothesis is that there is a difference between the two groups).

- Analyses of explorative MOCHA outcomes are not included in this SAP.

Section 3: Trial methods

9. Trial design

- The study is a 1:1 randomized, placebo-controlled, double-blind, single-center parallel group superiority trial. The study is conducted at the Pain Center, Department of Anesthesiology and Intensive Care, Odense University Hospital, Heden 7-9, 5000, Odense, Denmark. The setting is a tertiary care University Hospital pain center. Participants are recruited through advertisements (local papers and local radio), social media campaigns (LinkedIn and Facebook), and from the pain center waiting list. Recruitment via LinkedIn and Facebook are done through general posts and posts targeting special interests groups for people with chronic pain.
  Eligible patients signing the informed consent form are randomized to one of two groups:
  1. Melatonin 10mg, once daily (2 x 5mg pills)
  2. Placebo 10 mg, once daily (2 x 5mg pills)

  The treatments are described in detail in the trial protocol.

10. Randomization

- The randomization list was prepared by a data manager, who was not otherwise involved in the study. The allocation sequence was concealed in a password-protected computer file, which only the data manager had access to. The randomization list consisted of 220 sequential numbers (110 in each group) in permuted blocks of 2-6 individuals and was generated by the data manager using the REDCap electronic data capture tool. Patients were allocated to the melatonin- or placebo group with a 1:1 allocation ratio). The randomization list was sent to the pharmacy producing the study medicine, who labelled each medicine can with unique blinding codes according to the randomization list. The trial medicine was delivered to the trial site together with individual code-envelopes for every blinding code. The coded envelopes were stored behind double lock with 24/7 accessibility at the department of Anesthesiology and Intensive care at Odense University Hospital (OUH) (in case emergency unblinding of patients was required).

11. Sample size

- Based on an unpaired t-test, aiming to detect a between-group difference of 1 point or more in the change in pain intensity and assuming a SD of 2.5, 100 participants were needed in each group to achieve a power of 80% with a significance level of 5%. The intended analytical approach involves using baseline values as covariates instead of change scores, which is expected to result in a further gain in statistical power. Dropouts may decrease the statistical power; however, as a mixed model will be used for analysis, they will still contribute information. To account for any potential loss of power, the sample size was increased by 10%, i.e. we aimed at a total sample size of 220 patients (110 in each group).

12. Framework

- Both primary and secondary outcomes will be assessed using a superiority framework, expecting that patients randomised to melatonin will improve more than patients randomised to placebo. For the primary outcome the interpretation will follow the outlined interpretation rules in Table 1. A between-group difference of 1 point in the primary outcome was considered clinically relevant.

Table 1: Primary outcome trial interpretation for different estimated between group differences and 95% confidence interval scenarios.

Scenario	Estimate	Lower bound CI	Upper Bound CI	
1.	≥1	≥1		We have demonstrated an intervention effect of clinically relevant magnitude
2.	≥1	≥0, ≤1		We have demonstrated an intervention effect and obtained a positive intervention effect estimate of clinically relevant magnitude.
3.	≥1	≤0		We obtained a positive intervention effect estimate of clinically relevant magnitude, but we could not demonstrate an intervention effect.
4.	≥0, ≤1	≥0	≥1	We have demonstrated an intervention effect and obtained a positive intervention effect estimate.
5.	≥0, ≤1	≥0	≤1	We have demonstrated an intervention effect but also the absence of an intervention effect of clinically relevant magnitude.
6.	≥0, ≤1	≤0	≥1	We obtained a positive intervention effect estimate, but we could not demonstrate an intervention effect
7	≥0, ≤1	≤0	≤1	We obtained a positive effect estimate but also demonstrated the absence of an intervention effect of clinically relevant magnitude.
8.	≤0		≥1	We obtained a negative intervention effect estimate, but we could not exclude that the intervention effect is of clinically relevant magnitude.
9.	≤0		≥0, ≤1	We obtained a negative intervention effect estimate and demonstrated the absence of an intervention effect of clinically relevant magnitude.
10.	≤0		≤0	We have demonstrated the absence of a positive intervention effect.

13. Statistical interim analysis and stopping guidance

- The trial was planned to stop when patient number 220 was randomised, according to the a priori sample size calculation. No additional stopping rules were defined for the trial. No interim analyses of data were planned during the trial.

14. Timing of final analyses

- Analysis of the primary and secondary outcomes (to be included in the primary report/publication) for comparison of melatonin vs. placebo will commence after the 8-week safety assessment has been conducted for the last patient (anticipated to be medio April 2026).

15. Timing of outcome assessments

- Table 2 presents an overview of the timing of the assessment of the primary and secondary outcomes in the MOCHA trial (please also refer to the published protocol (1)).

Table 2: Timing of collection of primary and secondary outcomes in the MOCHA trial.

		Week					
	Baseline	**1**	**2**	**3**	**4**	**5**	**6**
NRS pain intensity	X	X	X	X	X	X	X
ISI	X			X			X
RMDQ	X						X
PROMIS-10 GH	X						X
GPE							X

NRS: Numeric rating scale; ISI: Insomnia Severity Index; RMDQ: Roland Morris Disability Questionnaire; PROMIS-10 GH: Patient-Reported Outcomes Measurement Information System Global Health v. 1.2.; GPE: Global Perceived Effect.

- Adverse events (safety measures) were collected at week 3, 6 and 8 (post study safety visit) and registered according to the time they occurred.

Section 4: Statistical principles

16. Confidence intervals and p-values

- 16: Level of statistical significance

  All statistical tests will be 2-sided and performed using a 5% significance level.
- 17: Adjustment for multiplicity

  As the MOCHA trial has one predefined primary outcome, and we consider all other outcomes as supportive outcomes, no adjustments for multiplicity will be performed.
- 18: Confidence intervals

  All presented confidence intervals will be 95% and be 2-sided. Please also refer to Table 1, for details about interpretation of the lower and upper bounds of the 95% confidence interval in relation to different between-group effect estimates for the primary outcome.

19. Adherence and protocol deviations

- 19a: Definition of adherence to the intervention

  Adherence will be determined based on medication count or self-report (for patients not returning the study medicine) as follows:

  - Adherent patients are defined as:
    - A patient taking 80% or more of the study medicine (melatonin or placebo). Over the 6-week intervention patients are required to take 84 pills (i.e. 6 weeks x 7 days x 2 pills/day [each 5mg]). Patients taking 68 pills according to the medication count (68/84 x 100 = 80.1%) will be considered adherent to the intervention. This 68 pills adherence rule will also apply in case a patient has reduction of the prescribed dose (from 10mg to 5mg daily) during the study.

      Patients are required to return any left-over study medicine at the 6-week visit (a medication count is performed by the study person responsible for the 6-week visit). We will assume that all non-returned medicine has been consumed by the patients.
    - A patient not returning the study medicine, and self-report having used 68 pills or more of the study medication.
  - Non-adherent patients are defined as:
    - A patient having used less than 80% of the prescribed dose according to the medication count.
    - A patient not returning the study medicine, and self-report having taken 67 pills or less.
    - Patients with complete lack of information medication count or self-report.

- 19b: Description of how intervention adherence will be presented

  The number and percentage of patients being adherent/non-adherent according to the definitions in 19a will be presented for each of the two intervention groups (i.e. melatonin or placebo).

- 19c/19d: Definition of protocol deviations for the trial and how they will be reported. The following are pre-defined as major protocol deviations, which may have direct effect on the primary outcome:
    - Reporting of new pain medication use during the treatment period.

  All major protocol deviations will be reported in the primary RCT report. We expect no cross-over between groups as this is a placebo-controlled trial with blinding of both patients, clinicians and study coordinators.

20. Analysis populations

- In the main analyses of the primary and secondary outcomes and adverse events, all patients will be included according to the treatment they were randomized to receive, following the Intention-To-Treat principle (ITT).

In addition, two different per protocol analyses will be performed (on the primary outcome):

- Per protocol (inclusive): The inclusive per protocol population include patients being adherent according to the medication count OR self-report (see definition in 19a).
- Per protocol (conservative): The conservative per protocol population only includes patients according to the medication count (see definition in 19a).

Section 5: Trial population

21. Screening data

- The duration of the recruitment period (start and end date) and the total number of patients screened for eligibility will be collected and reported in a flow-chart. See also item 23 and 24.

22. Eligibility

Below is a summary of the in- and exclusion criteria for the MOCHA trial.

<u>Inclusion criteria:</u>

- Adults aged 18 to 64 years with back pain in the area from T1 to the gluteal fold. Back pain must be present on ‘most days’ or ‘every day’ for the past 3 months, back pain must limit the daily life or work activities on ‘some days’, ‘most days’, or ‘every

day' during the past 3 months, and the average pain intensity over the past 7 days must be ≥4 on 0-10 Numeric Rating Scale [NRS].

- Participating fertile women must use safe contraception (spiral, birth control pills, contraceptive patch, contraceptive vaginal ring, or progestin injections) for 3 weeks before and 1 week after the trial. If female participants do not use safe contraception, they must provide oral and written informed consent that they will not engage in sexual activity with males during the trial. A woman is considered non-fertile if she is sterilized, hysterectomized, bilateral oophorectomized or is postmenopausal. A woman is considered postmenopausal when vaginal bleeding has been absent for 1 year as reported by the participant.
- Speak and understand Danish language.

Exclusion criteria:

- Known abuse of alcohol or other substances or people who use opioids.
- Known malignancies within past 6 months, known fractures within past 4 months, lumbar radiculopathy, spinal stenosis, and inflammatory/autoimmune arthritis.
- Severe psychiatric disorders, suicide and self-damage thoughts and/or psychotic symptoms.
- Pregnancy. A negative urine test for human chorionic gonadotropin [hCG] for pregnancy for fertile women before inclusion is required.
- Kidney or liver failure. Tested by a blood test (serum levels of alanine-aminotransefase (ALAT), creatinine, glomerular-filtration-rate (GFR)).
- Contraindications to use of melatonin according to the Danish Medicines Agency's approved product information.

23. and 24. Recruitment and withdrawal/follow-up

- The CONSORT flow-chart will include:
    - Number of patients assessed for eligibility
    - Number of patients excluded (with reasons)
    - Number of patients eligible for inclusion in the trial
    - Number of eligible patients not consenting to participate (with reasons)
    - Number of patients randomized to each treatment arm

- Number of patients with assessment of the primary outcome at week 1, 2, 3, 4, 5 and 6.
- Withdrawals/lost to follow-up (with reasons) and timing for both treatment arms
- Number of patients included in the ITT, per protocol (conservative) and per protocol (inclusive) analyses for each treatment arm.

25. Baseline patient characteristics

- 25a: List baseline characteristics to be summarized.
  Mock table 1 (below) presents an overview of the baseline characteristics that will be presented in the primary report. For further details, please refer to the published protocol paper (1).

- 25b: Details of how baseline characteristics will be descriptively summarized.
  Categorical data will be summarized as numbers with percantages (%). Continuous data will be summarized as mean (SD) or median (10 and 90% percentile) dependening on the shape of the distribution. No formal tests for significant differences between treatment groups at baseline will be performed.

Section 6: Analysis

26. Outcome definitions

Outcomes presented under Primary or Secondary Outcome Measures at ClinicalTrials.gov (NCT06476392) will be reported in the primary report.

- Table 2 presents and overview of the outcomes and their timing. Mock tables 2 and 3 illustrate how the results for the primary and secondary outcome analyses and the adverse events will be presented in the primary report.

- Primary outcome is the difference in improvement in the melatonin vs. placebo group in average pain intensity (last 7 days) assessed using a 0-10 numeric rating scale (NRS, 0=no pain and 10=worst imaginable pain) from baseline to 6 weeks.

- We will also compare the effect of melatonin, relative to placebo, on the following secondary outcomes:
    - Difference in the proportion of patients reaching a 30% decrease in average NRS pain intensity (last 7 days) from baseline to 6 weeks.
    - Difference in the proportion of patients reaching a 50% decrease in average NRS pain intensity (last 7 days) from baseline to 6 weeks.
    - Trajectory of weekly (at 0, 1, 2, 3, 4, 5 and 6 weeks) NRS back pain intensity scores from baseline to 6 weeks.
    - Difference in improvement in *back pain related disability* from baseline to 6 weeks. Back pain related disability is assessed using the 23-item Roland Morris Disability Questionnaire (RMDQ) with a score ranging from 0 (no disability) to 23 (extremely severe disability).
    - Difference in *Global Perceived Effect* (GPE) after 6 weeks, assessed with the question: 'How is your back pain now compared to when you entered this study', with 5 response options (much worse, worse, almost the same/unchanged, better and much better).
    - Difference in improvement in *Insomnia symptoms* from baseline to 6 weeks. Insomnia symptoms is assessed using the Insomnia Severity Index (ISI), score ranging from 0 (best) to 28 (worst).
    - Difference in improvement in *Physical and Mental Health* from baseline to 6 weeks. Physical and mental health is assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS-10) Global Health questionnaire version 1.2. The PROMIS-10 questionnaire comprises 10 items designed to evaluate different dimensions of global health. A Physical Health (4 items) and Mental Health (4 items) score will be calculated from 8 of the 10 PROMIS-10 questions (items).
- For a more detailed description of the outcomes please also refer to the published protocol (1).

- For unknown reasons it was discovered by the company that delivers the ear EEG equipment (outcome measures described under Other Outcome Measures in the ClinicalTrials.gov [NCT06476392] registration), that the quality of the EEG-data was not satisfactory. Therefore, the study steering committee decided to cancel the use of ear EEG in the study. This was done because the expiration day for the trial medication was approaching and it was therefore not possible to postpone recruitment of patients supposed to have EEG assessments in the trial.

27. Analysis methods

- Statistical methods for treatment effect estimation:
  Estimation of the treatment effect of continuous primary and secondary outcomes with a baseline measurement will be based on mixed linear models with time (baseline and any follow-up time point), treatment group (Melatonin or placebo) and the interaction between time and treatment arm, as fixed effects and intercept and slope as patient-specific random effects. The error variance will be allowed to vary over time and across the two groups, except at baseline. The variance-covariance matrix of the random effects will be allowed to vary across the two groups. Fitting of the mixed models will be based on the restricted maximum likelihood technique. In case of convergence problems, the model will be simplified by additional restrictions on the variance parameters with respect to equality over time and between the two groups. Interactions will be parametrized as time dependent treatment effects such that the treatment effect at week 6 corresponds directly with the efficacy parameter of interest. The treatment effect at baseline will be set to 0 to reflect randomization.

  For the primary outcome (i.e. between-group difference in change from baseline to 6 weeks in NRS pain intensity [mean of last 7 days]), the follow-up time points 1, 2, 3, 4, 5, and 6 weeks will be used. Table 2 describes the intended trial interpretation with respect to the primary outcome for all possible effect estimates and 95% CI scenarios. We consider a between-group difference of 1 point in the primary outcome clinically relevant.

  For the ISI secondary outcome, the follow-up time points 3 and 6 weeks will be used.

For the remaining continuous secondary outcomes (i.e. RMDQ, PROMIS-10 GH and pain sensitivity), only the 6-week follow-up time point will be used.

For the two responder indices outcomes (30% and 50% decrease in average NRS pain intensity), treatment effects will be reported as odds ratios based on a logistic regression model including the baseline pain intensity value as a covariate. These analyses will only include patients with primary outcome at 6 weeks.

The secondary outcome (GPE) is measured on an ordinal scale. The treatment effect will be expressed as an odds ratio from an ordinal logistic regression model.

For any estimated treatment effect, confidence intervals and p-values will be computed using the Wald-principle.

- Reporting treatment effect estimates
  Treatment effects (i.e. difference between Melatonin and Placebo) will be expressed as the gain in reduction (or increase – dependent on the outcome) observed in the Melatonin group, i.e. a positive number always expresses a favoring of Melatonin. Treatment effects will be reported with 95% confidence intervals.

  For each outcome also characteristics of the distribution in each arm will be reported.

- Mean trajectories
  For the primary outcome and ISI, the mean trajectories (baseline to 6 weeks) in each arm will be visualized. This will be based on estimates of the corresponding marginal means from the linear mixed model. In addition, the empirical curves (with SD) will be presented in the supplement.

28. Missing data

- Handling of missing data.

  The use of a linear mixed model for all longitudinal outcome measurements including baseline allows to include all randomized patients into the primary analysis

independent of the missing patterns observed. Consequently, the intention-to-treat (ITT) principle can be applied, assuming that missing outcome data satisfies the missing at random assumption.

Sensitivity analyses with respect to the missing at random assumption will be conducted. These analyses will be based on multiple imputation and follow two different approaches. First, we will consider a tipping approach adding to all generated outcome values a constant value δ, mimicking the expectation that missing outcomes values are in reality higher than those we would expect under the missing at random assumption. The second approach focus on patients in the Melatonin group, who stop participation in the trial, i.e. for whom both the outcome values as well as information on the medication is missing after the finally observed outcome. In these patients, the further increments are generated using the distribution of the increments observed in the placebo group in patients with similar values until drop out.

29. Additional analyses

- Details of any additional analyses:
    - We will investigate whether a certain level of insomnia at baseline may be a prerequisite for pain reduction from Melatonin. This question will be addressed by estimating the treatment effect as a function of the baseline ISI value. This will be approached by modelling the treatment effects as splines with 3 knots within the mixed linear model used to analyze the primary outcome. The knots will be placed at the 15^{th}, 50^{th} and 85^{th} percentile of the distribution of ISI.

Further exploratory analyses may be conducted in subsequent reports if considered relevant.

30. Harms

- Handling and reporting of adverse events

Adverse events (AEs) are collected at week 3, 6 and 8 (post study safety visit). Participants will complete a questionnaire regarding side effects and will also be interviewed by the investigator about any adverse events that occured. The severity of

harms will be assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. To determine whether an AE is related to the trial medication, the investigator will refer to the Summary of Product Characteristics (SmPC) for Melatonin.
A serious adverse event (SAE) is defined as any medical occurrence or effect that, at any dose, results in death, poses a life-threatening risk, necessitates hospitalization or extends an existing hospital stay, causes persistent or significant disability or incapacity.

Number of AEs and SAEs will be reported separately in the trial report, and both will be divided into events related or nonrelated to the trial medication, according to the definitions above. Adverse events reported by more than 10% in one of the groups will be described. Number of deaths will be reported separately. AEs and SAEs will be presented as illustrated in MOCK table 3.

31. Statistical software

- Details of statistical package used for analyses.
  STATA 19.5 (or an updated version if applicable) (StataCorp, College Station, TX, USA).

32. Operating procedures

- Data management and other procedures

  Participants will respond to questionnaires via the REDCap electronic data capture tool that enters data directly into the electronic Case Report File (eCFR). Investigator collected data will be entered directly into the eCFR during the visits. Range checks for data values will be used to improve the data quality in the eCFR. In the analyzing process, all the data will be transferred to a statistical program and the analyses will be performed by an independent statistician. The data will be anonymized and stored 25 years after the end of the trial. The Trial Master File (TMF) is saved in a safe and password-protected Sharepoint.

  To reduce the risk of interpretation bias, blinded results of primary and secondary

outcomes from the statistical analyses (excluding adverse events) performed by a blinded statistician (group A vs group B) will be presented to all authors, who will agree on two alternative written interpretations. One where group A is melatonin and one where group A is placebo (and vice versa for group B). After finalizing the blinded interpretation, the data manager, who was not otherwise involved in the study will unblind the groups.

During the study period unblinding of a single participant will only occur in case of a medical emergency and if the Sponsor/PI (KDB) finds it necessary to ensure the safety of the participant. Unblinding occurs by breaking the code-envelope related to the subjects blinding code.

References

1. Kilic K, Vaegter HB, Bruun KD, Vach W, Hartvigsen J, Koes BW, et al. Melatonin for chronic back pain (the MOCHA trial): study protocol for a randomized, double-blind, placebo-controlled trial. Trials. 2025;26(1):513.
2. Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Dore C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337-43.

Mock table 1: Baseline patient characteristics.

	Melatonin (n=XX)	**Placebo (n=XX)**
Female, no. (%)		
Age, years (SD)		
Body mass Index, kg/m^2 (SD)		
Work status, no. (%):		
Working (including students)		
Sick leave (partly or full)		
Disability pension		
Other public welfare support		
Education, no (%):		
Primary school		
Upper secondary		
Bachelor/vocational education		
Master degree or higher		
Pain medicine use, no. (%):		
Paracetamol		
NSAID		
TCA/SNRI		
Gabapentinoids		
Muscle relaxants		
Other		
Frequency of back pain last 3 months, no. (%):		
Most days		
Every day		
Activity limiting back pain last 3 months, no. (%):		
Some days		
Most days		
Every day		
Average NRS pain, last 7 days (SD)		
ISI score (SD)		
RMDQ score (SD)		
PROMIS-10, Physical Health (PH) score (SD)		
PROMIS-10. Mental Health (MH) score (SD)		
PPT, lower back (kPa)		
PPT, shoulder (kPa)		

NSAID=Non-steroidal antiinflammatory drugs; TCA=Tricyclic antidrepessants; SNRI=Serotonin and norepinephrine reuptake inhibitors; NRS=Numeric rating scale; ISI= RMDQ=Roland Morris Disability Questionnaire; PROMIS=Patient-Reported Outcomes Measurement Information System; PPT=Pain pressure threshold

No between group p-values will be reported for baseline characteristics.

Mock table 2: Outcomes at 6 weeks

	Score at 6 weeks melatonin group (mean, SD)	Score at 6 weeks placebo group (mean, SD)	Change baseline to 6 weeks melatonin group (mean, SD)	Change baseline to 6 weeks placebo group (mean, SD)	Between group difference in change* (mean, 95% CI)	Total no. of possible assessments in each group	No. of assessments (melatonin / placebo)
Primary outcome:							
NRS pain intensity						770	XX/YY
Secondary outcomes:							
ISI score						330	XX/YY
RMDQ score						220	XX/YY
PROMIS-10 PH score						220	XX/YY
PROMIS-10 GH score							
PPT, lower back (kPa)							
PPT, shoulder (kPa)						220	XX/YY
Global Perceived Effect:	**No. (%)**				**OR (95% CI)**	110	XX/YY
Much better							
Better							
Same/unchanged							
Worse							
Much Worse							
NRS pain intensity responders:							
30% improvement						110	XX/YY
50% improvement						110	XX/YY

*Baseline to 6 weeks between group mean difference in change estimated from mixed model, including all available follow-up time points for each outcome.

Mock Table 3: Adverse events

	Melatonin (n=xx)	**Placebo (n=xx)**
Serious adverse events:		
No. of patients (%)		
No. of events (%)		
No. of events related to trial medication (%)		
Deaths, no. (%)		
Adverse events:		
Total no. of patients (%)		
Total no. of events (%)		
Mild:		
No. of patients (%)		
No. of events (%)		
No. of events related to trial medication (%)		
Moderate:		
No. of patients (%)		
No. of events (%)		
No. of events related to trial medication (%)		
Adverse events reported by more than 10% in one of the groups:		
YYY		
XXX		
ZZZ		