Analytical Plan for Association between KOOS scores and OTC analgesic use in patients using knee-braces

DOCUMENT: SAP-2022-023-AD-v01

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2022-05-02

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Document version

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01	Initial version

1 ABBREVIATIONS

- CI: confidence interval
- KOOS: Knee injury and Osteoarthritis Outcome Score
- OTC: Over the counter
- SD: standard deviation
- VAS: Visual analog scale

2 CONTEXT

2.1 Objectives

Quantify the association between KOOS increase and frequency of use of over-the-counter analgesic over a 4-week period, controlling for pain reduction.

2.2 Hypotheses

In (P) patients 18 through 65 years old who suffer from medial osteoarthritis of the knee using an unloading knee brace, (E) the utilization of OTC analgesics (O) influences the KOOS score (T) over a 4-week period.

2.3 Study design

Cross-sectional, change from baseline study.

3 DATA

3.1 Raw data

The raw data base was received with KOOS and VAS pain measurements both at baseline and after the 4-week period of the study, as well as the weekly frequency of OTC analgesic use. The original data base had 8 variables collected on 10 observations.

3.2 Analytical dataset

From the pre and post measurements available in the raw data the differences between baseline and post KOOS scores were calculated, as well as the differences between baseline and post VAS pain scores. Baseline characteristics were kept for the descriptive analysis of the study sample.

After the cleaning process 8 variables were included in the analysis. The total number of observations excluded due to incompleteness and exclusion criteria will be reported in the analysis. Table 1 shows the structure of the analytical dataset.

Table 1 *Analytical dataset structure after variable selection and cleaning.*

id	age	sex	pain_pre	koos_pre	outcome	pain_reduc	frequency
1							
2							
3							
…							
N							

All variables in the analytical set were labeled according to the raw data provided and values were labeled according to the data dictionary for the preparation of production-quality results tables and figures.

4 STUDY PARAMETERS

4.1 Inclusion and exclusion criteria

N/A

4.2 Exposures

Frequency of use of OTC analgesics.

4.3 Outcomes

Specification of outcome measures (Zarin, 2011):

1. (Domain) Pain
2. (Specific measurement) KOOS score
3. (Specific metric) Mhange from baseline
4. (Method of aggregation) Mean

Primary outcome

Average increase in KOOS score after a 4-week period using OTC analgesics.

4.4 Covariates

VAS pain scale reduction, age and sex.

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

The epidemiological profile of the study participants will be described at baseline. Demographic (sex, age and BMI) and clinical variables (KOOS and VAS scores) will be described as mean (SD) or as counts and proportions (%), as appropriate. The distributions of participants' characteristics will be summarized in tables and visualized in exploratory plots.

5.1.2 Inferential analyses

All inferential analyses will be performed in the statistical models (described in the next section).

5.1.3 Statistical modeling

A multiple linear regression model will be adjusted to the study data to assess the association between the change in KOOS scores and the frequency of use of OTC analgesics, controlling for the change in VAS pain scores. Due to the small sample size available, the results interpretation will focus on the model's coefficients as a descriptive analysis. Despite this focus on description of possible trends, CI and p-values will be computed and reported for completeness sake.

In order to evaluate the impact of potentially relevant covariates, several models are planned to be specified in increasing complexity. A simple linear regression model will

be used to assess the crude estimate of the association between the change in KOOS score and the use of OTC analgesics. Other separate models will add the change in VAS pain score and the demographic covariates (sex and age) as control variables. The final model will include both the change in VAS score and the demographic variables as control variables.

5.1.4 Missing data

No missing data imputation will be performed. All evaluations will be performed as complete case analyses.

5.2 Significance and Confidence Intervals

All analyses will be performed using the significance level of 5%. All significance hypothesis tests and confidence intervals computed will be two-tailed.

5.3 Study size and Power

N/A

5.4 Statistical packages

This analysis will be performed using statistical software R version 4.1.3.

6 OBSERVATIONS AND LIMITATIONS

Risk of bias

Besides bio-mechanical and quality of life measurements the KOOS score also includes qualitative measures of pain. It could be possible that the VAS pain score is correlated with the KOOS score, which would introduce bias in the association being assessed.

Recommended reporting guideline

The adoption of the EQUATOR network (http://www.equator-network.org/) reporting guidelines have seen increasing adoption by scientific journals. All observational studies are recommended to be reported following the STROBE guideline (von Elm et al, 2014).

7 REFERENCES

- **SAR-2022-023-AD-v01** – Association between KOOS scores and OTC analgesic use in patients using knee-braces
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in

Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014 Dec;12(12):1495-9 (https://doi.org/10.1016/j.ijsu.2014.07.013).

- Zarin DA, et al. The ClinicalTrials.gov results database – update and key issues. N Engl J Med 2011;364:852-60 (https://doi.org/10.1056/NEJMsa1012065).
- Gamble C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337–2343 (https://doi.org/10.1001/jama.2017.18556).

8 APPENDIX

This document was elaborated following recommendations on the structure for Statistical Analysis Plans (Gamble, 2017) for better transparency and clarity.

8.1 Availability

All documents from this consultation were included in the consultant's Portfolio.

The portfolio is available at:

https://philsf-biostat.github.io/SAR-2022-023-AD/