

# Sample size for the verification of possible Interleukin-6 circadian rhythm in Alpha-1 Antitrypsin deficient patients

DOCUMENT: SAP-2021-020-LH-v01

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## Document version

Version	Alterations
01	Initial version

## 1 ABBREVIATIONS

- CI: confidence interval
- d: Cohen's D effect size
- SD: standard deviation

## 2 CONTEXT

### 2.1 Objectives

Determine the sample size to detect the difference of the daily range of Interleukin-6 blood levels between Alpha-1 Antitrypsin deficient and healthy patients.

### 2.2 Hypotheses

The circadian rhythm in patients induces a detectable amplitude between peak and lower daily IL6 levels. The average IL6 daily amplitudes differ between Alpha-1 Antitrypsin deficient and healthy patients.

## 3 DATA

### 3.1 Raw data

A unique study ID will be created for each participant to allow tracking of consecutive IL6 blood level measurements. IL6 data of each participant will be collected at three different times per day. Each datum will have its respective date and time of specimen collection recorded. Participant demographic characteristics to be collected are the group to which they belong (AAT-deficient or healthy), the date of birth, sex and BMI at the date of inclusion.

## Analytical Plan (SAP)

After the cleaning process the raw data will include 13 variables. Table 1 shows the structure of the raw dataset.

**Table 1** Raw dataset structure.

id	group	sex	dob	bmi	date	il6_time1	il6_measure1	il6_time2	il6_measure2	il6_time3	il6_measure3	outcome
1												
2												
3												
...												
n												

### 3.2 Analytical dataset

Age at inclusion will be computed between the date of birth and the date of the first specimen collection.

For each patient the peak level and the lower level of IL6 measurements will be calculated. The peak level (respectively, lower level) of each patient's IL6 will be calculated as the average of all peak level (respectively, lower level) measurements. The amplitude of each patient's IL6 blood level will be calculated as the difference between peak level and lower level.

All variables in the analytical set will be 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.

The analytical dataset will be included in the private version of the report, and will be omitted from the public version of the report.

## 4 STUDY VARIABLES

### 4.1 Primary and secondary outcomes

The primary outcome for the detection of a circadian rhythm will be defined as the amplitude of the IL6 blood level which will be calculated as the difference between the peak level and the lower level of daily measurements.

The secondary outcome will be defined as the the difference between the average IL6 daily amplitude between healthy and AAT-deficient patients.

## 4.2 Covariates

No covariates will be considered for the sample size calculation. Age, sex and BMI will be used to adjust the estimates of the primary and secondary outcomes. Both raw and adjusted estimates will be computed.

## 5 STATISTICAL METHODS

### 5.1 Statistical analyses

#### 5.1.1 Descriptive analyses

N/A

#### 5.1.2 Inferential analyses

N/A

#### 5.1.3 Statistical modeling

N/A

### 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

### 5.4 Statistical packages

This analysis will be performed using statistical software R version 4.1.2.

## 6 OBSERVATIONS AND LIMITATIONS

### Direction of the difference

The AAT deficient patient IL6 blood levels may be hypothesized to be lower (higher) than the levels observed healthy patients. If this hypothesis holds, a left tailed (right tailed) test will have more statistical power to detect significant differences than a two-tailed test. If there is support in the literature for an educated guess on the direction of

the difference this could improve the chance of having significant p-values in the final analysis, at the risk of not detecting a difference in the other direction.

For example, if the hypothesis is specified in the left direction (group of interest has lower levels of IL6 than the healthy group) and the actual observed levels indicate that the group of interest has higher levels of inflammatory biomarkers, then the actual difference will likely not be significant in the study. It is recommended that such decision be made with caution.

## 7 REFERENCES

- **SAR-2021-020-LH-v01** – Sample size for the verification of possible Interleukin-6 circadian rhythm in Alpha-1 Antitrypsin deficient patients

## 8 APPENDIX

### 8.1 Availability

Both this analytical plan and the corresponding analysis report (**SAR-2021-020-LH-v01**) can be downloaded in the following address:

<https://philsf-biostat.github.io/SAR-2021-020-LH/>