Analytical Plan for Implant failure rates in a knee prosthesis sub-population of the Helios Klinikum Berlin-Buch hospitals

DOCUMENT: SAP-2021-002-JF-v01

From: Felipe Figueiredo **To:** Jens Freitag

Date: 2021-05-16

TABLE OF CONTENTS

1 ABBREVIATIONS 2
2 INTRODUCTION 2
2.1 Context 2
2.2 Objectives 2
2.3 Hypotheses 2
2.4 Study design 2
3 DATA 2
3.1 Raw data 2
3.2 Analytical dataset 3
4 STUDY VARIABLES 4
4.1 Primary and secondary outcomes 4
4.2 Covariates 4
5 STATISTICAL METHODS 5
5.1 Statistical analyses 5
5.1.1 Descriptive analyses 5
5.1.2 Inferential analyses 5
5.1.3 Statistical modeling 5
5.1.4 Missing data 5
5.2 Significance and Confidence Intervals 6
5.3 Study size and Power 6
5.3.1 Statistical packages 6
6 EXCEPTIONS AND OBSERVATIONS 6
7 REFERENCES 6
8 APPENDIX 6
8.1 Availability 6

Analytical Plan for Implant failure rates in a knee prosthesis sub-population of the Helios Klinikum Berlin-Buch hospitals

Document version

Version	Alterations
01	Initial version

1 ABBREVIATIONS

- BMI: body-mass index
- CI: 95% confidence interval
- SD: standard deviation

2 INTRODUCTION

2.1 Context

2.2 Objectives

Perform a time-to-failure analysis to estimate implant loosening rates in a sample of knee prosthesis patient data from the Helios Klinikum Berlin-Buch hospitals

2.3 Hypotheses

N/A

2.4 Study design

Longitudinal retrospective study.

3 DATA

3.1 Raw data

The data will be pre-processed, rearranged and cleaned as follows:

- All variables will be standardized

  - variable names will be standardized for processing purposes, labels will be attributed for reporting purposes;
  - observations will be standardized according to variable type (numeric, dates, categorical, etc)
- All categorical variables will be standardized according to their categories pre-defined in the dictionary provided
  - Gender: M/W
  - Smoking status: No/Yes
  - Joint: L/R
- All dates will be standardized and invalid values removed
  - All invalid values like “xxxxxxxxxx”, “xxxxxxxxxxxxxxx”, etc will be removed before data processing;
- Age will be computed as whole years between birth and first surgery, with calendar accuracy;

Two observations appear to be test data (Names: Patient 1, Patient 2) and will be removed.

3.2 Analytical dataset

The analytic dataset will be composed from a selection of variables obtained from the original dataset. Study variables selected for this analysis are:

- Gender
- Date of birth
- Age
- BMI
- Joint operated on
- Smoking status
- Date of surgery
- Date of failure diagnosis

Other variables from the raw dataset will not be used for the analysis. The event occurrence and time under observation will be computed as defined in the section 4.1.

After all data cleaning and variable selection procedures the analytic dataset should have a similar structure as shown in Table 1.

Table1 *Mock-up example of analytic dataset*

id	gender	age	bmi	joint	uka_date	loosening_date	event	time
1								
2								
3								
…								
82								

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

Upon inspection of the dates of first surgery and dates of loosening for individual patients, it appears the study period is delimited between 2017-05-10 and 2021-02-25, so these will be the dates considered as study start and end.

Specification of outcome measures (Zarin, 2011):

1. (Domain) Transplant quality
2. (Specific measurement) Prosthesis loosening
3. (Specific metric) Time-to-event
4. (Method of aggregation) Kaplan-Meier estimator

Primary outcome

The event of interest in this analysis is the diagnosis of implant loosening. The time until the event of interest will be computed between the date of first surgery and date of implant loosening. Patients that reached study end date without implant failure will be censored. Considering the study period of approximately 4 years, Time under observation will be measured in years.

4.2 Covariates

Study outcomes will not be adjusted for covariates like age, gender or BMI.

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

Patient characteristics will be described with frequency and proportion for categorical variables and mean (SD) for numerical variables.

Table 2 *Mock-up example of descriptive analysis table*

Characteristic	N
Gender	
M	
W	
Age	
BMI	
Joint	
L	
R	
Loosening	
Success	
Failure	

5.1.2 Inferential analyses

The main study outcome (time-to-failure) will be presented in a Kaplan-Meier plot.

Time-to-failure will be cross-analyzed with all selected categorical variables, including gender, smoking status and joint. Univariate analyses will be performed using the log-rank test.

5.1.3 Statistical modeling

Study outcomes will not be adjusted for covariates like age, gender or BMI.

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.

5.3.1 Statistical packages

This analysis will be performed using statistical software R version 4.1.0.

6 EXCEPTIONS AND OBSERVATIONS

None.

7 REFERENCES

- **SAR-2021-002-JF-v01** – Implant failure rates in a knee prosthesis sub-population of the Helios Klinikum Berlin-Buch hospitals
- 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

Both this analytical plan and the corresponding analysis report (**SAR-2021-002-JF-v01**) can be downloaded in the following address:

https://philsf-biostat.github.io/SAR-2021-002-JF/