TEMPLATE RESEARCH PROTOCOL

for non-WMO-applicable research

23-04-2024, version 4.0

Full title of protocol	ASA prediction using health data and medication use
Short title or Acronym	ASA prediction
Protocol ID / Panama number	12006
Version	3.0

Date	23-04-2024
Coordinating investigator[1]/ Project leader	*S.F. van den Heuvel – s.vandenheuvel@erasmusmc.nl*
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Sponsor[4] (in Dutch: verrichter/opdrachtgever)	*Erasmus MC*
Subsidizing party[5]	*Health Holland – Ministry of Economic Affairs*

Name	**Signature**	**Date**
Sponsor or legal representative: *<please include name and function>* *<For non-commercial research,>* **Head of Department:**	**C. van der Marel** *Anesthesiology*	**24-04-2024**
Coordinating Investigator/Project leader/Principal Investigator: *<please include name and function>*	**J.-W. Korstanje** *prinicipal investigator*	**24-04-2024**

1. *Coordinating investigator: Investigator who bears the responsibility for the coordination of investigators operating in the various centers participating in multicenter research. Not all multicenter research will have a coordinating investigator. There is no requirement to appoint one. A project leader has the responsibility to develop a research protocol and to complete the study within the predefined goals.*
2. *Principal investigator: Investigator who has the overall responsibility to comply and to complete the study within the predefined goals.*
3. *Multicenter research: as an alternative you can also state that these are specified in the list with participating centers including principal investigator. This separate document with version date must be uploaded under category I1.*
4. *Sponsor: The party that commissions the organization or performance of the research, for example a pharmaceutical company, academic hospital, scientific organization or the investigator's employee. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidizing party.*
5. *Subsidizing party: A party that provides funding for a study but does not commission it*

Table of Contents

Please note that it is not allowed to remove paragraphs from this template protocol. If a paragraph is not applicable, please mention this in the specific paragraph, preferably with a short motivation.

List of abbreviations and relevant definitions*

CTA	Clinical Trial Agreement
De novo biobank	A new data, human material or imaging collection
DMP	Data Management Plan
DPIA	Data Protection Impact Assessment
DTA	Data Transfer Agreement
Exception consent	Form Care for data Template, in Dutch: Formulier uitzondering toestemming
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation in Dutch: Algemene Verordening Gegevensbescherming
IC	Informed Consent
IFU	Instruction For Use
MTA	Material Transfer Agreement
NWTC	Non-WMO Review Committee; in Dutch: Niet WMO Toetsingscommissie
UAVG	Dutch Act on Implementation of the General Data Protection Regulation; in Dutch: Uitvoeringswet Algemene Verordening Gegevensbescherming
WMO	Medical Research Involving Human Subjects Act, in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen

**Please add any new definitions that are used in the research protocol*

Summary

The summary should give a brief description of the central question that the research is intended to answer and its justification. It should specify the hypothesis (if applicable) and the research objectives. In addition, the synopsis should briefly describe the design, population, methods and procedures of the study. Finally, if applicable, the nature and extent of the burden and risks should be indicated.

Rationale: The development of a machine learning algorithm that predicts American Society of Anesthesiologist-Physical Status (ASA-PS) based on preoperative variables would not only improve clinical decision-making in patient risk stratification but also offer a more reliable tool for administrative and regulatory uses. Therefore, the development of such a machine learning tool presents a significant opportunity to advance both the science and practice of perioperative care. Incorporating medication use into the algorithm could further enhance its predictive power, as it is closely linked to systemic disease. This addition could help refine the ASA-PS classification, making it an even more valuable tool in the clinical setting.

Objective(s): To develop a machine learning algorithm that can predict the American Society of Anesthesiologists Physical Score (ASA-PS) I-IV based on gender, age, BMI, standard health questionnaire and medication use (ATC) and determine its performance.

Study type: A retrospective cohort study of routinely collected health data of patients who had surgery in the Erasmus MC.

Study population: All patients, 18 years or older, who underwent elective surgery in the Erasmus MC since the introduction of HiX and who have had a preoperative anesthesiological consultation.

Methods: Multiple machine learning algorithms predicting ASA-PS using age, sex, BMI, health questionnaires and ATC codes of used medication will be developed, validated and evaluated.

Burden and risks: none

Recruitment and consent: Based on art. 24 of the “Uitvoeringswet AVG”, this research will be performed under the exception consent:

- Obtaining informed consent of all patients in this database (>90.000 patients) demands an unreasonable effort.
- The study serves a general purpose (triage of patients for personalized preoperative screening)
- Data that is processed is stored in pseudonymized format and cannot lead to individual patients.
- Patients that have registered an opt-out for scientific research are excluded

1. Introduction and rationale

The American Society of Anesthesiologists Physical Status (ASA-PS) classification system is a widely used tool for assessing surgical fitness and other clinical contexts. However, its inherent subjectivity and heavy reliance on clinician judgment can lead to inconsistencies in patient risk stratification, a critical component of perioperative care. Furthermore, the ASA-PS system has been adopted for various administrative and regulatory purposes beyond its original intent, such as quality assessment by the Dutch Health and Youth Care Inspectorate (IGJ), compensation decisions by private payers in the USA, patient triage, and determining suitability for certain types of surgery.

Given the broad and critical applications of the ASA-PS system, enhancing its precision and objectivity is of paramount importance. One way to achieve this is through the development of a machine learning algorithm that predicts ASA-PS based on preoperative variables. Anesthesiologists base the ASA-PS score on the presence of systemic diseases, which can be inferred from medication use. By leveraging data such as ATC codes, BMI, sex, age, routinely collected preoperative health data, and medication use, this algorithm could provide a more consistent and objective measure of ASA-PS.

This would not only improve clinical decision-making in patient risk stratification but also offer a more reliable tool for administrative and regulatory uses. Therefore, the development of such a machine learning tool presents a significant opportunity to advance both the science and practice of perioperative care. Incorporating medication use into the algorithm could further enhance its predictive power, as it is closely linked to systemic disease. This addition could help refine the ASA-PS classification, making it an even more valuable tool in the clinical setting.

2. Objective(s)

To develop a machine learning algorithm that can predict the American Society of Anesthesiologists Physical Score (ASA-PS) based on sex, BMI, age and medication use (ATC) and routinely collected preoperative health data and determine its performance.

3. Study type

3.1. **Study type**

☒ Retrospective
☐ Prospective
☐ Combination Retrospective/Prospective

3.2. **Single center / Multicenter**

☒ Single center
☐ Multicenter

3.3 **Check all the applicable boxes**

☒ Medical records (re-use of data from healthcare, including AI)
☐ Case report

☐ Re-use data from research
☐ Evaluations of quality of healthcare (retrospective
☐ Research with additional use of residual material from regular healthcare
☐ Research with re-use of human material from research or existing biobank
☐ De novo biobank
☐ Phase IV research
☐ Healthcare evaluation research (prospective)
☐ Research with medical devices
☐ Research with In Vitro Diagnostic Tests
☐ Other research, describe

4. Study population

4.1. Study population

☒ Adults (16 years and older)
☐ Minors (younger than 16 years)
☐ Incapacitated adults (16 years and older)
☐ Incapacitated minors (younger than 16 years)

4.2. Population (base)

All patients who underwent a surgical, diagnostic or therapeutic procedure within the surgical suite of the Erasmus MC since 2018 (introduction new digital Hospital Information System, HiX) and who had a ASA-PS class recorded.

4.3. Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Underwent a surgical, diagnostic or therapeutic procedure within the surgical suite of the Erasmus MC
- ASA score recorded in electronic medical record
- A verified medication list in HiX, or a filled out preoperative anesthesiological health questionnaire registered in HiX

4.4. Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Age <18 at moment of surgery
- ASA V-VI
- Opt-out registered in HiX

4.5. Sample size calculation

It is widely acknowledged that robust development and accurate validation of AI-based prediction models necessitate large sample sizes. (van Royen et al. EHJ 2023) However, no sample size calculators are currently available for development of AI models to perform a formal *a priori* sample size calculation.

Nevertheless, we used sample size guidelines for regression-based prediction models as a starting point (Riley et al.,2020). For an upper limit of the minimum required sample size (for a relatively unbalanced, multiclassification model) we used a c-statistic of 0.77 (Mudumbai et al., 2019) for a prediction of ASA I-IV, 302 candidate parameters, and a prevalence of 0.04 (for ASA IV, Model #10 in Table 1) and targeted a shrinkage of 0.9. This led to a sample size of 67,116.

For a lower limit of the minimum required sample size (for a more balanced, binary classification model) we used a c-statistic of 0.88 (Zhang et al., 2018) for a prediction of ASA I&II vs. III&IV, 302 candidate parameters, and a prevalence of 0.31 (for ASA III&IV, model #15 in Table 1), targeting a shrinkage of 0.9. This led to a sample size of 6,663.

Based on ratios observed in the dataset and an approximate size of the dataset of approximately 150,000 cases, we estimate approximately 30,000 to remain after applying inclusion and exclusion criteria for these specific models, satisfying at least the minimal criteria.

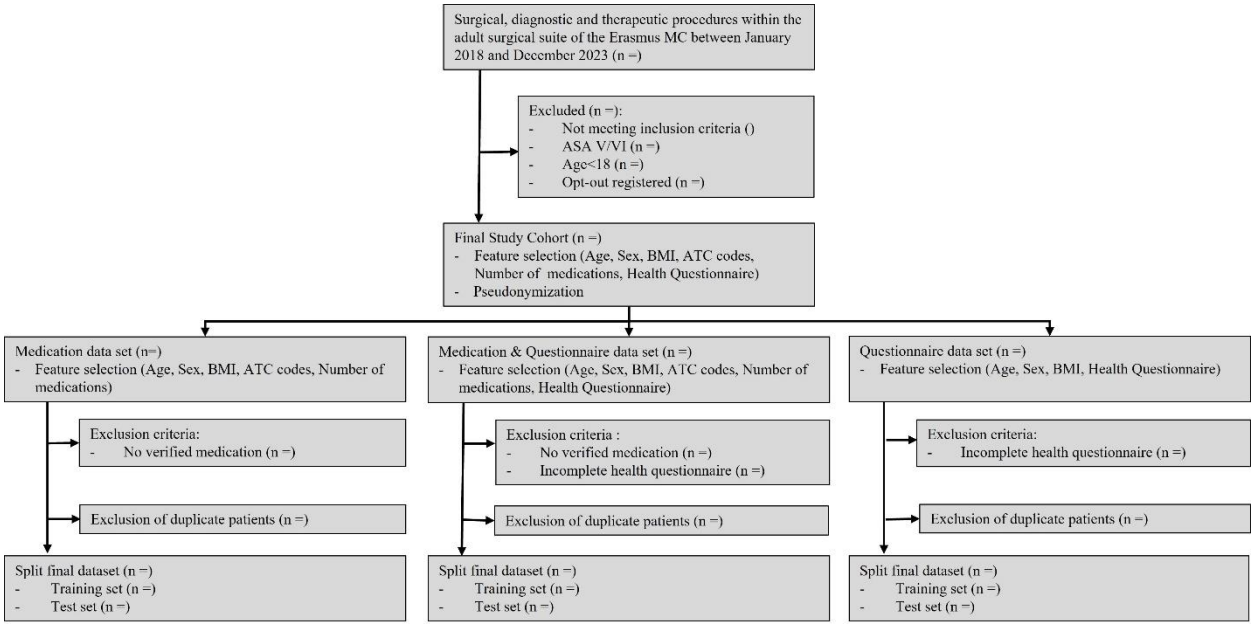
A larger sample size may be needed due to the higher complexity of AI-based prediction models, low prevalence (lower than 0.5) and expected high noise (van Royen et al. EHJ 2023). Therefore, a *posteriori* approach of plotting model errors against increasing sample percentages will also be used to justify the sample size (Rajput et al., 2023).

5.1. **Research methods**

Data collection: Health data obtained during the preoperative screening process for procedures registered in HiX from 2018-2023 will be extracted from the HiX database using a PowerBI query developed by ICON Healthcare in collaboration with the department of Anesthesiology under a data processing agreement. The patient ID's will be cross-referenced with the hospital's "opt-out' registry ("Baseline") and patients with an opt-out will be removed from the database. The resulting database will be stored on a secure, encrypted drive within DRE (Research environment) only available to the Principal Investigator. An extra Pseudonymized patient ID column will be added.

An extraction will then be performed of the following data: Pseudonymized patient ID, demographic information (sex, age), Body Mass Index (BMI), answers to questions in the standard anesthetic preoperative health questionnaire, medication use (represented by ATC codes), and ASA-PS scores. This resulting database will be used to construct the necessary datasets and be further preprocessed. (See DMP for further details).

Construction of data sets: all data will be processed according to the flow diagram in Figure 1. The split into a training and test set will be stratified on ASA-PS scores.



Data Preprocessing: The constructed (training and test) datasets data will be cleaned to handle missing values, outliers, and inconsistencies. Of patients that are present in the dataset with multiple procedures, procedures are first prioritized on the availability of both a verified medication list and a filled out preoperative health questionnaire, then the oldest record will selected and retained. Categorical variables, such as sex, will be encoded appropriately for the machine learning model. A variable on the total number of medication will be constructed. Other new features (variables) can be created based on existing data to improve the performance of our model (feature engineering). The exact nature of these new features is not predetermined, as they will be constructed based on the insights we gain during the exploratory data analysis and model training phases. Medication use will be recoded from the number of medicines a participant uses per ATC code, to the use of a medicine within a particular ATC code (yes/no). Variables will be normalized as required by the specific machine learning method.

Statistical Analysis and Model Validation: The development of a machine learning algorithm will be structured around the creation of predictive models using the H2O AutoML package, applicable in both Python and R environments. These models will undergo training on a meticulously preprocessed dataset, with a k-fold cross-validation strategy where 80% of the data is allocated for training purposes and the remaining 20% for validation. The primary outcome variable in focus is the ASA-PS score, with predictor variables encompassing age, sex, body mass index (BMI), responses to a health-related questionnaire, and ATC codes.

A suite of machine learning algorithms, bundled in the AutoML package, will be employed, including the Generalized Linear Model, Random Forest, Gradient Boosting Machine, and Deep Learning techniques. To enhance predictive performance, a Stacked Ensemble method, also known as Stacked Generalization, will be utilized to amalgamate the strengths of individual algorithms. The ensemble will be guided by a 'superlearner' or 'metalearner', with the Generalized Linear Model serving as the default choice.

Predictions for the response variable will be approached in two distinct manners:

1. A multiclass classification challenge, distinguishing between ASA scores I through IV.

2. A binary classification task, differentiating between the clinically significant groupings of ASA scores I&II and III&IV.

To tackle the multiclass classification, two primary strategies will be adopted:

1. The construction of a Multiclass Classification Ensemble, designed to model the ordinal ASA scores as a single entity.

2. The implementation of a Two-Stage One-vs-One Majority Voting scheme, where six binary ensemble models will be developed to discern between each pair of ASA scores. The collective output of these models will be synthesized through a majority voting mechanism, as facilitated by the diceR package in R.

The following combination of dependent variables (features) will be explored:

1. **Demographics and BMI only**
   To evaluate the predictive power of base characteristics of patients.
2. **Medication combined with demographic data (age, gender) and BMI**
   To evaluate the predictive power of a model based on medication and demographic data that should always be readily available.
3. **Health Questionnaire combined with demographic data (age, gender) and BMI.**
   As 2, but answers to a general anesthetic health questionnaire instead of medication.
4. **Health Questionnaire and medication combined with demographic data (age, gender) and BMI.**
   A combination of all above features.

This results in the following combinations of dependent (response) and dependent (predictor) variables:

Model	Dependent (response)	Independent (predictor)	Strategy
1	ASA 1 vs. 2 vs. 3 vs. 4	Demographics + BMI	Ensemble (multiclass)
2	ASA 1 vs. 2 vs. 3 vs. 4	Demographics + BMI	Two-stage OVO-Majority voting
3	ASA 1 vs. 2 vs. 3 vs. 4	Model 1 + Medication	Ensemble (multiclass)
4	ASA 1 vs. 2 vs. 3 vs. 4	Model 2 + Medication	Two-stage OVO-Majority voting
5	ASA 1 vs. 2 vs. 3 vs. 4	Model 1 + Questionnaire	Ensemble (multiclass)
6	ASA 1 vs. 2 vs. 3 vs. 4	Model 2 + Questionnaire	Two-stage OVO-Majority voting
7	ASA 1 vs. 2 vs. 3 vs. 4	Model 1 + Medication + Questionnaire	Ensemble (multiclass)
8	ASA 1 vs. 2 vs. 3 vs. 4	Model 2 + Medication + Questionnaire	Two-stage OVO-Majority voting
9	ASA 1 & 2 vs. 3 & 4	Demographics + BMI	Ensemble (binary)
10	ASA 1 & 2 vs. 3 & 4	Model 9 + Medication	Ensemble (binary)
11	ASA 1 & 2 vs. 3 & 4	Model 9 + Questionnaire	Ensemble (binary)
12	ASA 1 & 2 vs. 3 & 4	Model 9 + Medication + Questionnaire	Ensemble (binary)

Model development process is inherently iterative, commencing with the aforementioned methodologies. As the project progresses, the pursuit of the most efficacious model will lead to the exploration of additional refinements following the initial model constructions. Examples of possible refinements are: dimensionality reduction, dataset balancing, the modeling of data subsets, the incorporation of domain knowledge leading to the creation of more sophisticated features, and the identification of independent variables that may suffer from the perfect separation problem. This comprehensive approach ensures a robust and systematic development of a machine learning algorithm tailored to the specificities of the ASA-PS score prediction.

Validation: The models will be validated using a separate holdout test set (10% of original dataset). This will ensure that our models generalize well to unseen data. The validation process

will involve applying the models to the test set and comparing the predicted outcomes with the actual outcomes.

Model Evaluation: The performance of the models will be evaluated using metrics such as accuracy, precision, recall, AUC and F1-score. Confusion matrices and ROC's will be used to visualize the performance of our models. Misclassifications will be manually reviewed to gain qualitative insights into the model's performance, with special emphasis on "catastrophic error examples", e.g. ASA I instead of IV, or ASA IV instead of I.

SHAP (Shapley Additive exPlanations) and LIME (Local Interpretable Model-agnostic Explanations) will be explored as techniques for interpreting the models. The calibration of the models will be evaluated using calibration plots. The optimal method for a priori sample size calculation in machine learning algorithms lacks consensus. Consequently, we will utilize the entire available dataset and conduct a post hoc assessment by plotting model errors against increasing sample percentages (Rajput et al., 2023). To detect possible bias in the final model, the 'fairness' of the model will be assessed from different perspectives for different subpopulations.

5.2. **Standard clinical care versus extra for research**
Not applicable

5.3. **Burden and risks**
No burden or risk because of retrospective study design and pseudonymized data.

5.4. **Medical device(s) / In vitro diagnostic tests**
Not applicable.

Incidental findings

6.1. **Chance of incidental findings**
Is there a chance of incidental findings?
☐ Yes
☒ No

6.2. **Procedures**
Not applicable.

Statistical analysis
Describe how data will be analyzed

7.1 **Main study parameters/endpoints**
Please describe the main study parameters/endpoints.
The dependent response variable will be the ASA-PS class, both as a four-level variable (ASA-PS I, II, III and IV) and a two-level variable (ASA-PS I and II versus ASA-PS III and IV). The ASA-PS class was assigned to the patient and recorded in the patients file in the EMR by an anesthesiologist of resident anesthesiology as a part of the routinely performed preoperative anesthesiological screening in preparation for a procedure.

7.2 **Secondary study parameters/endpoints**
Please describe the secondary parameters/endpoints, how the analysis will be done for the outcome parameters.
- Performance metrics: The correct classification of the ASA-PS score will be evaluated using performance metrics of the machine learning algorithms. Common performance metrics include: Accuracy (the proportion of correctly predicted instances), precision (the ratio of true

positive predictions to the total positive predictions), recall (sensitivity or the ratio of true positive predictions to the actual positive instances), F1-score (the harmonic mean of precision and recall) and the Area Under the Receiver Operating Characteristic Curve (AUC-ROC, Measures the model's ability to discriminate between positive and negative instances).
- Calibration: calibration plots will be used to assess the agreement between predictions and the event rate (i.e. correct classification).
- Misclassifications. A manual review of a selection of misclassifications will be performed by two anesthesiologists to qualitatively assess the cause of the misclassification.
- Explainability: SHAP and/or LIME can offer insights into the contribution of each feature to the prediction of individual instances.
- Optimal sample size: Analysis of the learning curves to determine if additional data would likely improve the model's performance or if the current dataset is sufficient.
- Fairness: To detect possible bias in the final model, the 'fairness' of the model will be assessed from different perspectives for different subpopulations.

7.3 Other study parameters

Please describe the other parameters/endpoints.

As independent predictor variables information will be used that could be collected preoperatively with minimal effort for both patient and healthcare professional without the need for hospital visits or invasive procedures (e.g. blood sampling, ECG recording). We will extract basic demographic information (age, sex), general health information collected using a preoperative anesthesiological health questionnaire, medication use registered by the hospital pharmacy using ATC codes, and the Body Mass Index (BMI), all valid at the time of the preoperative anesthesiological screening and subsequent ASA-PS classification

7.4 Analysis

Please describe how the analysis will be done for the outcome parameters.

The performance of the models will be evaluated using metrics such as accuracy, precision, recall, AUC-ROC, AUC-PR and F1-score. Confusion matrices and ROC's will be used to visualize the performance of our models. Misclassifications will be manually reviewed to gain qualitative insights into the model's performance, with special emphasis on "catastrophic error examples", e.g. ASA I instead of IV, or ASA IV instead of I. Explainability will be explored using SHAP and LIME. The optimal sample size will be assessed using the learning curves of the models with increasing sample size. Fairness will be assessed by evaluating the performance on subpopulations.

Ethical considerations

8.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (version, date, see for the most recent version:), Gedragscode Gezondheidsonderzoek 2022 and in accordance with other guidelines, regulations and Acts (if applicable, please specify).

8.2 Informed consent

Will the subjects be asked for informed consent?

☐ Yes *(Upload Participant Information Letter and Informed Consent)*

☐ No, consent already given in previous study *(Upload Participant Information Letter and Informed Consent previous study)*

☒ No, this research will be performed under the exception consent *(Upload form Care for data Template, in Dutch: Formulier uitzondering toestemming)*

☐ Other (e.g. partly, indirectly) *Please describe the situation.*

8.3 **Recruitment and informed consent procedures**

If yes, please give a description of the recruitment and informed consent procedures. How and by whom (investigator, supervising doctor, other person) participants will be informed about the study and asked for their consent, how much time will they be given to consider the decision. The patient information letter with informed consent form should be attached as a separate document.

Not applicable

8.4 **Exception consent**

If no, exception consent: the opt-out registry will be consulted for all patients included in the database. See the attached Form Care for data Template.

Handling and storage of data / images / sound recordings / photos / film recordings

9.1 **Data / images / sound recordings / photos / film recordings**

Please describe which data / images / sound recordings / photos / film recordings is/are used, are they obtained for regular healthcare purposes or in the context a research project, or a combination.

Health data obtained during the preoperative screening process for procedures registered in Hix from 2018-2023 will be extracted from the HiX database using a PowerBI query developed by ICON Healthcare in collaboration with the department of Anesthesiology. This database will be stored on a secure, encrypted drive within DRE (Research environment). There an extraction will be performed of the following data: Pseudonymized patient ID, demographic information (sex, age), Body Mass Index (BMI), answers to questions in the standard anesthetic preoperative health questionnaire, medication use (represented by ATC codes), and ASA-PS scores. This resulting database will be used to construct the necessary datasets and be further preprocessed. (See DMP for further details)

9.2 **Privacy protection**

Describe how subject's privacy is protected. Describe how, when and by whom data is coded (unique code without initials or date of birth) and how the key table is safeguarded, mention the General Data Protection Regulation.

Please note: The handling of personal data has to comply with the EU General Data Protection Regulation and the Dutch Act on Implementation of the General Data Protection Regulation (in Dutch: Algemene Verordening Gegevensbescherming en Uitvoeringswet Algemene Verordening Gegevensbescherming).

Before further preprocessing the data is stored on an encrypted, secure location in a DRE Workspace. There, patient hospital IDs (PID) are deterministically encrypted using encryption packages in R. The key is stored on a separate password protected location within Microsoft Azure only available to the principal investigator. Age at the time of the preoperative screening is calculated using the birth date and date of the preoperative screening. Only 'age' is used for further analyses. All other data is not traceable to individual patients.

9.3 **Handling and storage of data**

Describe how data is handled and stored (i.e., which data management system/data capture system), anonymous / pseudonymized / coded / identifiable, who has access to the coded source data, how long data will be kept, which steps are taken to ensure data security, what happens with the data after the research has been completed.

In line with Erasmus MC guidelines, data will be kept 10 years after it is collected. The coded database will be stored on DRE. The key will be stored on a separate location (Sharepoint) only available to the principal investigator.

9.4 **Handling and storage of images / sound recordings / photos / film recordings**
Describe how images / sound recordings / photos / film recordings are handled and stored, how the subject's privacy is protected, anonymous / pseudonymized / coded / identifiable, what happens with images after the research has been completed.

Not applicable.

9.5 **Approval of access to data / images / sound recordings / photos / film recordings**
Describe how the access is approved. Is access granted by the Data Board, Department, Principal investigator of the collection or other?

Not applicable

Handling and storage of human material

10.1 **Human material**
Please describe which human material is used.
Not applicable

10.2 **Check all the boxes which are applicable to the human material origin:**

☐ Residual material from regular healthcare

☐ Research (material acquired from a previous study).
Add the reference of the study i.e., MEC-number Erasmus MC.

☐ Re-use of human material from existing biobank
Describe whether the human material originates from research into the same disease.

☐ Other, *please specify*

10.3 **Handling and storage of human material**
Not applicable

10.4 **Biobank**
Not applicable

10.5 **Approval of access to human material**
Not applicable

11. Exchange, sharing or transfer of data and/or human material and/or images

Data will be shared on DataVerse according to Erasmus MC policies. Please see the DMP.

12. Amendments

Amendments are changes made to the research after a favorable opinion by the NWTC has been given.

All amendments must be submitted to the NWTC that gave the favorable opinion.

Substantial amendments must be approved by the Niet WMO Toetsingscommissie before they can be implemented.

13. End of study report

Within one year after the end of the study a final study report will be submitted with the results of the study, including any publications/abstracts of the study.

In case the final study report will not be available within one year, another term should be defined including the reasons.

14. Publication

Do you have the intention to submit the study results in a manuscript for publication in a journal:

☒ Yes

☐ No, *please motivate*

Describe when the final study report with the results of the study will be submitted.

15. References

Include a list of all key references published in peer review journals that are relevant for the study and are discussed in the protocol

16. Attachments

☐ Participant information letter and Informed consent document

☒ Care for data Template – Formulier uitzondering toestemming

☐ Questionnaires

☒ Data Management Plan

☐ Data Transfer Agreement

☐ Material Transfer Agreement

☐ Clinical Trial (Site) Agreement

☐ Other, *please describe*