

retention

SMART HEART FAILURE MANAGEMENT

Horizon 2020 Project RETENTION

**“HEART FAILURE PATIENT MANAGEMENT AND INTERVENTIONS USING
CONTINUOUS PATIENT MONITORING OUTSIDE HOSPITALS AND
REAL WORLD DATA”**

**Research and Innovation Action
H2020-SC1-BHC-2018-2020
GA 965343**

**Duration: 48 months from 01/05/2021
Coordinator: Institute of Communication and Computer Systems**

Deliverable ID.:	D5.2	
Deliverable title:	RETENTION Analytics & Decision-making enabling mechanisms v1	
Planned delivery date:	31/12/2022	
Actual delivery date:	23/12/2022	
Deliverable leader:	SIEMENS	
Contributing partners:	FORTH, LSE, ICCS, SIESLR	
Dissemination Level:	X	PU = Public;
		CO = Confidential
		CI = Classified



This project has received funding from the European Union’s Horizon 2020 research and innovation programme under Grant Agreement No. 965343.

This deliverable reflects only the authors’ view and the Commission is not responsible for any use that may be made of the information it contains.



Document information and history

Deliverable description (from DoA)

Delivery of the first version of the models, processes and components enabling the analytics, decision-making, and data and model sharing capabilities of RETENTION.

Version N.	Date	Author [Person and Organisation]	Reviewer [Person and Organisation]	Milestone*	Notes
V. 0.1	28/10/2022	I. Nicolae, G. Danciu (SIESRL)		TOC	1st TOC version
V. 0.2	16/11/2022	I. Nicolae, G. Danciu (SIESRL), A. Pardalis, Y. Goletsis, M. Roumpi (FORTH), H. Hourani, E. Visintin (LSE), K. Bromis (ICCS)		1st initial draft version	1st round of contributions
V. 0.3	15/12/2022	I. Nicolae, G. Danciu (SIESRL), A. Pardalis, Y. Goletsis, M. Roumpi (FORTH), H. Hourani, E. Visintin (LSE), K. Bromis (ICCS)		ER, Proposed: Final draft version for review	Revised text
V. 0.4	20/12/2022		M. Colombo (i2Grow), I. Basdekis (STS), G. Del Torro (DM), O. Giannakopoulou, K. Bromis (ICCS)	Review checkpoint	Internal Review
V. 0.5	21/12/2022	I. Nicolae, G. Danciu (SIESRL)		ER, Revised: version after revision	Revised text
V. 0.5	21/12/2022		M. Haritou (ICCS),	Final Review	Minor comments
V. 0.6	22/12/2022	I. Nicolae, (SIESRL)		Final for submission	
V. 0.6	22/12/2022		I. Basdekis (STS)	Deliverable approved by TCo	Final released
V. 1.0	23/12/2022		M. Haritou (ICCS)	Deliverable approved	Deliverable Submitted



Table of Contents

Document information and history.....	1
Deliverable description (from DoA).....	1
Table of Contents	2
Table of Abbreviations.....	4
Table of Figures	6
List of Tables	7
1 Executive Summary	8
2 About this Document	9
2.1 Role of deliverable	9
2.2 Relationship to other RETENTION deliverables.....	9
2.3 Structure of the document	10
3 Data Analytics	11
3.1 Description.....	11
3.2 Components architecture.....	12
3.3 Applicability: Use-case scenario	16
3.4 Next developments	20
4 Decision Support for Interventions	21
4.1 Summary.....	21
4.2 Patient interventions and notifications.....	21
5 Disease Insights through Trustworthy & Verifiable AI	23
5.1 Description.....	23
5.2 Components	23
5.3 Applicability: use-case scenario.....	23
5.4 Next developments	25
6 Decision & Policy Support for Clinical & Public Health Experts: a methodological protocol	26
6.1 The overall objective	26
6.2 Conceptual framework and rationale.....	26
6.2.1 Phase I: Identify	26
6.2.2 Phase II: Define	26



6.2.3	Phase III: Validate	27
6.2.4	Phase IV: Integration	27
6.3	Completed Research: Phase I - Scoping Review	28
6.3.1	Definitions.....	28
6.3.2	Preliminary searches undertaken.....	28
6.3.3	Data source and search approach	29
6.3.4	Study selection process	29
6.3.5	Data extraction	32
6.3.6	Preliminary results.....	32
6.4	Next steps	34
7	Data & Model Sharing	35
7.1	Overall approach	35
7.2	Data sharing to RETENTION.....	35
7.3	Data sharing from RETENTION	41
7.4	Model sharing to RETENTION	44
7.5	Model sharing from RETENTION	49
8	Conclusions.....	53
9	References	54
10	Annex.....	57
	Annex A: Model run instructions for third party users	57



Table of Abbreviations

.NET	Domain NETwork
ADB	Adaptive Boosted Decision trees
AI	Artificial Intelligence
API	Application Programming Interface
AUC	Area Under Curve
AWS	Amazon Web Services
BDA	Big Data Analytics
CHD	Cardiovascular Heart Disease
CSB	Clinical Side Backend
CVD	CardioVascular Disease
DM	DATAMED
DoA	Document of Action
DSS	Decision Support System
ESC	European Society of Cardiology
FHIR	Fast Healthcare Interoperability Resources
FORTH	Foundation for Research and Technology Hellas
GBC	Gradient Boosting Classifier
GIC	Global Insights Cloud
GUI	Graphical User Interface
HF	Heart Failure
HL7	Health Level 7
HR	Hazard Ratio
HTTP(s)	(Secure) Hyper Text Transfer Protocol
i2g	i2Grow
ICCS	Institute of Communication & Computer Systems
JSON	JavaScript Object Notation
LG	Logistic Regression
LSE	London School of Economics and Political Science
LVAD	Left Ventricular Assist Device
MAE	Mean Absolute Error
ML	Machine Learning
NN	Neural Networks
NYHA	New York Heart Association



OR	Odds Ratio
PICOT	Population, Intervention, Comparator, Outcome, and Time
pkl	Python Pickle File
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised Clinical Trial
RDBMS	Relational Database Management System
REST	Representational state transfer
RF	Random Forests
RMSE	Root Mean Squared Error
RRR	Relative Risk Ratio
RWD	Real World Data
RWE	Real World Events
SHAP	SHapley Additive exPlanations
SIESRL	Siemens SRL
SQL	Structured Query Language
SSL	Secure Sockets Layer
SVM	Support-Vector Machines
URL	Uniform Resource Locator
VPN	Virtual Private Network
XGB	XG Boost



Table of Figures

Figure 1. The integrated flow of the data analytics architecture	14
Figure 2. The flow applied on the “patient evolution” scenario	15
Figure 3. The ML Model Training flow.....	20
Figure 4. Diagram that represents the workflow of generating notifications through the DSS component..	22
Figure 5. Metadata attached to the model	24
Figure 6. Variable importance as resulted from SHAP	25
Figure 7. PRISMA Flow diagram.....	33
Figure 8. Login screen of “Data Sharing to RETENTION platform” tool.	36
Figure 9. The main menu screen of “Data Sharing to RETENTION platform”.	37
Figure 10. Import a .csv file that includes the patients’ data.	38
Figure 11. An example of .csv file.	38
Figure 12. Save option of the data to the GIC database.	39
Figure 13. An example of .json structure for a FHIR variable.....	40
Figure 14. An example of .json structure for a non-FHIR variable.	40
Figure 15. The login screen menu of "Data sharing from RETENTION" tool.....	41
Figure 16. The main menu of "Data sharing from RETENTION" tool.	42
Figure 17. RETENTION data extracted from GIC (example).	43
Figure 18. RETENTION Implementation Guide (IG).	43
Figure 19. An example of body weight variable, as it is depicted in IG).	44
Figure 20. Login page of "Model Sharing from RETENTION platform" tool.	45
Figure 21. Main menu of "Model Sharing to RETENTION platform" tool.	46
Figure 22. Example of available datasets.	47
Figure 23 Features selection for survival rate dataset	47
Figure 24. Confirmation screen of the chosen features and classifiers.	48
Figure 25. Results of model training though analytics.	49
Figure 26. Login screen of "Model Sharing from RETENTION platform" tool.	50
Figure 27. Main menu screen of "Model Sharing from RETENTION platform" tool.	51
Figure 28. Use cases selection for the trained models.....	52



List of Tables

Table 1 – Rationales for choosing the scenario.....	16
Table 2 – Variables values that were used in first scenario	17
Table 3. Normal value ranges in adults	18
Table 4. Variables used in scenario	18
Table 5. Detailed variables used in first scenario.	18
Table 6. Diagram that represents the workflow of generating notifications through the DSS component...	22
Table 7. - Grey literature organizations searched by country	30
Table 8 - Extractions categories for literature review	34



1 Executive Summary

Deliverable D5.1 entitled “Analytics & Decision-making enabling mechanisms v1” is the first deliverable of “WP5 Enabling Technologies & Secure, Privacy-aware by Design Data Handling”.

The objective of this work package is to provide the models and the tools that enable the platform analytical processing and decision support features. Also, this work package is responsible with creating a platform where ML models can be developed, tested, and integrated in an easy manner. As additional output, this work package provides decision and policy support capabilities for both clinical as well as public health experts relevant to the project. These actors are patients, clinicians, caregivers, policy makers, health organisations, data scientists and administrative staff. All of them could have an interest in the platform and the benefit that this module brings to each of them will be detailed in this deliverable.

This document describes the results of how the delivery of the first version of the models, processes and components enabling the analytics, decision-making, and data and model sharing capabilities of RETENTION have been completed. It documents the infrastructure and analytics development activities which focuses on delivering components associated with the management of analytics and needed for the RETENTION infrastructure, including (external) tools supporting the ML pipeline.

In Chapter 3 we have described the entire framework that handles the model management from its creation to its delivery for prediction purpose, by exemplifying a scenario inspired from a documented study. In Chapter 4 the Decision Support for Interventions mechanism is described at a birds-eye-view level. Chapter 5 continues the model management with more explicit details about how the explanations have been achieved. In Chapter 6 we present the initial procedures considered for further implementing the Decision & Policy Support for Clinical & Public Health Experts task.

Finally in Chapter 7 we present the deployment of compiled models to the clinical site backend so that dashboard users can use them for prediction and further data analysis processes.



2 About this Document

The general concept of RETENTION is to combine various medical and consumers' health monitoring devices to enable the collection of continuous data from the daily life of patients with heart failure (HF), which will be analysed to obtain the necessary evidence to provide personalized advertising activities their healthy and independent lives. RETENTION will use (big) data analysis and learning capabilities, enabling large-scale analysis of collected data to generate the evidence needed to make decisions about individual interventions. Privacy protection-by-design design data management capabilities covering data at rest, processing and migration will fully cover the RETENTION platform. The goal of RETENTION is to develop and deliver a new platform to support improved clinical monitoring and interventions designed to improve the clinical management of patients with chronic heart failure.

The RETENTION platform will support the clinical decision by collecting various type of data from patients, analysing these data using big data techniques, artificial intelligence algorithms, detecting similar patterns in HF progression.

The current report, D5.1 "Analytics & Decision-making enabling mechanisms v1" (M20), cumulates the development within WP5 "Analytics & Decision-making for Personalised Management & Interventions" and relates to the delivery of the first version of the models, processes and components enabling the analytics, decision-making, and data and model sharing capabilities of RETENTION. The second and final iteration will be presented within version D5.2 "Analytics & Decision-making enabling mechanisms v2" (M36).

2.1 Role of deliverable

This deliverable presents the current state of implementations that were prepared within the scope of Work Package 5. The main purpose of this delivery is to present the first version of implemented process that allows the ML management, the developed models in relation to the scenarios agreed with clinicians, the decision making as well as the explainability of the models. Another important aspect of this deliverable is to present the status of model sharing component of RETENTION, which will prove its use in the deployment of trained models to the CSB side, so that the models will be used for various predictions.

2.2 Relationship to other RETENTION deliverables

This deliverable is following the work presented in D3.2 (RETENTION Architecture) that presents the high-level framework of RETENTION, in compliance with the actions of the DoA and the proceedings of D3.1 RETENTION Requirements, and utilises the specification of the FHIR based model and the well-defined semantics that use widely adopted ontologies defined in D4.1 The RETENTION Data Model and D4.2 RETENTION Data Management enabling mechanisms v1 for the representation of the clinical data that will be collected in the RETENTION project. RETENTION is committed to support open standards, while considering the heterogeneity, volume and velocity of data points collected by the project as presented in D4.1 The RETENTION Data Model. Considering the interoperability and open access focus of RETENTION, HL7 Fast Healthcare Interoperability Resources (FHIR) standard is utilised for the representation of the clinical data that will be collected, along with widely adopted ontologies and well-specified value sets for each resource, also supporting integration with other FHIR-compatible datasets. The repositories where patient's data is collected (to serve as input for the ML models), are managed in accordance with what has been presented in deliverable D2.2 Year 1 project report and project plan updates.



Using such a standardised representation of the data collected, WP5 activities aiming in streamlining the development of analytics and decision ML models to provide accurate personalised predictions. The analytics approaches presented in this deliverable are linked to specific clinical scenario(s) that: i) handle the usage data generated by devices and sensors and those of patients' medical data, to create and deploy ML models for a continuous learning pipeline, that in turn provides personalised scenarios/suggestions approved by clinicians. The outputting of the mentioned functionalities and results to GIC (at first) and CSB (later on) end-users in a meaningful and user-friendly manner supported by open-source tools integrated within the RETENTION platform, and the RETENTION Dashboard (to be presented in D6.1 RETENTION Interfacing, Device Federation and Visualisation components v1)

The technical indicators associated with the execution of test scenarios presented in D8.2 RETENTION Clinical Trial Protocol & Evaluation Framework (i.e., series of actions leading to a predefined/expected result) will confine the satisfaction of the functional and non-functional requirements and the overall performance of the solution.

2.3 Structure of the document

This report is structured in eight sections. The first section is the introductory part, where we inform the reader about the content of this document. The second section, namely Chapter 2 entitled 'About this Document' provides information about this report in terms of the goal, its relation to other relevant RETENTION deliverables and the current subsection summarizing the structure of the document. Chapter 3 provides a description of data analytics model management in relation to task T5.1 "Data Analytics: Models & Components", followed by Chapter 4 which includes details of the Decision Support System for interventions related to task T5.2 "Decision Support for Interventions: Models & Components". Chapter 5 is in relation with task T5.3 "Disease Insights through Trustworthy & Verifiable AI: Processes & Components" and described the mechanisms undertaken towards the development of trustworthy and transparent AI. Chapter 6 provides an overview of the work performed for offering policy support for public health experts, in connection with task T5.4 "Decision & Policy Support for Clinical & Public Health Experts". Chapter 7, connected with task T5.5 "RETENTION Data & Model Sharing" refers to the data & model sharing considering 3rd party users, as from and to the RETENTION. Summing up, the final chapter provides the general remarks and conclusions of the presented work.



3 Data Analytics

Specifications of the RETENTION data analytics models, tool support for the creation and editing of said models, as well as the design and implementation of the components needed to execute T5.2 Decision Support for Interventions: Models & Components.

3.1 Description

There are many data analytics tools developed for general purposes in the ML community, each designed with a specific scenario in mind. Choosing the right analytical tool implies knowing a few aspects: how large is the dataset, what type of data is involved, what are the end-users working with the tool, etc.

A study where a large-scale empirical analysis on 4031 ML projects, including 1116 ML Tools and 2915 ML applied projects, was conducted (Rzig et al. 2022), considers all the above exposed aspects, as well as one of the most important for RETENTION: how is the model deployment management realised. In this analysis, they found evidence of lower adoption of DevOps tools in Applied ML projects, as well as different practices and development efforts around these files, which tended to be less effective than those of ML Tool and Non- ML.

Going further in the healthcare domain, Healthcare has adopted IoT and ML, allowing automated machines to process medical records, predict diagnoses, and most importantly, perform real-time patient monitoring. ML and Data Modelling techniques tend to be more and more used in clinical decision support systems to support clinicians in the decision-making process (Ray and Chaudhuri, 2021). Using data analysis methods, progresses in making more accurate and efficient decisions, eliminate medical errors, improve patient health, and reduce costs.

As a general note, computerized ML algorithms can identify correlations between descriptive variables in complex, non-linear, multi-dimensional systems, superior to standard statistical methods when predicting risk of events, as for example, in estimating HF mortality risk score (Greenberg et al., 2021). However, individual ML algorithms perform differently on different datasets. This may affect the overall results as the estimation results vary (Aldahiri et al., 2021). Careful attention, however, is to be considered in curating the data, selecting the variables, verifying the validity of the model performance and fine-tuning the results (Greenberg et al., 2021).

In a recent review (Bazoukis et al., 2021) on 122 clinical studies on HF patients, left ventricular assist device patients, healthy individuals and patients with risk of developing HF, the implementation of ML techniques in the management of heart failure (HF) patients was investigated in comparison with conventional clinical methods. The investigation concluded that ML techniques may play an important role for the efficient construction of methodologies for diagnosis, management, and prediction of outcomes in HF patients. The ML methods reached to an improved performance compared to conventional techniques.

Similar research studies involve AI within the Heart Failure Management. For example, the researchers in (Fahmy et al., 2021) identified the progression of Hypertrophic Cardiomyopathy patients from the New York Heart Association (NYHA) class I/II towards NYHA class III/IV. The investigated ML models ranged from logistic regression (LG), random forests (RF), support-vector machines (SVM), gradient boosted decision trees (GBC), adaptive boosted decision trees (ADB), and neural networks (NN), and the best approach was an ensemble of LG-GBC-SVM achieving an AUC of 0.81.



Other applicability showing further the major technological applications of AI in healthcare, refers, for example, to risk stratification or optimal titration of medical therapy, as the review in (Averbuch et al., 2022) shows, among other possibilities.

The need for patient-doctor communication, follow-up visits, and availability of clinicians has also become obvious. Innovation and technological advances can be the solution to the problems of our modern healthcare system. These innovations range from swallowable microchips that alert doctors when drugs are being taken, to large-scale data analysis to determine which drugs are most effective (Bhardwaj et al., 2017).

However, it should be noted indeed that due to the absence of a regulatory framework for the implementation of AI and ML into the clinical practice, the role of AI is still an auxiliary decisional role and at the moment cannot replace clinical cardiologists. Once with the advancement of AI, optimizations on the trustworthy and transparent mechanisms, and the completion of regulatory actions such as the EU AI Act (<https://artificialintelligenceact.eu/>), the AI could play a higher role for patients interventions and decisions. Even though, such technologies will probably never be able to completely replace physicians and it should not even be this goal, they have the potential to transform the healthcare sector, benefiting both patients and healthcare providers (Bhardwaj et al., 2017).

In RETENTION, there are various use-cases for data analysis such as days lost (%) due to unplanned cardiovascular hospitalisations or all-cause death or cardiovascular mortality during the individual follow-up time (to a maximum of 575 days, i.e., the 574 days of the patient monitoring period plus 28 days from the final study visit). These use-cases are split into primary endpoints and secondary endpoints. With respect to patient types, three types are considered as follows: heart failures patients, heart transplanted patients and patients implanted with assisted devices called LVAD.

Benefiting from both, standard statistical models such as the parametric t-test or non-parametric rank sum test, Kaplan-Meier estimates, Log-rank test for comparison distributions, and secondly, using various ML supervised and un-supervised algorithms, ensemble methods, and investigating the optimal performance, we consider building a system that understands what endpoints are related to each other, so that the model will have an optimal efficiency with respect to the targeted use-case.

3.2 Components architecture

The RETENTION platform architecture detailed in D3.2 comprises the Model Specification Tool and BDA Engine components, as defined in D3.2 “RETENTION Architecture”, primary constituted by the MLFlow and Jupyter Notebooks platforms.

MLflow¹ is an open-source platform for end-to-end machine learning (ML) lifecycle management. It has the following main components:

- Tracking: Allows tracking of experiments and storing parameters and results for further comparison

¹ <https://mlflow.org/>



- Models: Lets you manage and deploy models from a given list of ML libraries to a variety of model service platforms.
- Projects: Allows you to package your ML code in a reusable and reproducible format for further sharing with other data scientists
- Model Registry: Allows the centralization of a model store to manage the stage transitions of the complete model lifecycle: from staging to production, with versioning and annotation capabilities.
- Model Service: Lets you host MLflow models as REST endpoints.

The MLflow functionality that was used in RETENTION is mainly the Tracking one.

MinIO comes with a high-performance offering of S3 compatible object storage. MinIO is the only object storage suite available on every public cloud, every Kubernetes distribution, the private cloud, and the edge.

MinIO was used in RETENTION as a replica of AWS S3 services, without installing the AWS libraries on premise. It allowed formatting the storage way and delivering the models and meta-data attached to the model in an easy manner.

Postgres is a free and open-source relational database management system (RDBMS) emphasizing extensibility and SQL compliance. It was used here for storing the obtained models after the training phase.

Nginx² is a web server that can also be used as a reverse proxy, load balancer, mail proxy and HTTP cache. Here it was used to host the Jupyter notebooks that contain the data pre-processing pipeline.

Jupyter Notebook³ is the latest web-based interactive development environment for Python notebooks, code, and data. The integrated flow is depicted in the following figure (Figure 1):

² <https://www.nginx.com/>

³ <https://jupyter.org/>

Integrated workflow

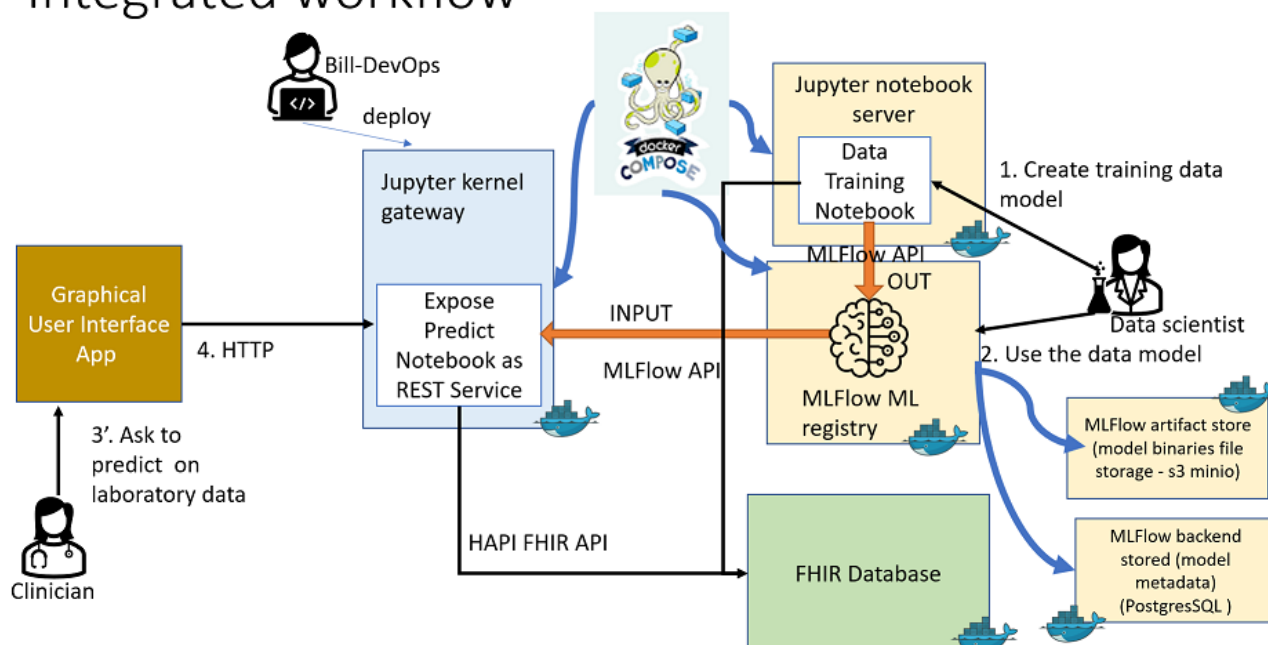


Figure 1. The integrated flow of the data analytics architecture

The “data training notebook” is a Python script that reads data from the GIC repository (i.e., both the FHIR and the nonFHIR Databases store the previously anonymised data been transmitted by all CSB instances) and using a ML Model namely a Gradient Boosting Classifier will create a model that responds to a given scenario. The models are trained on the GIC side and exposed via the Jupyter Kernel Gateway to the CSB side so that they can be “consumed” for prediction by clinicians that use the CSB@Dashboard.

The patient evolution prediction will be graphically represented via the Clinician view screen. This entire flow is presented in Figure 2.

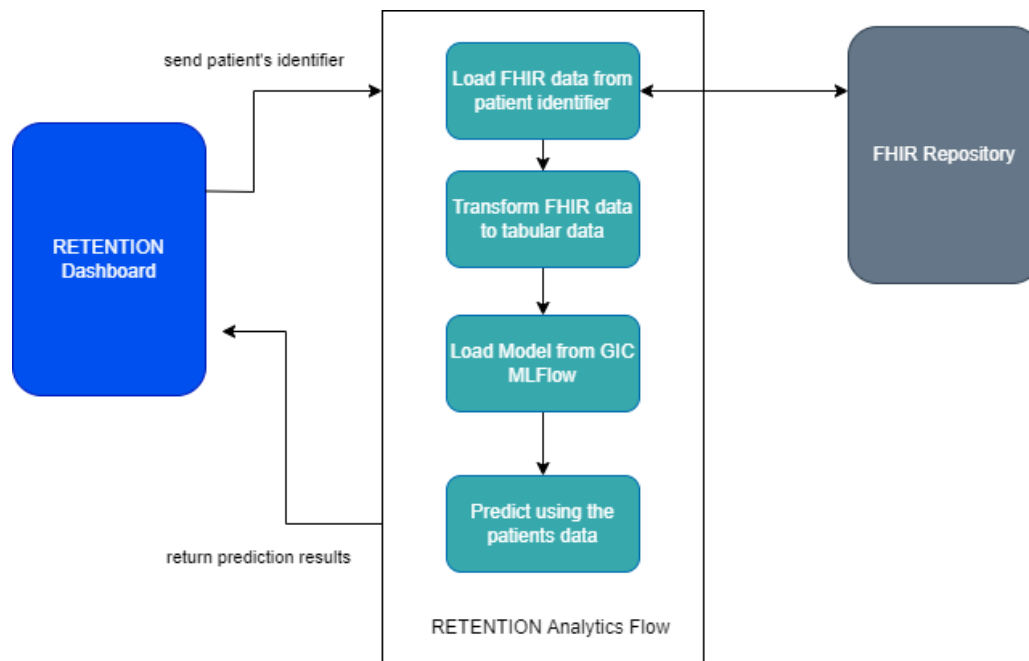


Figure 2.The flow applied on the “patient evolution” scenario

The machine learning process starts on the GIC (Global Insights Cloud) server, where only the data scientists and technicians have access to. There the training for the models of machine learning takes place, phase where the use cases needed for the clinician are designed and put together by the data scientists in a Jupyter Notebook environment hosted on the GIC server as a docker container. The Jupyter Notebook is protected in the current state via username and password, and the connection to the GIC server is realised in a secure manner using VPNs and *https ssl* certificates. After the training is done the model is ready to make predictions on new provided data.

Also, on the GIC server the MLFlow server is hosted as a docker container, and it is secured with a username and password, that is exposed as a REST API, the MLFlow server helps the data scientists to save and manage the machine learning models they create. Not only the models are saved but also the model's metadata like confusion matrix or SHAP outcomes, and parameters of the model, such as metrics for the accuracy of the model. All the data about the model and the model itself are stored on an Amazon S3 like bucket with help of Minio that is automatically installed with the MLFlow installation.

Then on the CSB (Clinical Side Backend) server, the trained model from the GIC server is fetched using the MLFlow REST API. MLFlow has a mechanism that allows transferring the model from the repository where the model was initially created to the machine that calls the *load_model* function.

Then, with this loaded model the clinicians can make predictions on the data they get from doing medical analysis on their patients, as well the data that came from the wearable devices associated with these patients.

The CSB server hosts the dashboard that presents clinicians with assigned patient data, and through this dashboard clinicians can choose the models they want to use to get predictions for their patients on different use cases, such as rate of patient survival. who suffer from heart failure diseases

As previously mentioned, clinicians call the trained model through the REST API with a particular patient's data, which is stored in a FHIR database and is also called through the REST API. The data that came from the REST call is in *json* format, so the data needs to be normalized into a tabular form so that it can be fed to the trained model and retrieve the prediction.

After the call to the trained model is made, the data that came from that call is displayed on the dashboard so that clinicians can analyse and make decisions, for the specific patient, not only with the data from the prediction, but also with their knowledge.

3.3 Applicability: Use-case scenario

The purpose of this ML project is to demonstrate on how the proposed Model Specification Tool can be utilised to support the clinical use-cases within RETENTION scope. The first scenario to which the ML Tool functionality will be demonstrated is named "Survival analysis for heart failure patients", which has the purpose to predict the time to death for each patient (i.e., study participant) with severe heart conditions. It relates with the secondary endpoint 2.b (defined in D8.2) of Cardiovascular mortality during the individual follow-up time.

The architecture presented in previous section was applied on the "Survival analysis for heart failure patients" scenario, considering that in this period of the RETENTION project the pilots have not yet started to produce the necessary input data for the ML process. The explicability of the AI model, further presented in section 5.3 Applicability: use-case scenario is done via SHapley Additive exPlanations (SHAP) library (Sundararajan et al., 2019). Along with the model, in the PostgreSQL database are saved Model Key Performance Indicators Validation measures (via ML Flow) as well: AUC (Area Under Curve), MAE (Mean Absolute Error), RMSE (Root Mean Squared Error), r^2 score (coefficient of determination - regression score function) and the Confusion Matrix.

The particular ML project provides a survival prediction for a chosen Heart Failure patient in the following 250 days, based on (similar RETENTION data model) data from a survival analysis study with 299 patients from Institute of Cardiology and Allied hospital Faisalabad-Pakistan during April-December (2015) (Ahmad et al., 2017; Chicco and Jurman, 2020). Data consists in information from demographics, baseline history and lab measurements. After testing multiple ML classification models, we concluded the GBC is the most appropriate one for this task.

The model uses Gradient Boosting Classifier to classify the patient's event as death (= 1) or not (= 0) and will provide the probability of the event happening.

Table 1 provides motivations and purpose for selecting the scenario as the first for demonstrating the ML Tool.

Table 1 – Rationales for choosing the scenario

Rationale	Description
Goal	Predicting the risk of death within 250 days for a chosen heart failure patient using Machine Learning Models
Reason	diagnosis is crucial to allow timely initiation of evidence-based treatments
Needs fulfilled	Be able to prevent death by detecting earlier the risk of death of heart failure

	Be able to provide adequate treatment and advice to patients that are at the risk of heart failure
	Be able to efficiently share understandable information with the patient and other medical personnel
	At a patient level, these estimates can allow informed discussions and shared decision making about treatment options and advanced care planning

3.3.1 Clinical perspective

Survival analysis of heart failure patients' study from Institute of Cardiology and Allied hospital Faisalabad-Pakistan during April-December (2015) (Ahmad et al., 2017; Chicco and Jurman, 2020). Study contains 299 patients of Heart Failure (HF), 105 women and 194 men, aged 40 years or above, having left ventricular systolic dysfunction, belonging to NYHA class III and IV.

The follow up time was 4–285 days with an average of 130 days. Up to end of follow-up period 96 patients (32%) died due to Cardiovascular Heart Disease (CHD) and 203 patients survived. Disease was diagnosed by cardiac echo report or notes written by physician.

- The model utilises information from demographics, baseline history and lab measurements to estimate the risk of death within the coming days.
- It provides a percentage risk of death within the following 250 days, and more specifically regarding the type of death, it can estimate the percentage risk of stroke within 250 days.
- The variables used are previous cases of Death Events (/Individual Follow-Up Time), Gender, Age, Smoking status, Diabetes, Hypertension, Anaemia, Ejection Fraction values, Serum Sodium, Serum Creatinine, Platelets and Creatine Phosphokinase (similar to those of RETENTION data model)
- After the selection or search for the specific patient considered for predicting the survival rate in the following 250 days within the "Heart Failure Study Group", the respective estimated prediction will be represented as a percentage of risk of death. The threshold for deciding on the probability percentage would be around 50%, meaning patient is estimated to die if probability is above 45% (high risk) and estimated to survive if probability is below 45%, with medium (15-45%) or low risk (0-15%) of Heart Failure. For values in the range 45-55%, it is hard to decide on the probability but is considered as high risk.

An example of such values is presented in the following Table 2.

Table 2 – Variables values that were used in first scenario

Report note date	Age	Gender	Diabetes	HBP	Anaemia	Smoking	Sodium	Creatinine	Ejection Fraction	Platelets	CPK	TIME	Event
2022-09	43	0	0	0	1	0	135	1.3	50	237000	358	97	0

Based on the above data measurements, the estimation (prediction) showed: 75% risk of death in the following 250 days, meaning that after Sept'22 there is high risk of death with a probability of 75%.

Note: Is useful to consider the range of variable values for a healthy individual, as shown in the following table, Table 3.

Table 3. Normal value ranges in adults

Variable	Value Range	Measurement Unit
Ejection Fraction	50 - 75	%
Serum sodium	136 - 145	Micromol per blood liter ($\mu\text{mol/L}$)
Serum creatinine	Men: 0.7 - 1.2 Women: 0.6 - 1.1	mg/dL
Platelet	150 - 400	Kiloplatelets per microliter of blood ($\text{K}/\mu\text{L}$)
CPK	< 190	milli-international units per milliliter (mIU/ml)

Therefore, considering the data in Table 2 and 3, this patient had abnormal values for CPK.

3.3.2 Data scientist perspective

The scope of the presented study is **survival prediction**: predicting the risk of death within 250 days and the corresponding probability percentage for a chosen heart failure patient using Machine Learning Models.

The variables that were used are presented in Table 4.

Table 4. Variables used in scenario

Variable type	Variable
Demographics	Gender, Age
Patient history	Smoking status, Diabetes, Hypertension, Anaemia
Laboratory values	Ejection Fraction, Serum Sodium values, Serum Creatinine, Platelets and Creatine Phosphokinase

In Table 5 we have presented the explanations and ranges for each variable used in this scenario (also presented in detail in D4.2 report, along with FHIR resources specifications).

Table 5. Detailed variables used in first scenario.

Feature	Explanation	Measurement Unit	Range
Birth Date	Birth Date of the patient	Date	Jan 1927 – Dec 1982
Gender**	Woman, man	Binary	0, 1 [0=Male, 1=Female]

Anemia	Decrease of red blood cells or hemoglobin	Boolean	0, 1 [0=No, 1=Yes]
Arterial Hypertension	If a patient has hypertension	Boolean	0, 1 [0=No, 1=Yes]
Diabetes	If the patient has diabetes	Boolean	0, 1 [0=No, 1=Yes]
Smoker	If the patient smokes	Boolean	0, 1 [0=No, 1=Yes]
Creatinine phosphokinase (CPK)	Level of the CPK enzyme in the blood	mIU/ml	[23,..., 7861]
Ejection fraction	Percentage of blood leaving the heart at each contraction	Percentage	[14,..., 80]
Platelets	Platelets in the blood	K/ μ L	[25 ,..., 850]
Serum creatinine	Level of creatinine in the blood	mg/dL	[0.50,..., 9.40]
Serum sodium	Level of sodium in the blood	μ mol/L	[114, ..., 148]
Time	Follow-up date / Date of Death	Date	[Jan – Sept '22]
DEATH	If the patient died during the follow-up period	Boolean	0, 1 [0=No, 1=Yes]

The risk of death is estimated via a Gradient Boosting Classifier (GBC) model, offering a percentage risk of death within the following 250 days for a specific patient. Regarding the type of death, it also estimates the percentage risk of stroke within 250 days.

The method returns a binary classification (0 or 1) meaning either the patient will survive or not. Data was pre-processed before it was fed to the ML model according to the below steps, as well as depicted in Figure 3.

Note: Other models have been investigated, like XG Boost, and other generic models, logistic regression; however, the performance was better with GBC.

The implemented flow necessary for this scenario

- A new group of patients was created as a FHIR resource per Study analysis: Heart Failure Study Group, and was exposed via REST API

- New patients were created and their information (e.g., names) was generated randomly in FHIR format based on the Synthea⁴ tool.
- The initial survival study dataset was transformed from a csv format to FHIR medical resources. Specific details for the data model and FHIR resources were presented in the D4.2 “RETENTION Data Management enabling mechanisms v1” report.
- The last preparation step was to associate the generated patients with the corresponding FHIR medical resources and ingested accordingly into the FHIR resource database (repository)

For the purpose of creating the ML Model, the data has been called from the FHIR repository into the data scientist environment (Jupyter Notebook), and transformed back to linear data as csv form, since the ML Mode requires tabular data format.



Figure 3. The ML Model Training flow

- The data was first normalized as to assure a common scale for all variables, since they have different ranges, as depicted in Figure 3. Then, the data was split into training (75% = 224 patients) and validation (25% = 75 patients) sets:
- Training: 75% survival study data in csv format used for training (224 patients records randomly chosen: 157 survivors and 67 deaths)
 - Output: ML model (.pkl file), metadata and artifacts stored in ML Flow.
- Validation: 25% study data in csv format used for model validation (75 patients: 46 survivors and 29 deaths)
 - Output: performance indicators via Validation Measures stored in ML Flow.
- Prediction/Test: 1 patient artificially generated data via Synthea (selected from the FHIR database)
 - Output: Probability of death estimation via Clinician screen view.

The REST API that facilitates this flow as well as the graphical user interfaces are detailed in deliverable D6.1 RETENTION Edge Mobile Application.

3.4 Next developments

Next, we intend to analyse the primary and secondary endpoints as described in D8.2, as to create scenarios that would be of value to RETENTION platform, scenarios like the one presented in this deliverable.

⁴ <https://synthea.mitre.org/>



4 Decision Support for Interventions

Focus on the specification of the RETENTION decision making and verified and non-verified intervention models, as generated by the platform; tool support for the creation and editing of said models and the components needed to execute the analytics and interventions based on these models at RETENTION CSB instances.

4.1 Summary

The DSS component of RETENTION platform accomplished some tasks that concern all the RETENTION platform users. In that context, DSS provides beneficial features for clinicians, patients and scientists. In order the DSS to provide those useful results, a certain amount of input data is necessary. The data stored in the FHIR database, which allow the required information to be processed and analysed by the DSS in order to provide useful outcomes. In the following section, all the features that are supported by the RETENTION DSS are outlined and briefly described.

4.2 Patient interventions and notifications

The DSS component provides a mechanism that continuously monitors measurements and statuses from the devices. For each intervention group, the DSS is sending a request every minute through the FHIR API to the FHIR Database to get the clinical data of interest (e.g., heart rate). When an outlier has been detected in predefined clinical characteristics set by the clinicians (described in Deliverable 8.2), a notification is being generated and is stored along with the intervention ID (type of intervention – low/critical level for each of the predefined clinical characteristics) in the non-FHIR Database. Concurrently, the Dashboard sends a request to the Non-FHIR Database through the Security Component to get the notifications that their status is active. Once this process is completed and the clinicians have been notified through the Dashboard, the status of the notifications stored in the Non-FHIR Database changes from active to send. This process is illustrated in detail in Figure 4.

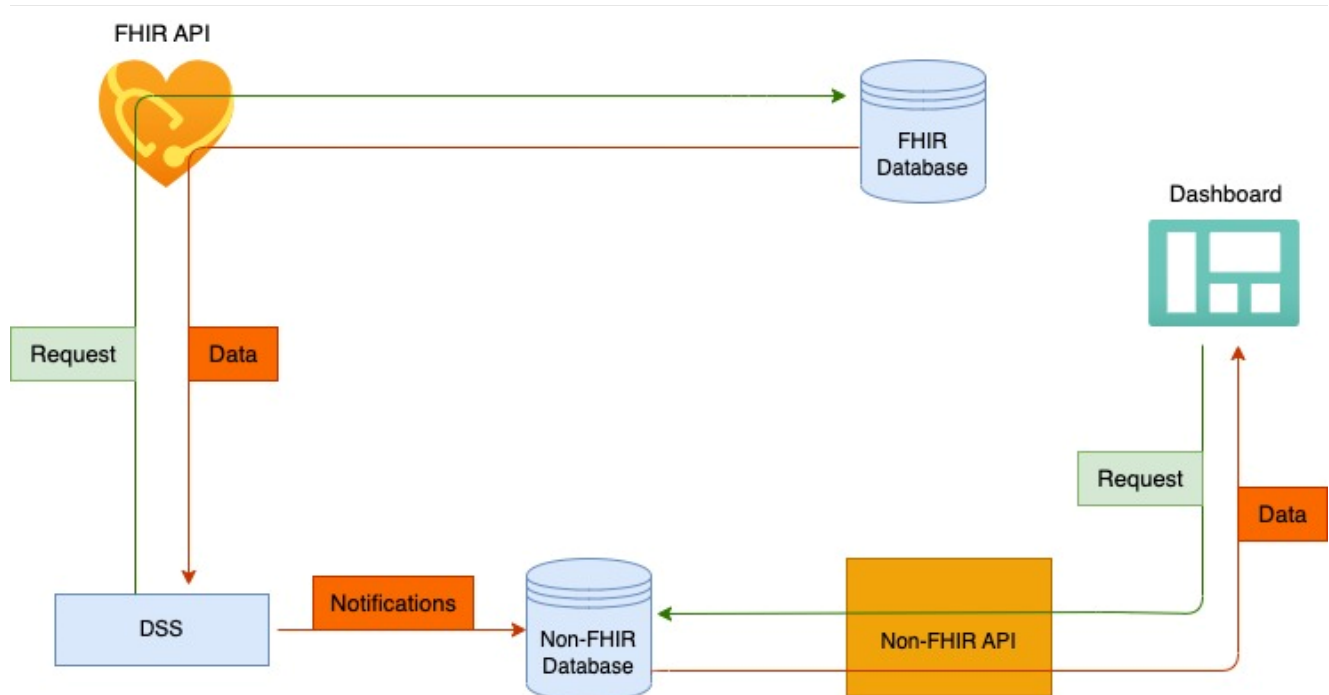


Figure 4. Diagram that represents the workflow of generating notifications through the DSS component

Table 6. Diagram that represents the workflow of generating notifications through the DSS component

Related Component	Details
FHIR Database	Access device measurements
Non-FHIR Database	Device usage and status
Dashboard	Interface for the clinicians to examine the proposed intervention alterations
Security Component	Transmit the notifications

The DSS was developed using the C# programming language which runs on the .NET Framework. No other tools were used for the notifications and interventions. The development is custom made by ICCS and the notifications are generated as rule based. This information is explained in detail in D8.2 where all the rules (cut-off values), the types of notifications as well as the categorization has already been addressed by the clinicians. The monitored variables as recorded by devices are e.g., weight, blood pressure, heart rate, oxygen saturation, temperature, activity, sleep, adherence to treatment, pulsatility index, flow, watts, driveline. An example of cut-off rule for a critical level notification for DSS, is a heart rate value of below or above 150 bpm, which will trigger a respective notification.

5 Disease Insights through Trustworthy & Verifiable AI

This task will focus on the development of verification capabilities (processes and associated components) for the models learned, leveraging the enablers of Data Analytics and Decision Support for Interventions, and applying ML techniques at the RETENTION GIC to generate disease insights which are transparent, explainable, and trustworthy.

5.1 Description

We see 3 directions of development when it comes to enhancing ML approaches for predictions with explanations for decision making. These are:

- Building intrinsically explainable models, such as regressions (e.g., linear regressions, logistic regressions, symbolic regressions, etc.);
- Offering a ranking of feature importance and their contribution to final decision scores, such as SHAP, Random Forest Feature importance etc,
- Model agnostic, Ad hoc explanations for specific instances, such as LIME and Anchor.

We have started with the second scenario, since this would be the most intuitive for non-technical staff to understand how their decisions are influenced by the support ML models. In the current version of the framework, the feature importance for prediction is explained via SHAP. The SHAP approach is based on game theory and the SHAP values represent a feature's responsibility for a change in the model output.

To get an overview of the most important features for a model we can plot the mean absolute value of the SHAP values over all samples and for every feature. The SHAP value for each sample (in this case, a patient survival prediction) shows the contribution of the feature to push the model output from the base value (the average model output over the training dataset we passed) to the model output. The features cumulated for each sample, can push the prediction higher or lower (see example in Section 5.3 Applicability: use-case scenario).

5.2 Components

The components are common as the MLFlow presented in section 3.2 Components architecture. Also, XAI library namely SHAP was used, accuracy metrics computing module are two more components. It comprises the Disease Insights component defined in D3.2 RETENTION Architecture.

The description on correlation and confusion matrix are components that create the meta-data of the models.

5.3 Applicability: use-case scenario

Validation measures for model's performance: AUC (Area Under Curve), MAE (Mean Absolute Error), RMSE (Mean Squared Error), r^2 score (coefficient of determination - regression score function), Confusion Matrix.

According to the AUC value of 0.799, one can interpret that the model was able to correctly recognize the event of death for 79% patients from the validation dataset (i.e., 79% from 75 patients), meaning for 59 patients.

The confusion matrix shows the classifier performance between classes (0 - survival; 1 - death). Confusion matrices are useful because they give direct comparisons of values like True Positives, False Positives, True Negatives and False Negatives. Therefore, it is easy to see whether the system is confusing the two classes (i.e., commonly mislabelling one as another).

Figure 5 presents the confusion matrix, and the accuracy metrics with their interpretation.

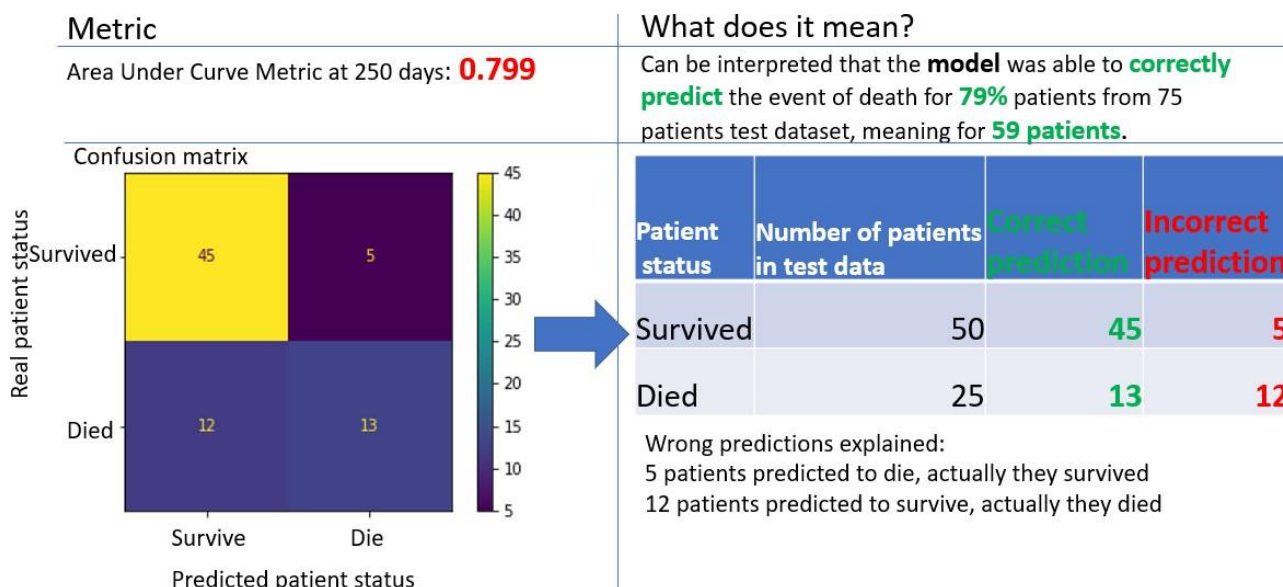


Figure 5. Metadata attached to the model

Looking at our results above, from the 55 patients correctly classified, 45 were correctly classified in the survival class (out of actual 50) and 13 correctly as death (out of 25). As we can see in this shallow example, the performance of 79% refers to: 90% performance for the survival class and 52% performance for the death class, and at this level it is not enough, but this exercise acted as a functionality demo.

The plot in Figure 6 sorts features by their average contribution over all samples given by SHAP values, showing the impact each feature has on the model output. This reveals that the bars in blue, impacted positively on average (over patients), the model output, while the rest had on average no beneficial contribution.

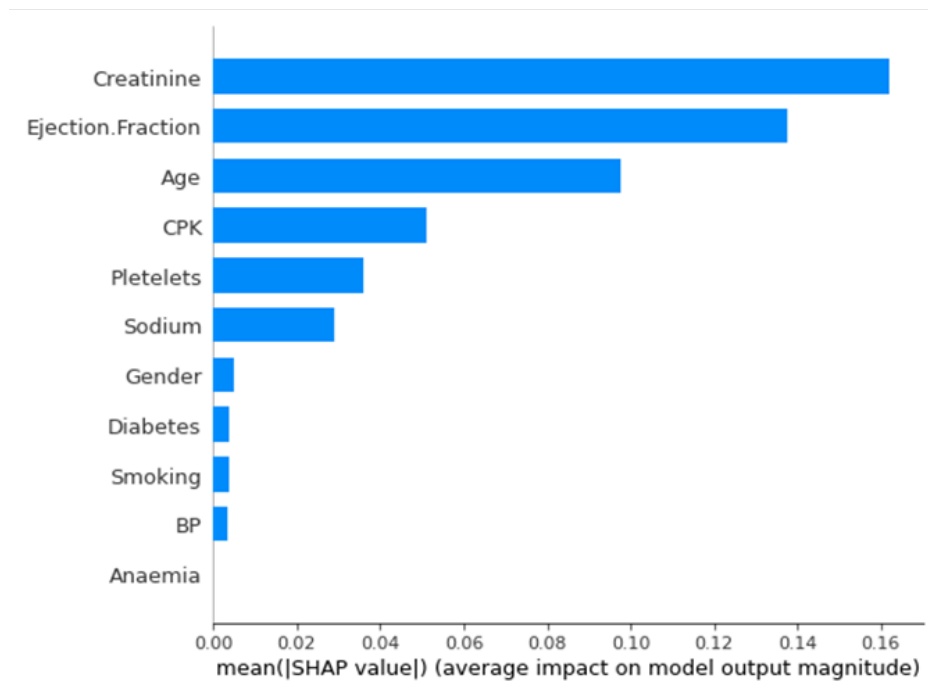


Figure 6. Variable importance as resulted from SHAP

The most relevant variables that influenced the prediction are Creatinine (0.16 orders of magnitude, changing the predicted survival probability on average by 16 percentage points), Ejection Fraction (0.14 = +14%), Age (0.10 = +10%), CPK (0.05 = +5%), Platelets (0.04 = +4%), Sodium (0.03 = +3%). First, probably because they offer a range of values providing more information for the predictor, compared to Gender, Diabetes, Smoking status, Blood Pressure (BP), Anaemia (<0.0005 = +0.05%) which are binary values and constant.

5.4 Next developments

In the further steps we plan to explore the next scenarios like "Time to first unplanned HF hospitalisation" or "Time to first unplanned cardiovascular hospitalisation", building intrinsically explainable models that have a readable mathematical function, and explaining the most significant feature values that lead to a decision per patient at prediction time.

6 Decision & Policy Support for Clinical & Public Health Experts: a methodological protocol

Provides the platform's decision and policy support capabilities of the platform which, combining the outputs of Data Analytics, Decision Support for Interventions and Disease Insights through Trustworthy & Verifiable AI, will provide clinical experts as well as public health experts at the RETENTION GIC with the necessary outputs to continuously improve HF patient management, to enhance the relevance of results from controlled clinical trials targeting HF and to refine protocols, regulations and public health policies pertaining to HF.

6.1 The overall objective

The main objective of Task 5.4 is to provide policy makers with a dashboard of key criteria/indicators to facilitate the analysis of the data collected through the clinical trial for the purposes of policy development. The vision is for RETENTION to provide decision makers with real patient data (registry) on which they can base the continuous evaluation and improvement of existing HF policies and the development of new ones as part of their cardiovascular strategy within the overall health vision of their respective countries or regions.

6.2 Conceptual framework and rationale

To fulfil the task's objective, the following research plan was developed, based on an adaptation of the European Society of Cardiology (ESC)'s framework for developing quality indicators for quantifying cardiovascular care and outcomes. The framework was adjusted to fulfil the project's objectives and the specific requirements of HF policies.

The methodology is a multistage qualitative analysis of HF policies that allows the selection of Key indicators (KI) that would form the basis of the policy dashboard to be developed as part of the RETENTION platform.

6.2.1 Phase I: Identify

The first phase of our methodology aims to identify the main HF policies implemented or proposed in the study country. To fulfil this objective, a scoping literature review of peer-reviewed and grey literature was carried to (a) identify the main policies and proposals of policies developed in the study countries, (b) identify the current policy needs for HF and c) select three or four policies that can be used to develop a policy dashboard that showcases how RETENTION can support HF policy assessment and development. This mapping exercise captures the status quo in HF management and policies, and identifies key initiatives developed and/or adapted to respond to current and future clinical and patient needs. As the team is about to conclude this phase at the time of this deliverable's submission, a detailed description of the scoping review is presented in section 6.3 Completed Research: Phase I - Scoping Review.

6.2.2 Phase II: Define

The second stage of our research plan aims to define the main clinical and quality indicators used in the policies selected in phase I. For each of the selected policies, a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) systematic literature review will be conducted. For each policy, the main endpoints will be identified, and for each endpoint, the literature will be screened to identify the association between the endpoints and the heart failure outcomes. In this systematic literature review,



national registers and clinical trial results will be included to identify the HF outcomes that can be associated with a particular endpoint.

The policies selected should have endpoints that match the endpoints included in the study protocol. In other words, any policy that has an endpoint that is not monitored in the study cannot be selected. The studies included in the literature research will exclude reviews or clinical studies that do not provide odds ratio (OR), hazard ratio (HR) or relative risk ratio (RRR) data.

6.2.3 Phase III: Validate

To successfully use the platform as a policy evaluation tool, it is crucial to engage relevant stakeholders early in the process to ensure their views and priorities are fully captured and catered for. Within this phase, a series of workshops, focus groups and/or questionnaires will be designed and carried out during the project's lifetime to gather the views of distinct stakeholders - namely policy makers, patient organisations and clinicians - regarding the current trends in HF policies and the impact RETENTION can have on improving HF management and policy.

The main aims of this phase are: (a) to elicit consensus on the relevance of the selected policies and indicators among policymakers and patient representatives and (b) to validate with clinicians the list of indicators compiled by the research team through phases I and II.

For this reason, a series of workshops will be organised. The first workshop aims to introduce RETENTION to a selected group of policymakers and patient organisations from the four study countries and for European (supranational) organisations. The workshop will take the form of a roundtable discussion to capture the stakeholders' opinions and requirements regarding the current gaps and needs in HF management policy, and to collect their feedback on the platform's features and its benefits to them. This will serve as an introductory workshop, paving the way for further discussions in the following workshops on the value and sustainability of the RETENTION platform and the different options for funding it in the future (serving the objectives of WP9 as well as WP5).

The second workshop aims to validate the indicators selected in phase II and will take the form of a focus group, with the clinicians involved in the project (consortium partners), to ensure the most relevant clinical outcomes are considered. This workshop may be complemented with a questionnaire distributed to the consortium clinicians to make sure differences in clinical practice are well captured.

6.2.4 Phase IV: Integration

Phase IV will use the results of the previous phases to design a policy dashboard that showcases to decision-makers how the RETENTION platform can make use the RWE collected in the clinical trial to evaluate the effectiveness of HF management policies.

As such, the LSE research team will collaborate with the technical partners in WP5 to develop a dashboard featuring the Key Indicators validated in phase III to assess the selected policies identified in phases I. It will follow the PICOT framework (Population, Intervention, Comparator, Outcome, and Time) whereby each one of the PICOT fields will have a drop-down menu to select the appropriate data to be analysed for each policy selected.



The platform will provide the analysis in graphs depicting the change in the outcome measure of interest over time for the intervention group vs. the control, as well as an overall % reduction/improvement in that outcome. The dashboard visual outcome will be in the form of graphs appropriate for each outcome selected.

6.3 Completed Research: Phase I - Scoping Review

In this first phase we'll provide initial definitions of the terms related to the heart diseases and the policies relevant for this clinical spectrum. In that sense we describe the preliminary effort that have been undertaken, as well as the research methodology plan that we intent to perform in the next period.

6.3.1 Definitions

Heart failure: HF is a clinical syndrome characterized by typical symptoms (e.g., breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in reduced cardiac output and/or elevated intracardiac pressures at rest or during stress (Ponikowski et al., 2016)

Post-discharge care: medical care provided on an outpatient/non-hospitalised basis, including diagnosis, observation, consultation, treatment, intervention, and rehabilitation services (MedicineNet, 2021).

Disease management policy: the concept of reducing health care costs and improving quality of life for individuals with chronic conditions by preventing or minimizing the effects of the disease through integrated care. Disease management policies are designed to improve the health of persons with chronic conditions and reduce associated costs from avoidable complications by identifying and treating chronic conditions more quickly and more effectively, thus slowing the progression of those diseases (AMCP, 2019).

Telehealth/ Remote Monitoring: telehealth is the use of digital information and communication technologies to manage health care and access health care services remotely. Technologies can include computers and mobile devices, such as tablets and smartphones. This may refer to technology that can be used from home, or a nurse or other health care professional providing telehealth from a medical office or mobile van, such as in rural areas (Mayo Clinic, 2022).

Remote monitoring is a method of healthcare delivery that uses the latest advances in information technology to gather patient data outside of traditional healthcare settings and uses specific technologies that allow clinicians or health care teams to check patients' health remotely (Mayo Clinic, 2022; Care Innovations, 2022). Remote monitoring is a type of telehealth delivery system and the term telehealth may, in turn, also refer to remote monitoring (Care Innovations, 2022).

6.3.2 Preliminary searches undertaken

Initially a brief literature review was undertaken to gain insight on post-discharge HF management practices in the study countries. This review facilitated the development of the scoping review strategy and the eligibility criteria. The search strategy was updated in an iterative process in order to select important papers encompassing the broader management of HF. This search gave insight into the alternative terms to use and how to narrow down the search.

6.3.2.1 Sample search strategy

TITLE ("heart failure*" OR "coronary failure" OR "heart infarct*" OR "postmyocard*" OR "coronary disease" OR "cardiomyopathy")

AND TITLE ("polic*" OR "guideline*" OR "recommendation*" OR "regulat*" OR "strateg*" OR "pathway*" OR "care plan*" OR "lifestyle change*" OR "rehabilitation" OR "monitor*" OR "follow-up")

AND ALL ("post discharge" OR "hospital discharge*" OR "outpatient*" OR "communit*" OR "secondary prevention" OR "primary care" OR "relapse" OR "post hospitalisation*" OR "disease management")

AND TITLE-ABS-KEY ("United Kingdom" OR "england" OR "english" OR "greece" OR "greek" OR "italy" OR "italian" OR "france" OR "french" OR "german*" OR "spain" OR "spanish" OR "eu" OR "europ*")

AND TITLE ("heart failure*" OR "coronary failure" OR "heart infarct*" OR "postmyocard*" OR "coronary disease" OR "cardiomyopathy")

AND TITLE ("remote" OR "telehealth" OR "telemedicine" OR "tele health" OR "tele medicine" OR "telemonitor*" OR "telerehab*" OR "virtual" OR "smartphone" OR "ehealth" OR "text messag*" OR "wearable*" OR "tech*" OR "tele* support")

AND ALL ("post discharge" OR "hospital discharge*" OR "outpatient*" OR "communit*" OR "secondary prevention" OR "primary care" OR "relapse" OR "post hospitalisation*" OR "disease management")

AND TITLE-ABS-KEY ("United Kingdom" OR "england" OR "english" OR "greece" OR "greek" OR "italy" OR "italian" OR "france" OR "french" OR "german*" OR "spain" OR "spanish" OR "eu" OR "europ*")
2010 - PRESENT

6.3.3 Data source and search approach

This search strategy aimed to review both peer-reviewed and grey literature using Medline and Scopus databases. The search was limited to the period January 1st, 2015 to May 30th, 2022. The start date was chosen as to include up-to-date telehealth policies, given the rapid development of digital health technologies. The search included publications in English and local languages where applicable. Sources that fall within our inclusion criteria were included and their reference lists searched for additional appropriate sources.

For grey literature, a list of relevant organizations was created (as per the inclusion criteria), and their websites were searched using key words such as “heart failure”, “management policy”, “care plan”, “post-discharge”, “rehabilitation”, “remote monitoring”, “telemonitoring”.

Additionally, a Google search was carried out using the above-mentioned key terms to find any outliers.

6.3.4 Study selection process

In this section we introduce the inclusion and exclusion criteria for the study process, steps that will define our next steps of the research plan.

6.3.4.1 Inclusion criteria

The scoping review methodology encourages a broad literature review, so the following were included:



- Both peer-reviewed and grey literature
- Any literature pertaining to policies, strategies and care plans followed/implemented in the post-discharge management of HF
- Any literature on digital health solutions for HF management
- Outpatient management does not have to be the main focus of the literature; however, it must be applicable and not be focused on a mutually exclusive area such as acute or emergency care
- Studies, reports & grey literature relevant to the study countries. Additional literature is included if it is general and thus its scope covers the study countries
- Studies published between January 1st, 2015 and May 30th, 2022
- Grey literature from relevant organisations in each country, as well as global or region-specific literature which includes the study key countries (see table 7 for organizational websites by country)

Table 7. - Grey literature organizations searched by country

Country/Region	Organisation & website
England/UK	National Institute for Health and Care Excellence (NICE)
	British Heart Foundation (BHF)
	National Health System (NHS) England
	Scottish Heart Failure Hub
	Public Health Scotland
	National Institute of Cardiovascular Outcomes Research (NICOR)
	The British Cardiovascular Society
	The Healthcare Quality Improvement Partnership (HQIP)
France	Santé Publique France
	Haute Autorité de Santé (HAS)
	Fondation Recherche Médicale
	Ministère des Solidarités et de la Santé
	French Society of Cardiology
Germany	Ärztliches Zentrum für Qualität in der Medizin
	Gemeinsame Bundesausschuss
	Institut für angewandte Qualitätsförderung und Forschung im Gesundheitswesen
	Allgemeine Ortskrankenkasse (AOK)
	Bundesärztekammer (BÄK)



	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
Greece	Hellenic Heart Failure Association
Italy	Ministero della Salute
	Ministero della Salute: Direzione Generale Della Programmazione Sanitaria.
	Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO)
	Centro nazionale per la prevenzione e il controllo delle malattie
	AIFA – Agenzia Italiana del Farmaco
Spain	Gobierno de España – El ministerio de Sanidad
	Sociedad Española de Cardiología.
	Sociedad Española de Medicina Interna.
International	The Heart Failure Policy Network
	World Health Organization (WHO)
	OECD/European Observatory on Health Systems Policies.
	European Society of Cardiology.
	European Observatory on Health Systems and Policies
	Global Heart Hub
	Heart Foundation
	DG- Sante – European Commission
	American College of Cardiology
	American Heart Association

6.3.4.2 Exclusion criteria

- Studies are excluded if they are not relevant to heart failure (i.e., studies on CVD in general)
- Studies are excluded if they do not refer to outpatient / post-discharge HF management/monitoring
- Studies are excluded if their focus does not include the study countries
- Studies are excluded if they are based on RCT or pilot study results
- Studies are excluded if they are not available in full text
- Papers are excluded if they correspond to “reviews, opinion articles, letters to editorials, commentaries, and viewpoints”



6.3.5 Data extraction

After searching all mentioned databases and webpages, the identified articles were uploaded to Zotero software and duplicates were removed. Two independent researchers extracted and screened titles and abstracts. Following that, the selected articles, with full text available, were carefully read by the two researchers, and their references list were mined for additional literature. Articles that satisfied the eligibility criteria were included. Any disagreement and discrepancies were resolved by a third researcher. All the steps of the study screening and selection process were reported in a PRISMA flow chart (Figure 7).

Data was extracted in a qualitative manner following the JBI Reviewers manual (Peters et al., 2020) by including key information from each paper, such as:

- Author, title, year of publication and the name of the journal/website where the relevant policy is discussed
- Country/region in which it was applied
- Relevant policy mentioned
- Outcomes/Indicators targeted by the relevant policy
- Performance, feasibility, and level of implementation of the relevant policy in the country where applicable
- Other key findings

The two researchers independently charted the data and discussed the results to determine whether the data charting form should be updated to include additional variables. Quantitative data synthesis was not performed since quantitative analysis is not required.

6.3.6 Preliminary results

A total of 68 peer reviewed articles and 32 reports and guidelines were identified for inclusion in the review. The flow of the inclusion for peer-reviewed papers is shown in **Error! Reference source not found.7**.

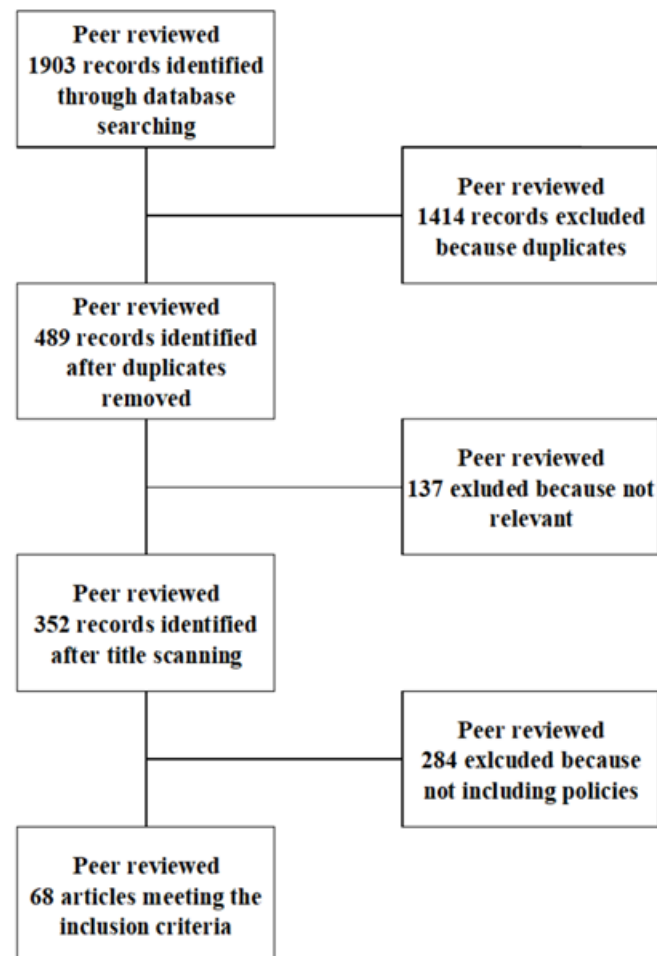


Figure 7. PRISMA Flow diagram

Information from the literature was extracted according to the type of telemonitoring system they considered, and the policies considered.

Across the literature, we identified three main categories of technologies (Bansilal et al. 2015; Benzer et al. 2016; Störk et al., 2017; Pekmezaris et al., 2018; Brahmhatt and Cowie, 2019; Dieckelmann et al., 2019; Negarandeh et al., 2019; HFPN. 2020a, b, c; Koehler et al., 2020; Farwati et al., 2021; Singhal et al., 2021):

- **Telemonitoring system:** This category includes non-implantable telemonitoring systems consisting of autonomous devices connected externally or wearable devices that allow regular self-measurements to be transmitted electronically to doctors.
- **Teleconsultations:** This category includes structured telephone support with doctors or nurses. This type of monitoring is usually included in more comprehensive disease management programs.
- **Telerehabilitation apps:** This category includes non-implantable telemonitoring systems that are implemented using applications software installed on the patient's phone.

The policy topic included in the extraction of the data pertained to three main areas: (i) Management of clinical symptoms (ii) Management of mental health symptoms (iii) Organization of the health care system and efficiency. A detailed description of each category is presented in Table 8.

Table 8 - Extractions categories for literature review

Macro policy area	Main policy aims	Sought outcomes
Management of physical symptoms	Reduction of hospitalization	To reduce the relapse of patients leading to early re-hospitalization by detecting early symptoms of relapse.
	Improvement of generic physical symptoms	To improve and monitor physical symptoms to re-adjust the titrations or the dose of diuretics and monitor weight.
	Improvement of home-based cardiac rehabilitation	To monitor the frequency and to educate patients on home-exercises to improve the HF prognosis.
Management of mental health symptoms	Monitoring of patients' mental health	To offer psychological therapy and educational support to patients and caregivers to avoid adverse effects on HF prognosis.
Organization of the health care system and efficiency	Multidisciplinary management programs	To implement integrated care pathways to make the delivery of optimal HF care efficient.
	Reduction of inpatient and outpatient' visits	To reduce the number of visits and reduce the costs to the health system.

6.4 Next steps

The next steps of this research involve the analysis of the literature review results. The final outcome will be the most relevant policies related to HF monitoring, on which a systematic literature review will be conducted to extract the main key indicators pertaining to the identified policies.



7 Data & Model Sharing

Considering the RETENTION models defined in Data Model, Data Analytics, Decision Support for interventions to provide an open data sharing specification and model that will form the basis for clinical and RWD data sharing, as well as model sharing, from and to the RETENTION platform. This will enable new partners to leverage RETENTION, bringing new clinical trial data, new AI algorithms, as well as new types of smart devices into the platform, and linking it to additional domains and relevant piloting activities. Moreover, it will allow others to exploit the validated RETENTION intervention and decision-making models in pertinent applications.

7.1 Overall approach

In the framework of T5.5 “RETENTION Data & Model Sharing”, an open data and model sharing specification is provided in order to allow external users and stakeholders to use data and knowledge (models) produced in RETENTION for further (clinical) research needs. This will allow others to exploit the data, RWD and the validated RETENTION intervention and decision-making models in pertinent applications. In a similar way, this open specification allows external users to create their own models based on RETENTION models, as well as to expand the data collected to RETENTION by bringing additional compliant data to the project. This leads to the definition of four use cases, which are presented in detail in the following paragraphs: (a) Data sharing to RETENTION platform, (b) Data sharing from RETENTION platform, (c) Model sharing to RETENTION platform and (d) Model sharing from RETENTION platform.

A specific tool is created for these four cases. The user will be able to download this tool from RETENTION platform and/or from a relevant software repository such as GitHub.

Note: Model sharing refers to sharing data & ML models to external parties (outside the project). The main external users of RETENTION data models are the clinicians and the data scientists. These users will be able to get RETENTION data and models. However, the Policy Makers users (outside the project) are expected to be able to use project results and analytics as users but not to obtain the models themselves (in a way that they can experiment with the model settings).

7.2 Data sharing to RETENTION

The main goal of the specific use case is to enable third-party users to bring new data to the RETENTION platform. The data that the third-party users will introduce to the platform should be in the same structure and format as the RETENTION one, in order to be in line with the project scope and have a meaningful impact on the rest of the functionalities of the platform such as models training and predicting clinical outcomes. Data outside of the scope of the RETENTION project will not be accepted.

In the framework of “Data sharing to RETENTION platform” the external parties (e.g. hospitals) will be able to leverage RETENTION, bring their data to the platform and in this way join the RETENTION initiative and the relevant study. From the RETENTION platform’s side, the advantages are great, since the external data can increase the additional data points used for model training which in turn can further increase model accuracy and/ or generalization.

Towards this direction, the proposed is based on the development of an application of a simple to use graphical user interface, that will allow a third party to import data according to the RETENTION data model and a prototype .csv, by providing structure and format specification.

The process of uploading new data to the RETENTION platform is as follows: Firstly, the third-party user needs to communicate with the administrator of the Global Insights Cloud (GIC) database to complete his/her registration to the RETENTION Platform. The communication takes place via email that the user sends to the RETENTION administrator. Specifically, the third-party user will need to send out some personal details such as First and Last name, name of organisation/institution, date of incorporation/establishment/registration, function of person submitting the registration and a small description including the reason of using the data.

Based on the above, the administrator evaluates the validity of the aforementioned data and provides credentials for the specific “Data sharing to RETENTION platform” tool.

The steps that are followed the successful access of the user to the RETENTION platform are presented below:

The third party connects to the tool by filling in the provided credentials (Figure 8). Automatically a token-based authentication takes place on the background where a post request takes place, sending the credentials to the RETENTION security component server, where a validation takes place. Upon confirmation, the security component responds by sending back to the tool a unique access token, which then will be used automatically by the tool to upload the imported data to the global insights cloud database.

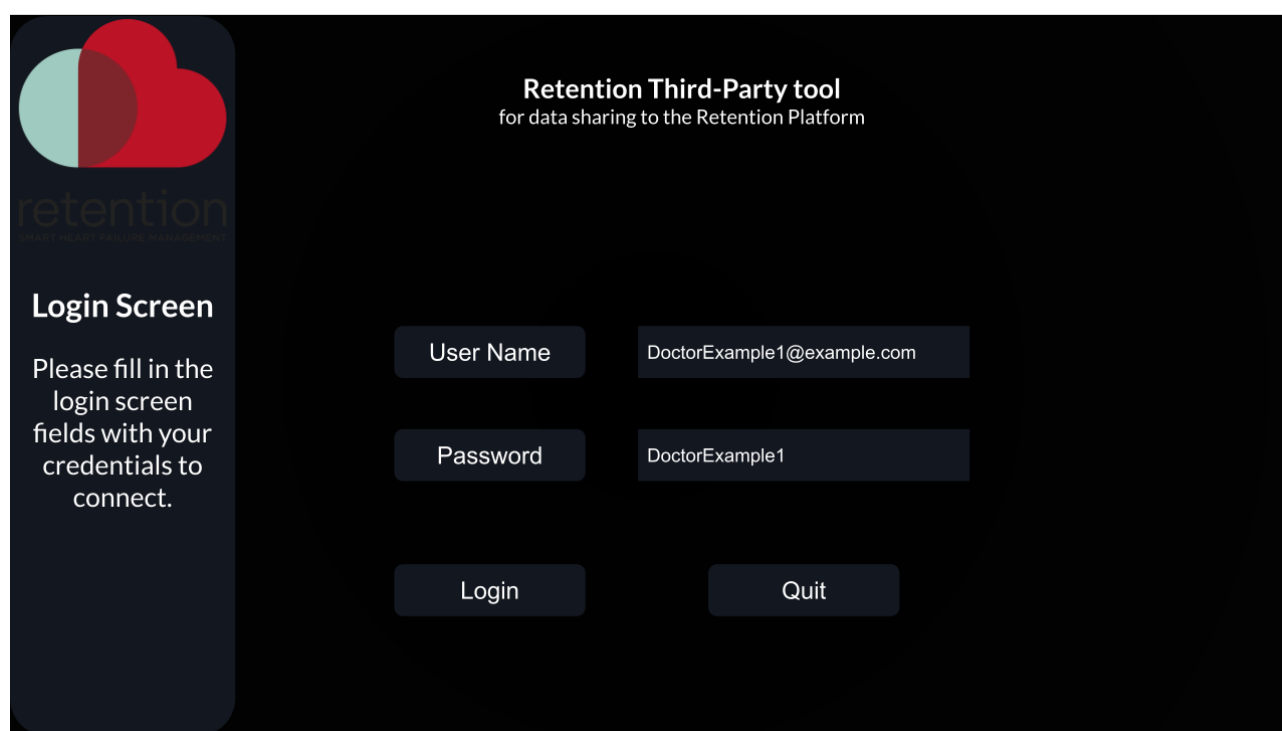


Figure 8. Login screen of “Data Sharing to RETENTION platform” tool.

The next figure presents the main menu screen of the tool where two options are demonstrated for the user.

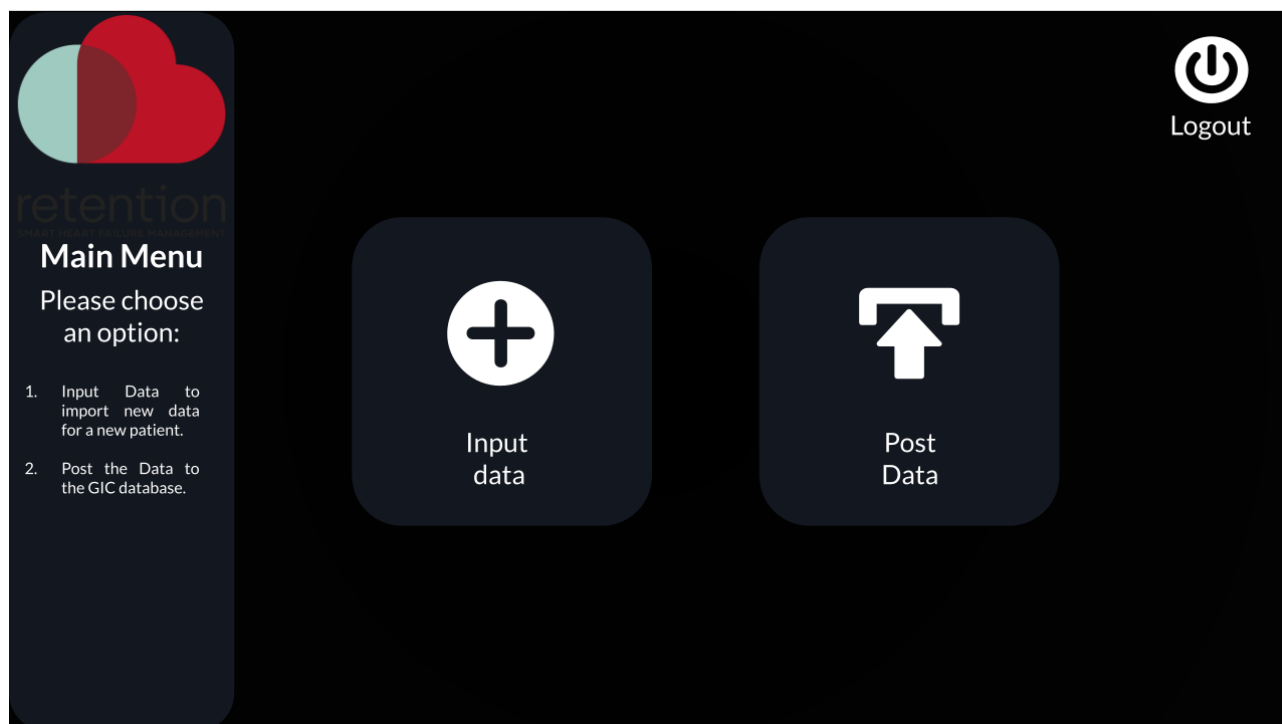


Figure 9. The main menu screen of “Data Sharing to RETENTION platform”.

By clicking the “Input data” option, the user is able to import new data to the platform that will be corresponding to new patients. For each patient pseudo-IDs will be created by the security component.

In case the data doesn’t follow the exact specified format, to match with the format of the RETENTION platform data, the user will need to convert them on his/her own before importing them. The data should match exactly a predefined csv structure that will be presented next.

At each screen of this graphical tool, there is a space on the left providing thorough instructions on all the available options, guiding the third-party user, so he/she can handle the mechanism without problems.

By clicking input data, the next screen is presented to the user so he/she can import the available data by uploading a .csv file.




retention
HEART HEALTH DECISION-MAKING
Import Data
Please import the necessary data by choosing the corresponding csv file
Import csv
! WARNING
Please make sure the csv is in the right format.
It can contain observations, conditions, medication and questionnaires.
Back

Logout

Figure 10. Import a .csv file that includes the patients' data.

An example .csv file containing some variables in this format can be seen in the following figure.

Sample of Example Patient Data

A	B	C	D	E	F	G	H	I	J	
UserId	6 Minute Walk Test	ALAT measurement	ALB measurement	ALP measurement	ASAT measurement	Acenocoumarol Medication	Acute cellular graft rejection	Allograft vasculopathy	Amiloride Medication	
PatientId1	120	120	120	120	120	150mg/day	Acute cellular graft rejection	Allograft vasculopathy	150mg/day	
K	L	M	N	O	P	Q	R	S	T	
UserId	Amiodarone Medication	Amlodipine Medication	Anaemia	Angina	Antibiotics Medication	Aorta root Diameter by US 2D	Aortic stenosis (Mild)	Aortic stenosis (Moderate)	Aortic stenosis (Severe)	
PatientId1	150mg/day	150mg/day	Anaemia	Angina	150mg/day	120	Aortic stenosis (Mild)	Aortic stenosis (Moderate)	Aortic stenosis (Severe)	
U	V	W	X	Y	Z	AA	AB	AC	AD	
UserId	Aortic aneurysm	Aortic mechanical valve	Aortic valve regurgitation (Mild)	Aortic valve regurgitation (Moderate)	Aortic valve regurgitation (Severe)	Apixaban Medication				
PatientId1	Aortic aneurysm	Aortic mechanical valve	Aortic valve regurgitation (Mild)	Aortic valve regurgitation (Moderate)	Aortic valve regurgitation (Severe)	Apixaban Medication				
AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO
UserId	Arterial Hypertension	Ascites	Questionnaire KCCQ	Questionnaire HF-CQ	Questionnaire MNA	Questionnaire MoCA	Questionnaire PHQ9	Questionnaire Symptoms		
PatientId1	Arterial Hypertension	Ascites	answer1	answer1	answer1	answer1	answer1	answer1		
PatientId1			answer2	answer2	answer2	answer2	answer2	answer2		
PatientId1			answer3	answer3	answer3	answer3	answer3	answer3		
PatientId1			answer4	answer4	answer4	answer4	answer4	answer4		
PatientId1			answerx	answerx	answerx	answerx	answerx	answerx		

Figure 11. An example of .csv file.

To include data coming from other studies and not necessarily include the vast number of variables of the RETENTION data model, missing values are allowed. Only the values that have correspondence with the RETENTION variables will be posted to GIC.

The user then can click on the “Import csv” option and find locally from his/her computer the csv file that he/she created with all the necessary data and import it. In case of errors and inconsistency in formatting the users get specific notifications so that he properly adjusts the .csv file.

The second option of the main menu is the “Post data” option. Having imported the .csv file with the data, the user then clicks back and is ready to send the data to the cloud. This happens by pressing the “Post Data” button in the main menu. Then the user is redirected to the following user interface of the graphical tool.

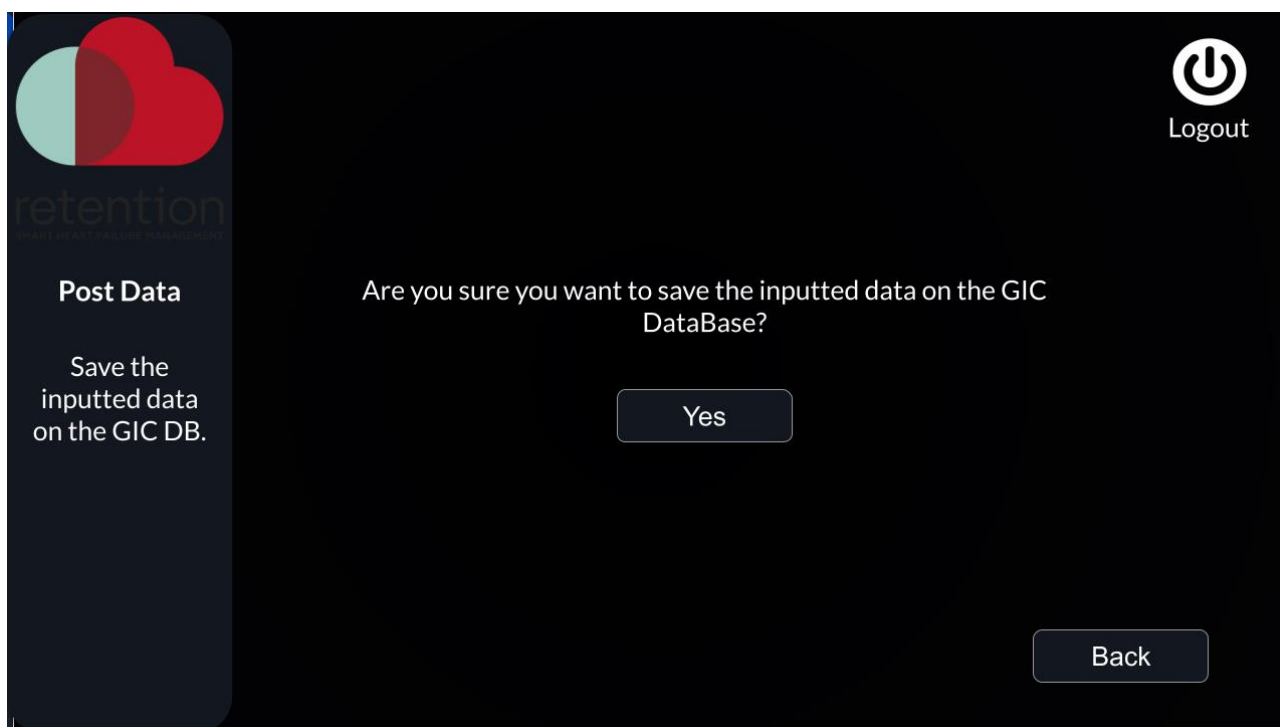


Figure 12. Save option of the data to the GIC database.

By pressing “yes”, the user triggers a process of multiple post requests, one for each variable of the .csv file. Two main endpoints are being used for the posting of the data, one for FHIR data and one for the non-FHIR data. The background process of this tool makes use of the authorization token received on the login stage and passes it as a header of the post request. Finally, the patient pseudo-Id is passed in the body of each post request, when uploading each field of the data. One example .json file, as it is posted is as following:

```
{
  "resourceType": "Observation",
  "id": "Bodyweight",
  "text": {
    "status": "generated",
    "div": "<div xmlns='\"http://www.w3.org/1999/xhtml\"'><p><b>Generated Narrative</b></p><div style="
  },
  "status": "final",
  "code": {
    "coding": [
      {
        "system": "http://snomed.info/sct",
        "code": "726527001",
        "display": "Body weight"
      }
    ]
  },
  "subject": {
    "reference": "Patient/1"
  },
  "effectiveDateTime": "2021-05-21T09:29:23.356+00:00",
  "valueQuantity": {
    "value": 120
  }
}
```

Figure 13. An example of .json structure for a FHIR variable.

The above figure shows the .json structure that the tool creates internally before posting a FHIR value, in this instance the body weight. These data then will be stored in the online database in the GIC.

Regarding the non- FHIR data, the software creates the necessary .json structure internally before posting to the non- FHIR database the data and has the following format:

```
weather.json x
{
  'userId': 'P103',
  'serialNumber': '123456789017\n',
  'measurementItems': [{ 'state': '12.939999999999998',
  'type': 'temperatureExternal',
  'deviceId': 'rpi',
  'measurementDatetime': 1669487334}]
}
```

Figure 14. An example of .json structure for a non-FHIR variable.

The figure above illustrates an example of the patient with pseudo-Id P103, with a device with serial number / package Id '123456789017' and the non- FHIR variable specified with this patient is external temperature.

It should be noted that when a third-party user will bring non- FHIR data, the package id will be preconfigured to a static statement as the data that he/she brings, doesn't come in from a RETENTION device and so no package Id is available, but only a pseudo-Id/userId.

Finally, it should be mentioned that the "Data sharing to RETENTION Platform" tool runs locally on the machine of the third-party user and the only prerequisite is to have installed the programming language that the tool was developed on, which is python, along with the necessary libraries PYQT5, . json, requests, .csv and NumPy. The tool can run in each operating system including Windows 10, Linux and macOS.

7.3 Data sharing from RETENTION

The "Data sharing from RETENTION" task has the goal to enable third-party users to receive the project's data and use them for their own research needs. This task makes the open-source distribution of the data possible, and several key outcomes can be achieved, such as the exploitation of data for training the models of external users. Thus, it is important to implement a process of enabling third-party users to easily and automatically download all of the data, i.e. FHIR and non-FHIR ones, to their local machines. Although data is open, it is given after an approval of the GIC administrator (following provision of name, contact details, organisation/institution and the reason access the data).

Taking into consideration the above a simple GUI tool is being developed that facilitates the registration of the user, the download of all data stored on the GIC database and the provision of the implementation guidelines.

In the following figure, the login screen of this tool is presented.

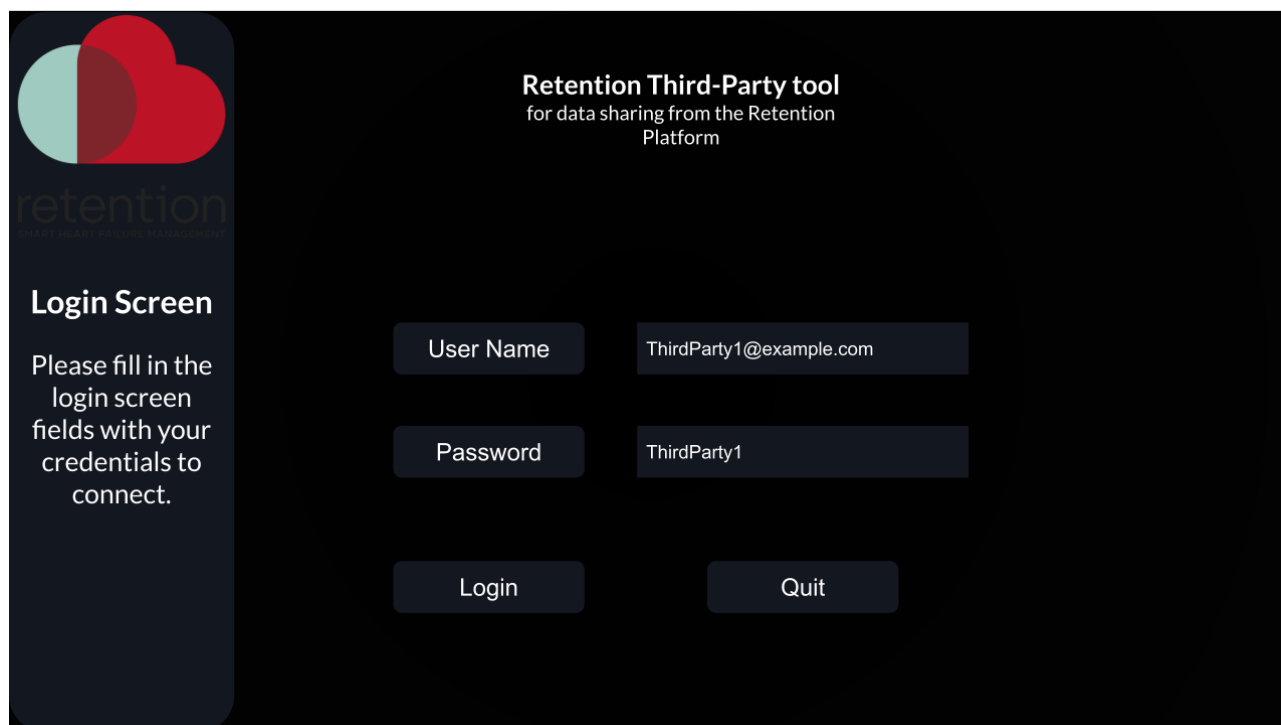


Figure 15. The login screen menu of "Data sharing from RETENTION" tool.

The authentication is token-based like the previous task and so when the login button is pressed the same process occurs. A request is sent to the security component that checks if the credentials exist in its registry. If yes, an access token with specific duration is provided, during its life the user can use it for the acquisition of data.

After logging in, three options are presented to the user as seen in the figure below.

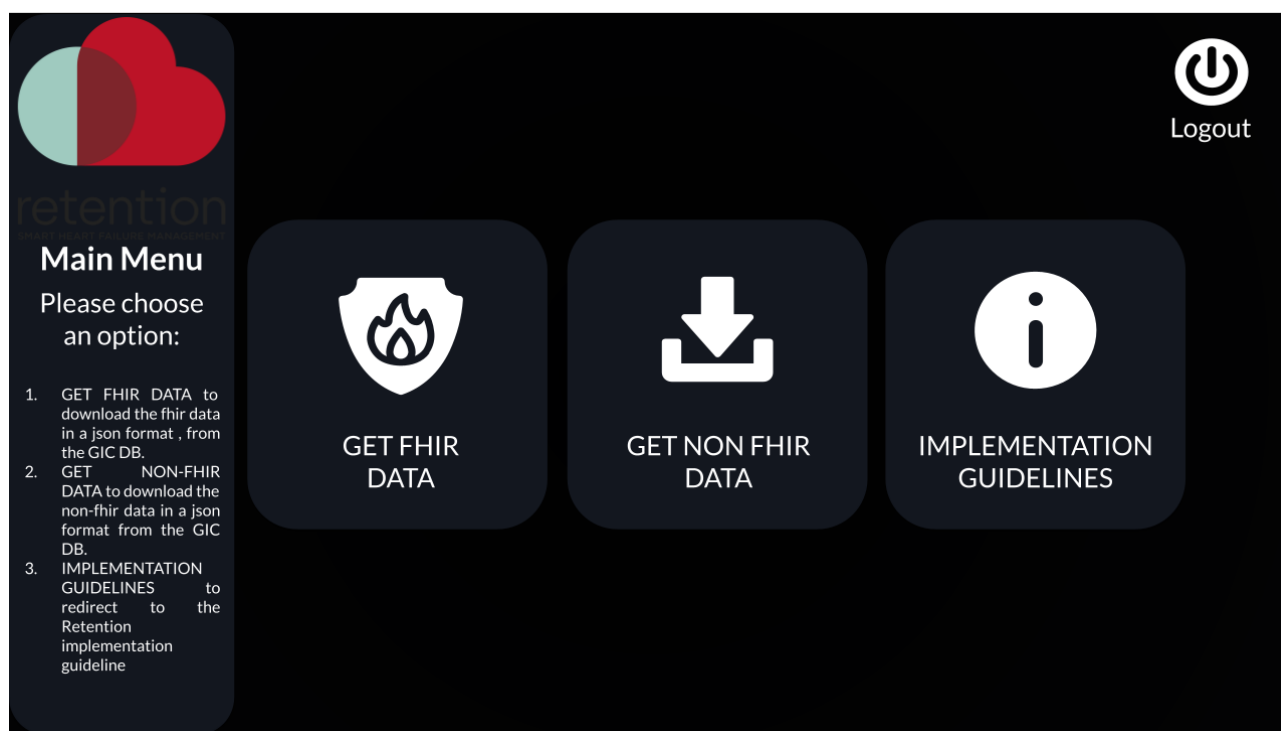


Figure 16. The main menu of "Data sharing from RETENTION" tool.

The data are separated to non-FHIR and FHIR as can be observed and different get requests are implemented to different endpoints to fetch the data for both.

When the user clicks on "GET FHIR DATA" a background process is initialised that implements multiple GET requests, for each patient in the GIC database to the FHIR endpoint. A similar process is followed for the non-FHIR endpoints. When the process is finished, the software will have created a local folder called "RETENTION_data", that will contain all the exported *json* files inside, one for each patient in an anonymous way.

In the following figure an example of this folder with 5 patients can be observed.

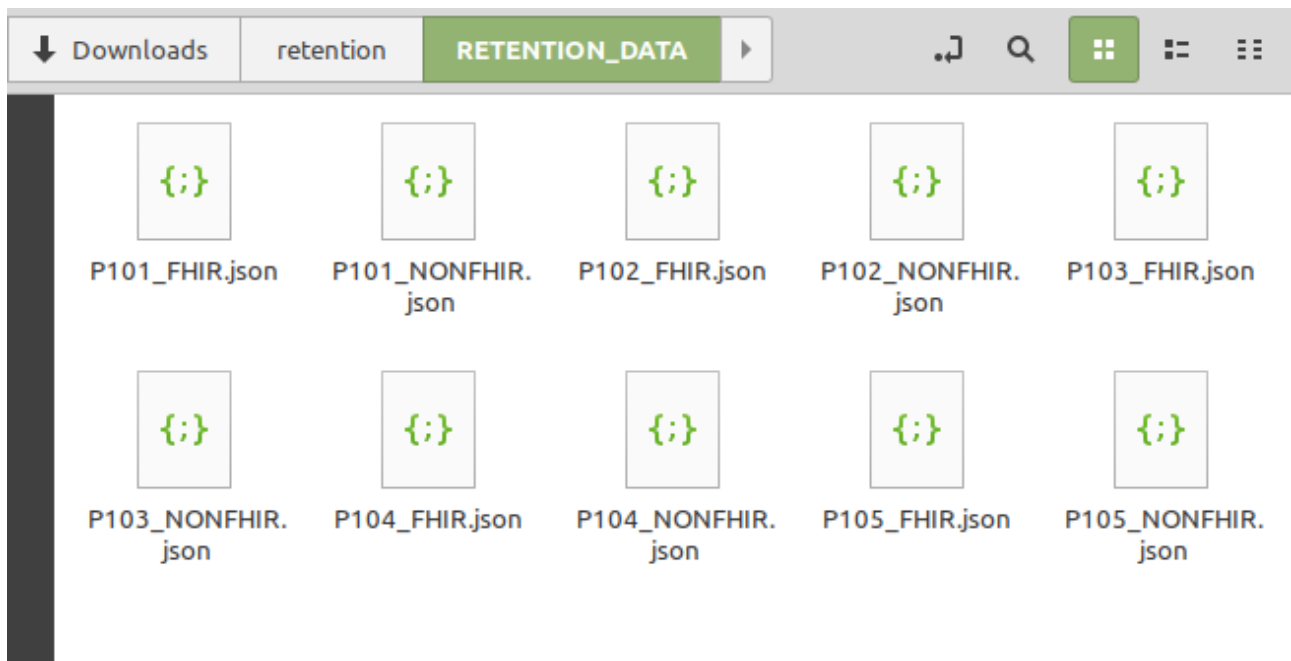


Figure 17. RETENTION data extracted from GIC (example).

Finally, through clicking the appropriate button, the user is redirected to the IG that gets information about the data structure.

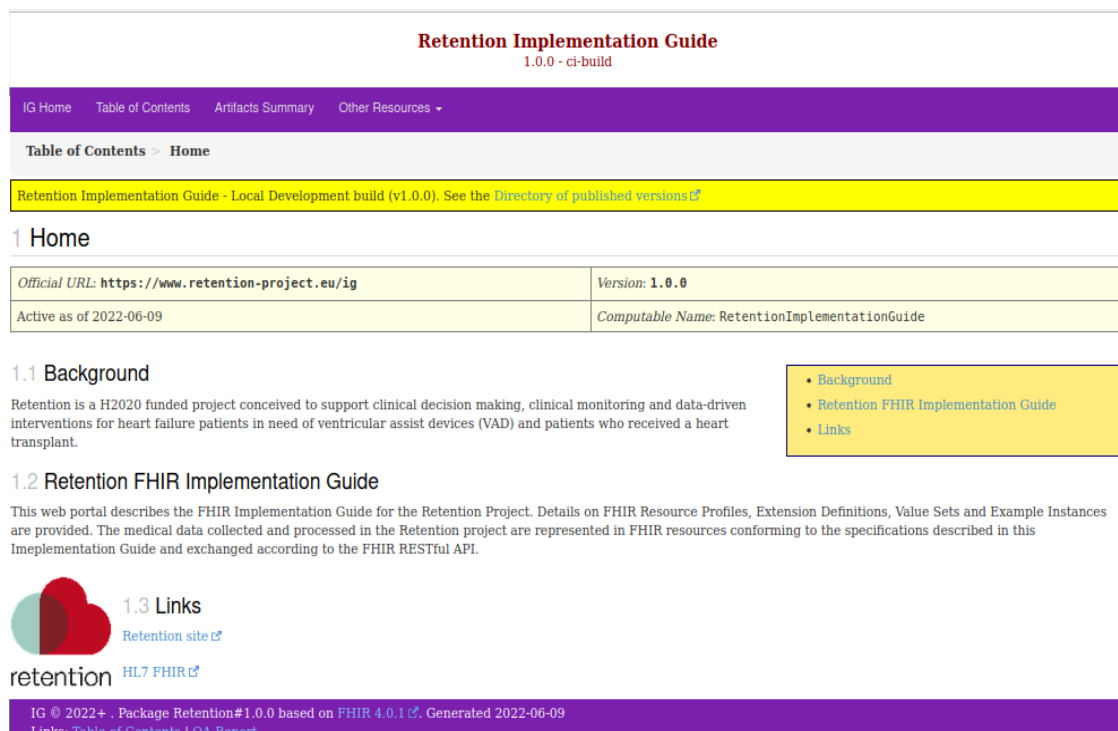


Figure 18. RETENTION Implementation Guide (IG).

The following figure presents one variable (body weight) and its code system (SNOMED-CT).

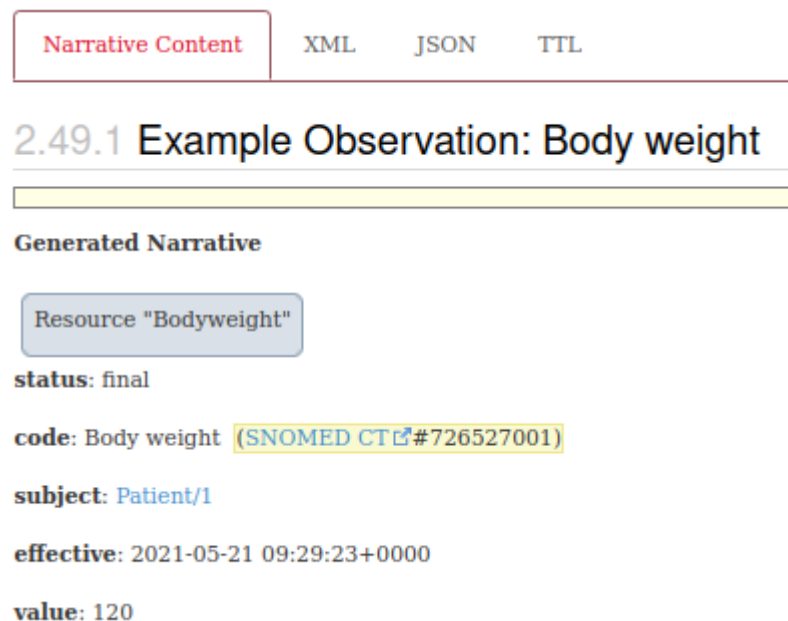


Figure 19. An example of body weight variable, as it is depicted in IG).

7.4 Model sharing to RETENTION

The “Model sharing to RETENTION platform” task has the main goal of enabling third-party users to create their own models based on RETENTION models specifications. Specifically, in order that the new models to be created to be meaningful and functional in the context of the project scope, they need to depend on the pre-existing model templates that the project makes use of. Taking this into consideration the final objective of “model sharing to”, is to allow third-party users, and especially analysts and data engineers, to modify, adjust and configure RETENTION models. In this way, researchers and data analysts can experiment on models already developed by RETENTION by approaching the Machine Learning (ML) cases of the project from another point of view (different algorithms, different parameters etc.). New models are uploaded and stored to the RETENTION database.

For the accomplishment of this goal, a graphical user interface tool facilitating the “Model sharing to RETENTION Platform” task will be employed. The main functionalities of this tool are the authentication of the third-party analyst, the provision of access to the pre-existing ML problems and respective models. Then, the analyst is given access to these datasets, can select of relevant features and choose available algorithms. For each of the newly created model selected parameters are returned to the user so he can evaluate the model performance.

Similarly, in order the third-party analyst to be able to use this tool, will be provided with the necessary credentials by the administrator of the GIC database. The following figure presents the login screen of the tool.

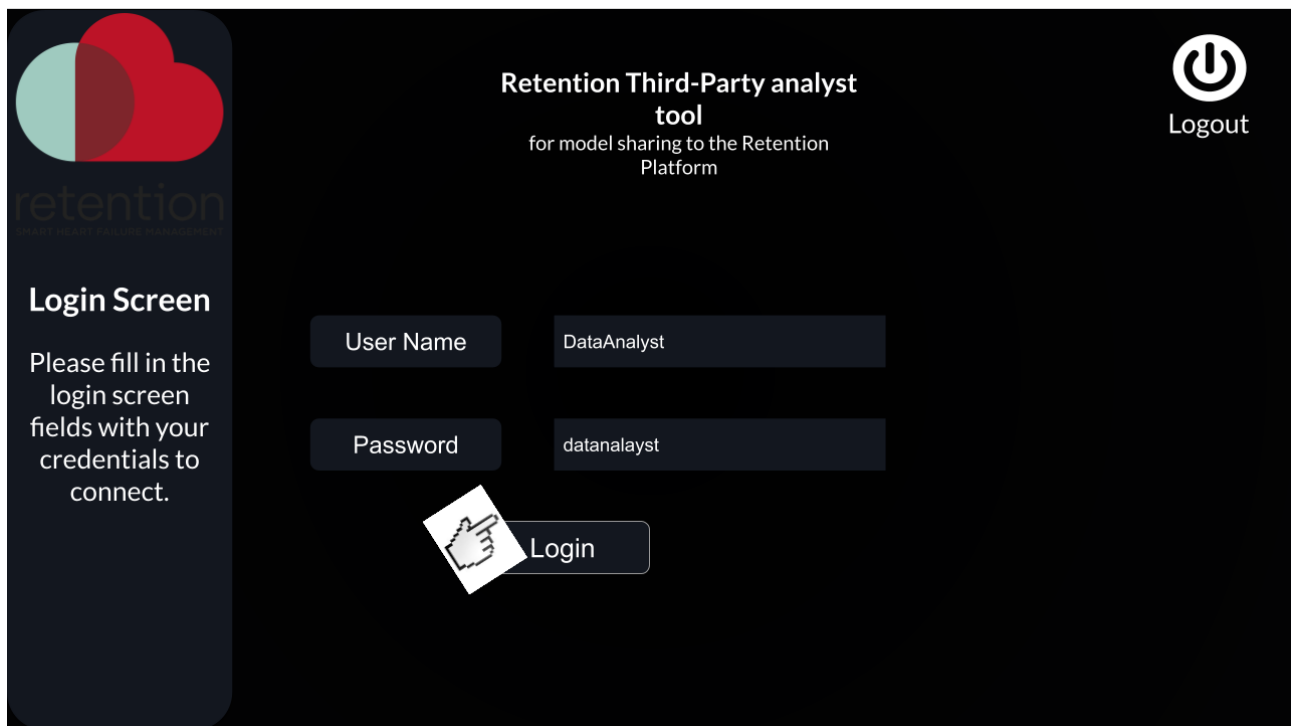


Figure 20. Login page of "Model Sharing from RETENTION platform" tool.

After this process, the analyst can access the web application that hosts the MLflow API, with which the user can accomplish all of the main functionalities of the machine learning processes such as training of the models. MLflow, as described in previous sections, is an open-source platform for managing machine learning workflows and is used in the context of RETENTION to handle machine learning models. Taking all this into consideration, ML flow is used by this tool for model exchange.

Next the main menu screen of the "Model sharing to RETENTION platform" tool is presented.

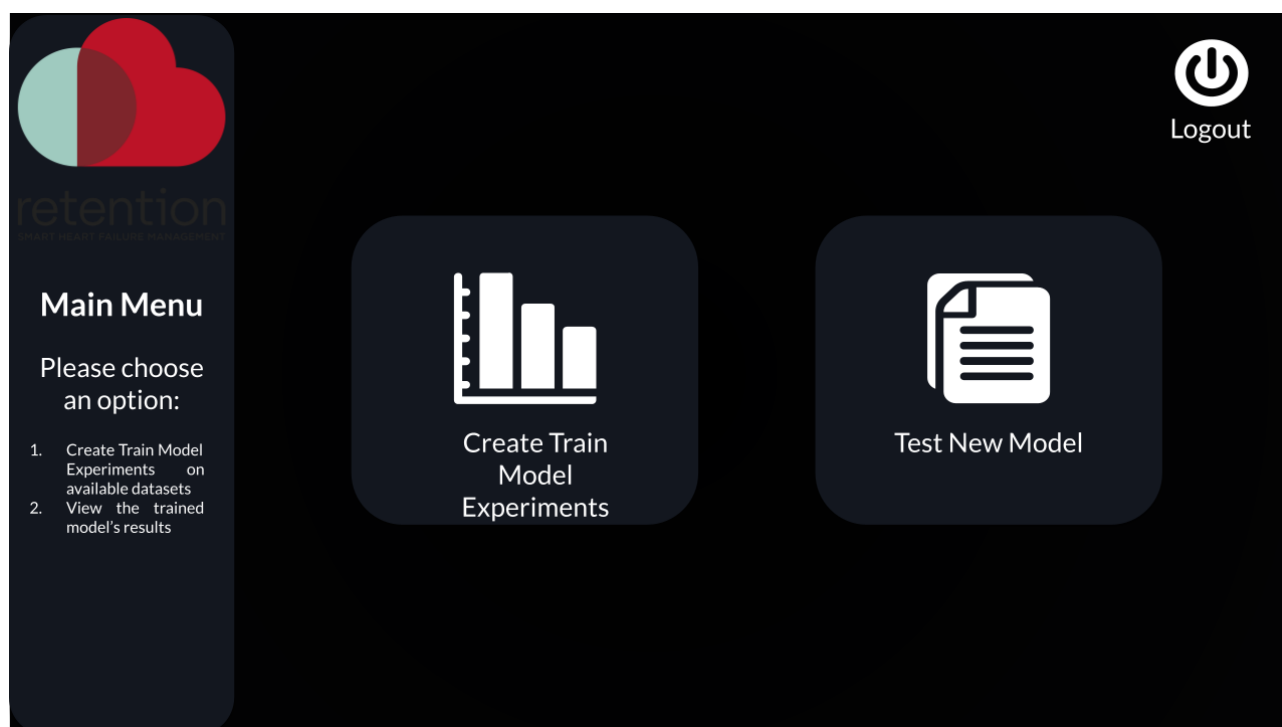


Figure 21. Main menu of "Model Sharing to RETENTION platform" tool.

Two functionalities are presented to the analyst: (i) Create Train Model experiments and (ii) Test new Model. By choosing the first one the analyst can choose the use case/ dataset, adjust the necessary features and algorithms, and execute the relevant model. The second functionality presents relevant results and analytics.

In the following figure two example datasets for survival rate and heart failure are demonstrated.

The screenshot shows the 'Available clinical trials datasets' interface. On the left, a sidebar contains the 'retention' logo and a 'Model Template' section with the text 'Please choose an option:' and a numbered list: '1. Choose among the available datasets'. The main area is titled 'Available clinical trials datasets' and features a 'Logout' button with a power icon in the top right. Below the title, there are two input fields: 'Survival rate' and 'Heart Failure'. The 'Survival rate' field has a green checkmark icon to its right. At the bottom, there are 'Apply' and 'Back' buttons.

Figure 22. Example of available datasets.

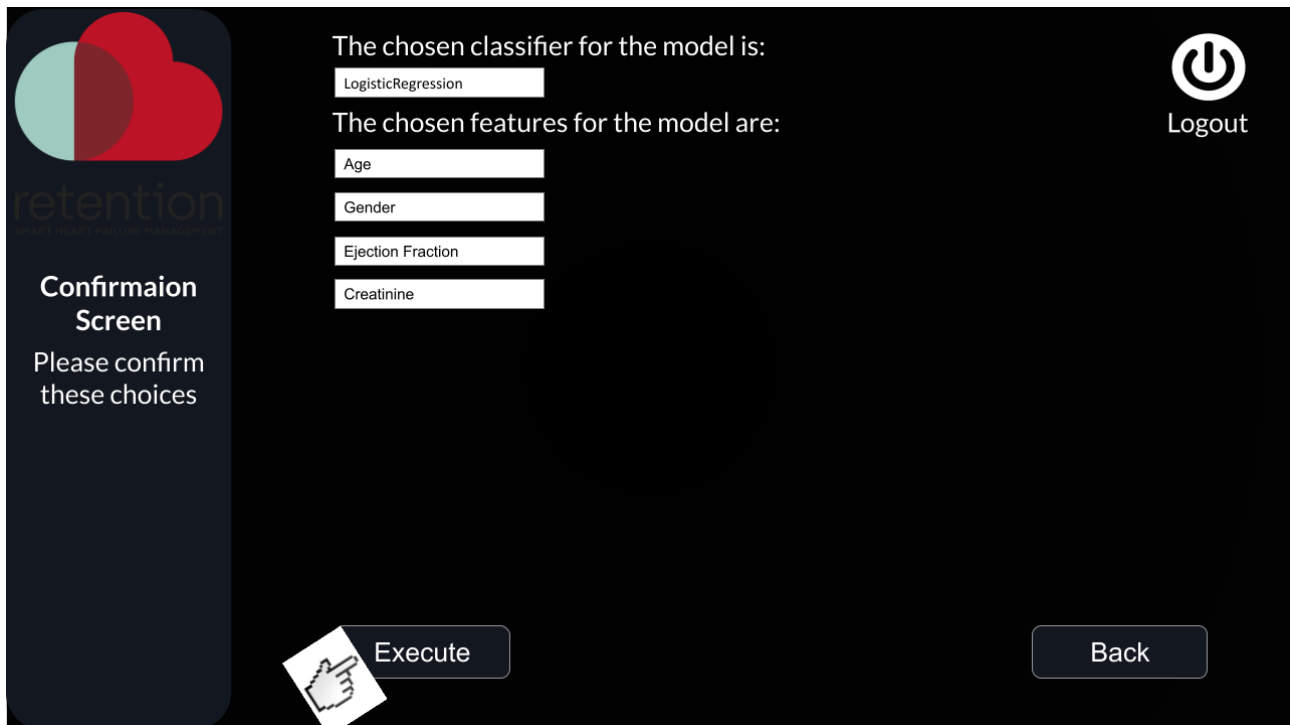
Then, the analyst clicks “Apply” and the following screen appears.

The screenshot shows the 'Training preparation of survival rate' interface. On the left, the sidebar is identical to the previous screen. The main area is titled 'Training preparation of survival rate' and features a 'Logout' button with a power icon in the top right. Below the title, there are two sections: 'Choose from the Features for survival rate' and 'Choose algorithm'. The 'Choose from the Features for survival rate' section contains a list of features: 'Age', 'Gender', 'Ejection Fraction', 'Creatinine', 'Sodium (Na)', and 'Potassium (K)'. Each feature has a green checkmark icon to its right. The 'Choose algorithm' section contains a dropdown menu with 'Select' as the current selection, and two options: 'LogisticRegression' and 'GradientBoostingClassifier'. At the bottom, there are 'Apply' and 'Back' buttons. A hand cursor icon is positioned over the 'Apply' button.

Figure 23 Features selection for survival rate dataset

After the appropriate use case has been selected, the relative to this dataset features and also the supported classifiers/algorithms that are able to be applied to the dataset, are being presented to the user so that he can choose during the creation of the new model.

The final step before executing the model is the confirmation screen where all of the choices regarding the training parameters and classifiers are presented to the user (Figure 24).



The chosen classifier for the model is:
LogisticRegression

The chosen features for the model are:
Age
Gender
Ejection Fraction
Creatinine

Confirmation Screen
Please confirm these choices

Execute

Back

Logout

Figure 24. Confirmation screen of the chosen features and classifiers.

Thus, by clicking “execute” of these chosen features and classifier, the model training will take place at GIC.

After the training is completed, the user by clicking the option “Test New Model”, will be able to view the model’s results through analytics.

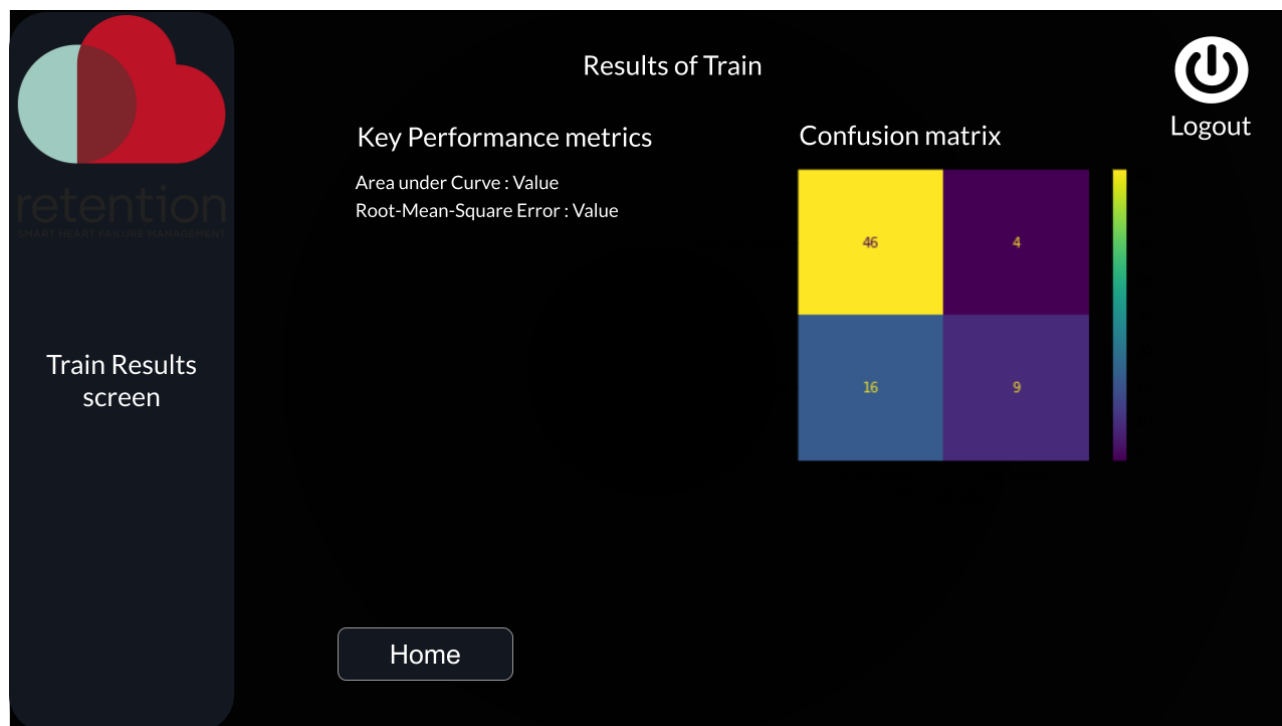


Figure 25. Results of model training through analytics.

The “Test New Model” provides the user with the necessary metrics and analytics to evaluate the performance of the model. For example, in the Figure 18, the Root-Mean-Square Error, the area under curve along with the relevant confusion matrix are presented. This information becomes available to the presented graphical tool through the MLFlow REST API interaction. Specifically, the two metrics will come as a JSON response of the REST API train service. They are automatically saved in the MLflow metadata repository. The image of the confusion matrix will come as a URL to the MLFlow artefacts storage (MinIO signed URL). It will also be contained in the JSON response. So, this means that this information is stored both on the GIC server and received locally to be displayed on the proposed tool.

7.5 Model sharing from RETENTION

The main goal of the “Model Sharing from RETENTION platform” is to enable third-party users to acquire the trained models and use them with their own similarly structured data. A basic prerequisite for this, is that the third-party analysts to be able to use efficiently the trained models, they need to have installed the ML flow, a pickle file (that contains the trained model), the programming language that the tool was developed on, which is python, along with the necessary libraries PYQT5, .json, requests, .csv, numpy, pandas, requests, scikit and Flask. The tool can run in each operating system including Windows 10, Linux and macOS.

A simple step by step guide with all the necessary software and libraries that are required is going to be distributed to the users that wish to run these models with their own data. An example of this file for an indicative model is shown in the Annex A: Model run instructions for third party users.

A simple GUI allows for model acquisition after authentication. Authentication follows the similar process as described in previous sections.

The login screen of the tool is presented next and is similar with the previous login screens.

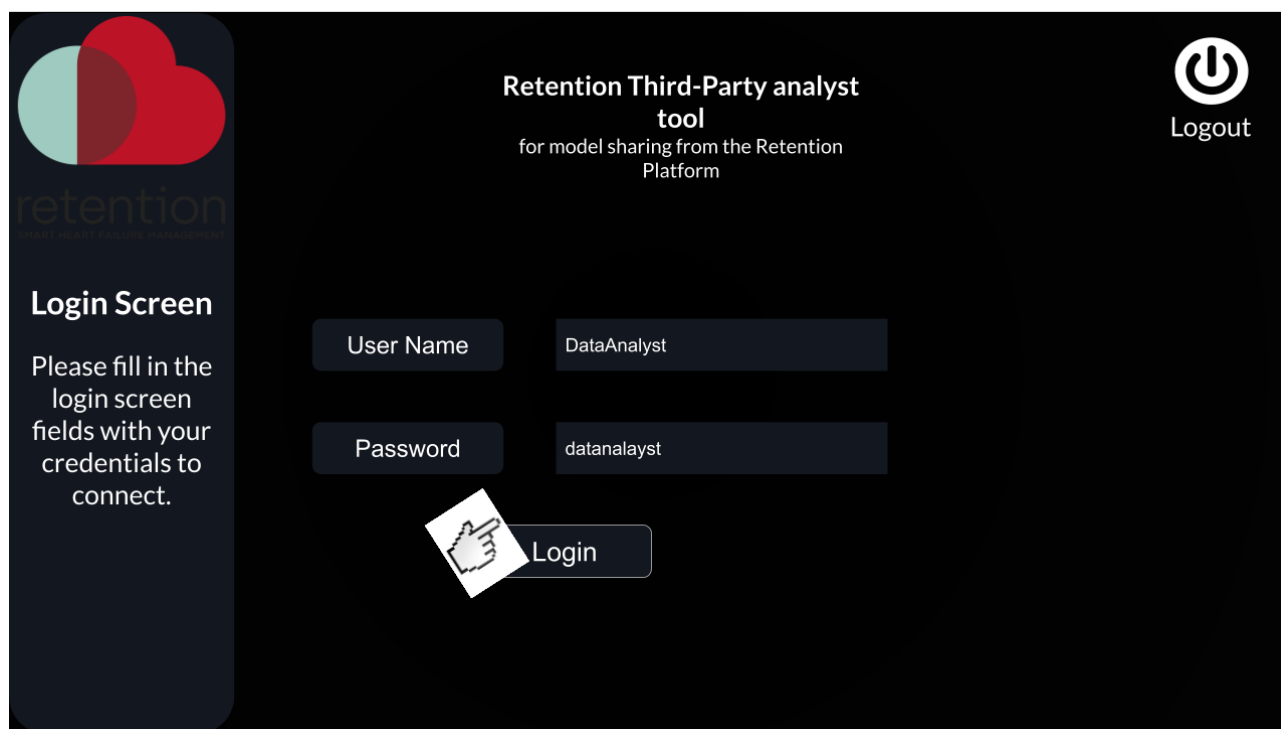


Figure 26. Login screen of "Model Sharing from RETENTION platform" tool.

Next the main menu screen of the tool is presented. Two main functionalities are presented in this screen: (i) The model download and (ii) Model statistics. By choosing the first one a list of all the available trained models regarding the specific use cases is presented, and so the user by selecting the use case of interest, he/she will be able to obtain the pickle file on the local machine for use. The "Model statistics" gives the basic characteristics of the model including performance, features employed, features importance for the model etc. so that the user can select the most appropriate model.

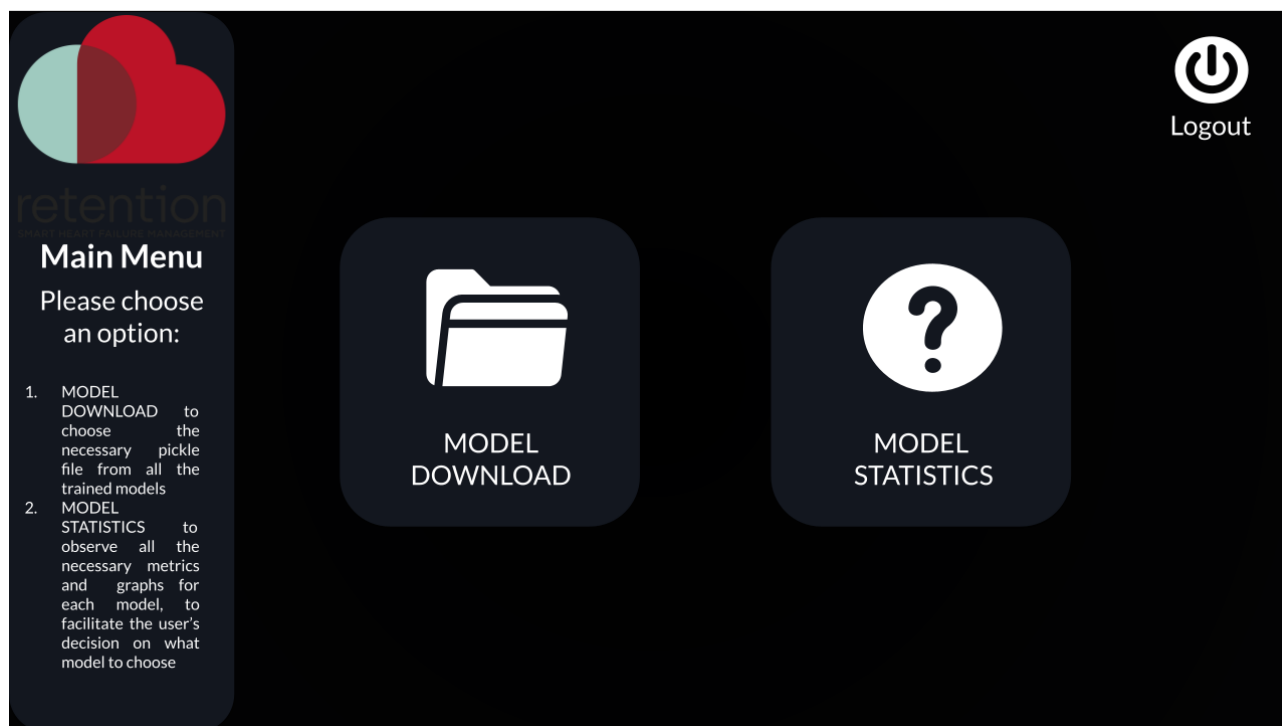
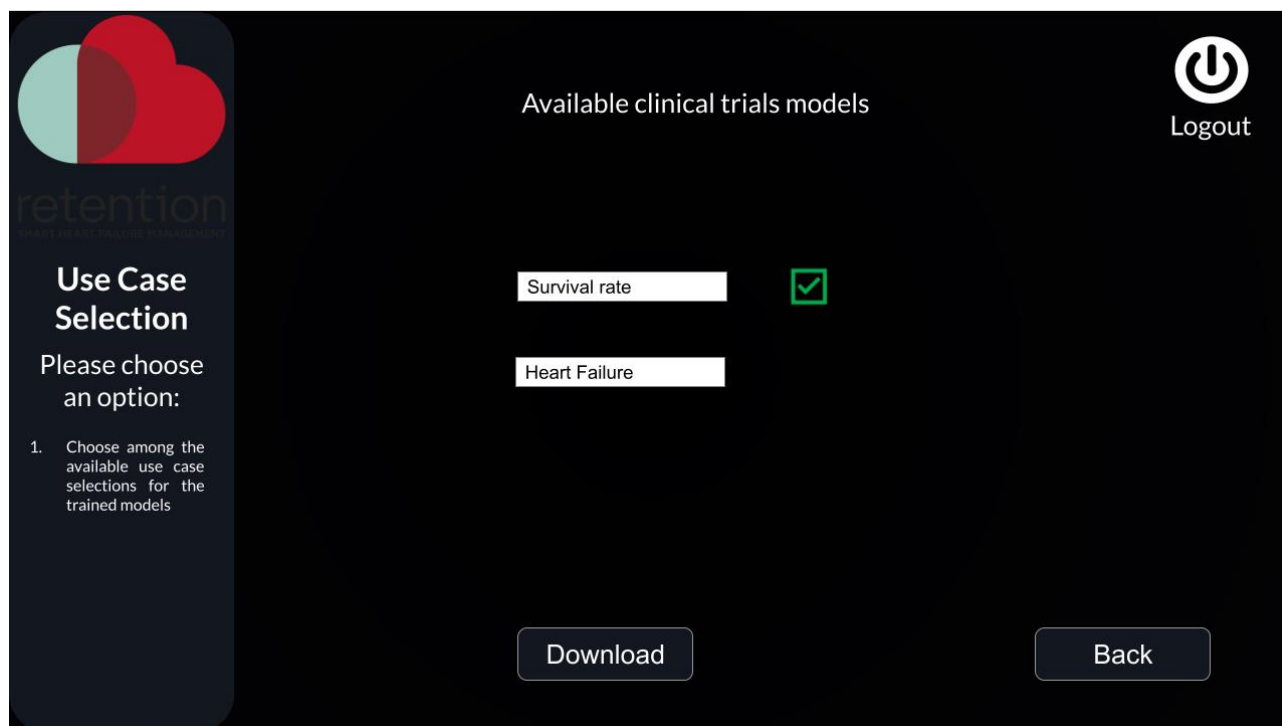


Figure 27. Main menu screen of "Model Sharing from RETENTION platform" tool.

Following, the "Model download screen", the user can make the necessary use cases selections to download the necessary models on his/her local machine. Indicatively, in the next figure are presented the use cases of "Survival rate" and "Heart Failure".



Available clinical trials models

Logout

Use Case Selection

Please choose an option:

1. Choose among the available use case selections for the trained models

Survival rate ☒

Heart Failure

Download Back

Figure 28. Use cases selection for the trained models.

In the model selection screen, the analyst chooses the model of interest and clicks download. Then a background process occurs that communicates with the MLFlow's REST API, (as we already mentioned MLFlow is running as a web application on GIC and the communication between the tools and MLFlow occurs via a REST API) and requests the pickle file of the model with a get request. The file then is retrieved in the local machine of the user, and he/she is ready to use it with his/her own data.



8 Conclusions

The D5.1 RETENTION Analytics & Decision-making enabling mechanisms v1 is the first iteration of documentation that presents the work done within WP5 work package. The efforts will be focused on creating models based on patients' data.

Tasks like data processing, big data handling, model explainability and model sharing will be continuously monitored by all partners involved in this package.

The final purpose of this effort will be to assure that clinicians will enjoy a tool that allows them to perform various predictions, analysis that potentially will provide a better insight to the evolution of heart diseases.



9 References

- Ahmad T, Munir A, Bhatti SH, Aftab M, Raza MA (2017) Survival analysis of heart failure patients: A case study. PLoS ONE 12(7): e0181001. <https://doi.org/10.1371/journal.pone.0181001>
- Aldahiri, A.; Alrashed, B.; Hussain, W. Trends in Using IoT with Machine Learning in Health Prediction System. Forecasting 2021, 3, 181-206. <https://doi.org/10.3390/forecast3010012>
- Averbuch Tauben, Kristen Sullivan, Andrew Sauer, Mamas A Mamas, Adriaan A Voors, Chris P Gale, Marco Metra, Neal Ravindra, Harriette G C Van Spall, Applications of artificial intelligence and machine learning in heart failure, European Heart Journal - Digital Health, Volume 3, Issue 2, June 2022, Pages 311–322, <https://doi.org/10.1093/ehjdh/ztac025>
- AMCP. 2019. Academy of Managed Care Pharmacy. Concepts in Managed Care Pharmacy; Disease Management. Available at: <https://www.amcp.org/about/managed-care-pharmacy-101/concepts-managed-care-pharmacy/disease-management>
- Bansilal S, Castellano JM, Fuster V. Global burden of CVD: focus on secondary prevention of cardiovascular disease. Int J Cardiol. 2015 Dec;201 Suppl 1:S1-7. doi: 10.1016/S0167-5273(15)31026-3. PMID: 26747389.
- Bazoukis G, Stavrakis S, Zhou J, Bollepalli SC, Tse G, Zhang Q, Singh JP, Armondas AA. Machine learning versus conventional clinical methods in guiding management of heart failure patients-a systematic review. Heart Fail Rev. 2021 Jan;26(1):23-34. doi: 10.1007/s10741-020-10007-3. PMID: 32720083; PMCID: PMC7384870.
- Benzer W, Rauch B, Schmid JP, Zwisler AD, Dendale P, Davos CH, Kouidi E, Simon A, Abreu A, Pogossova N, Gaita D, Miletic B, Bönner G, Ouarrak T, McGee H; EuroCaReD study group. Exercise-based cardiac rehabilitation in twelve European countries results of the European cardiac rehabilitation registry. Int J Cardiol. 2017 Feb 1;228:58-67. doi: 10.1016/j.ijcard.2016.11.059. Epub 2016 Nov 11. Erratum in: Int J Cardiol. 2017 Sep 1;242:50. Kouidi, Evangelia [corrected to Kouidi, Evangelia]. PMID: 27863363.
- R. Bhardwaj, A. R. Nambiar and D. Dutta, "A Study of Machine Learning in Healthcare," 2017 IEEE 41st Annual Computer Software and Applications Conference (COMPSAC), 2017, pp. 236-241, doi: 10.1109/COMPSAC.2017.164.
- Brahmbhatt DH, Cowie MR. Remote Management of Heart Failure: An Overview of Telemonitoring Technologies. Card Fail Rev. 2019 May 24;5(2):86-92. doi: 10.15420/cfr.2019.5.3. PMID: 31179018; PMCID: PMC6545972.
- Care Innovations. 2022. Population Health Insights; All insights; What Is Telehealth? What Is Remote Patient Monitoring? How Are They Different? Available at: <https://resources.careinnovations.com/population-health-insights>
- Chicco Davide, Giuseppe Jurman: Machine learning can predict survival of patients with heart failure from serum creatinine and ejection fraction alone. BMC Medical Informatics and Decision Making 20, 16 (2020)
- Dieckelmann M, Reinhardt F, Jeitler K, et al. Chronic heart failure patients' experiences of German healthcare services: a protocol for a scoping review. BMJ Open 2019;9:e025685. doi: 10.1136/bmjopen-2018-025685



Fahmy Ahmed S., Rowin Ethan J., Manning Warren J., Maron Martin S., Nezafat Reza, "Machine Learning for Predicting Heart Failure Progression in Hypertrophic Cardiomyopathy", *Frontiers in Cardiovascular Medicine*, vol. 8, ISSN=2297-055X, 2021, DOI: 10.3389/fcvm.2021.647857.

Farwati M, Riaz H, Tang WHW. Digital Health Applications in Heart Failure: a Critical Appraisal of Literature. *Curr Treat Options Cardiovasc Med*. 2021;23(2):12. doi: 10.1007/s11936-020-00885-z. Epub 2021 Jan 16. PMID: 33488049; PMCID: PMC7812033.

Greenberg, B., Brann, A., Campagnari, C. et al. Machine Learning Applications in Heart Failure Disease Management: Hype or Hope?. *Curr Treat Options Cardio Med* 23, 35 (2021). <https://doi.org/10.1007/s11936-021-00912-7>

HFPN. 2020a. Heart Failure Policy Network. Heart failure policy and practice in Europe: Germany. London: HFPN. Available at: <https://www.hfpolicynetwork.org/wp-content/uploads/Heart-failure-policy-and-practice-in-Europe-Germany.pdf>

HFPN. 2020b. Heart Failure Policy Network. Heart failure policy and practice in Europe: England. London: HFPN. Available at: <https://www.hfpolicynetwork.org/wp-content/uploads/Heart-failure-policy-and-practice-in-Europe-England.pdf>

HFPN. 2020c. Heart Failure Policy Network. Heart failure policy and practice in Europe. London: HFPN. Available at: <https://www.healthpolicypartnership.com/app/uploads/Heart-failure-policy-and-practice-in-Europe.pdf>

Koehler F, Koehler K, Prescher S, Kirwan BA, Wegscheider K, Vettorazzi E, Lezius S, Winkler S, Moeller V, Fiss G, Schleder J, Koehler M, Zugck C, Störk S, Butter C, Prondzinsky R, Spethmann S, Angermann C, Stangl V, Halle M, von Haehling S, Dreger H, Stangl K, Deckwart O, Anker SD. Mortality and morbidity 1 year after stopping a remote patient management intervention: extended follow-up results from the telemedical interventional management in patients with heart failure II (TIM-HF2) randomised trial. *Lancet Digit Health*. 2020 Jan;2(1):e16-e24. doi: 10.1016/S2589-7500(19)30195-5. Epub 2019 Dec 12. PMID: 33328035.

Mayo Clinic. 2022. Healthy Lifestyle; Consumer Health. Telehealth: Technology meets health care. Available at: <https://www.mayoclinic.org/healthy-lifestyle/consumer-health/in-depth/telehealth/art-20044878>

MedicineNet. 2021. MedTerms Dictionary. Medical Definition of Ambulatory Care. Available at: https://www.medicinenet.com/ambulatory_care/definition.htm

Negarandeh R, Zolfaghari M, Bashi N, Kiarsi M. Evaluating the Effect of Monitoring through Telephone (Tele-Monitoring) on Self-Care Behaviors and Readmission of Patients with Heart Failure after Discharge. *Appl Clin Inform*. 2019 Mar;10(2):261-268. doi: 10.1055/s-0039-1685167. Epub 2019 Apr 17. PMID: 30995686; PMCID: PMC6469982.

Ray Arkadip, Avijit Kumar Chaudhuri, Smart healthcare disease diagnosis and patient management: Innovation, improvement and skill development, *Machine Learning with Applications*, Volume 3, 2021, 100011, ISSN 2666-8270

Singhal A, Cowie MR. Digital Health: Implications for Heart Failure Management. *Card Fail Rev*. 2021 May 11;7:e08. doi: 10.15420/cfr.2020.28. PMID: 34035953; PMCID: PMC8135017.



Störk S, Handrock R, Jacob J, Walker J, Calado F, Lahoz R, Hupfer S, Klebs S. Treatment of chronic heart failure in Germany: a retrospective database study. *Clin Res Cardiol.* 2017 Nov;106(11):923-932. doi: 10.1007/s00392-017-1138-6. Epub 2017 Jul 26. PMID: 28748266; PMCID: PMC5655600.

Pekmezaris R, Torte L, Williams M, Patel V, Makaryus A, Zeltser R, Sinvani L, Wolf-Klein G, Lester J, Sison C, Lesser M, Kozikowski A. Home Telemonitoring In Heart Failure: A Systematic Review And Meta-Analysis. *Health Aff (Millwood).* 2018 Dec;37(12):1983-1989. doi: 10.1377/hlthaff.2018.05087. PMID: 30633680.

Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). *JBIM Manual for Evidence Synthesis*, JBI, 2020. Available from <https://synthesismanual.jbi.global>. <https://doi.org/10.46658/JBIMES-20-12>

Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J.* 2016 Jul 14;37(27):2129-2200. doi: 10.1093/eurheartj/ehw128. Epub 2016 May 20. Erratum in: *Eur Heart J.* 2016 Dec 30;: PMID: 27206819.

Rzig Dhia Elhaq, Foyzul Hassan, Marouane Kessentini, An empirical study on ML DevOps adoption trends, efforts, and benefits analysis, *Information and Software Technology*, Volume 152, 2022, 107037, ISSN 0950-5849, <https://doi.org/10.1016/j.infsof.2022.107037>.

Sundararajan, Mukund, and Amir Najmi. "The many Shapley values for model explanation." arXiv preprint arXiv:1908.08474 (2019)



10 Annex

Annex A: Model run instructions for third party users

These instructions relate to the case of loading and running the model on a third-party user's PC after the respective model pickle file has been downloaded via the 'Model download screen'. For running the model, Python 3 environment is to be used with platforms like Jupyter Notebooks or IDEs (Integrated Development Environments). These are momentary instructions and can be changed during the further development of the 'Model Sharing from RETENTION' component, as well as the libraries and versioning. The exemplification relates to the Survival Rate Analytics scenario further described in section 3.3 Applicability: Use-case scenario.

Requirements.txt

```
json5==0.9.5
```

```
pandas==1.2.4
```

```
requests==2.25.1
```

```
numpy==1.20.2
```

```
scikit-learn==1.1.2
```

```
Flask==2.1.2
```

First Step:

Download the requierments.txt file and run this 'pip install -r requirements.txt' in a terminal that is open in the same location as the requierments.txt.

For using the model and for running prediction, ML Flow is optional to be used, since the model already includes the pickle file.

If still desired, this line should be added to the requirements file: mlflow==1.22.0

Second Step:

Download the pickle file, where the trained model resides, and then run the following python code in the same directory as the downloaded pickle to deserialize the pickle file

and to run the model as a REST API:

```
import pickle
```

```
import pandas as pd
```



```
from flask import Flask, jsonify

with open('name_of_model.pkl', 'rb') as f:
    model = pickle.load(f)
    model = model.model

app = Flask(__name__)

@app.route('/predict', methods=['POST'])
def predict():
    json_ = request.json
    query_df = pd.DataFrame(json_)
    query = pd.get_dummies(query_df)
    prediction = model.predict(query)
    return jsonify({'prediction': list(prediction)})
```

The features that can be used with this model are:

Age, Sex, Chest Pain Type, Blood Pressure, Cholesterol, Blood Sugar, ECG, Heart Rate, Angina, ST, ST Slope

An example of a list of features is:

40,1,0,140,289,0,0,172,0,0,2

For prediction, only one record of features is required.

To use this list with the model you need to do a POST method to <http://localhost:5000/predict> with the data in the following format:

```
{
  "Age": 40,
  "Sex": 1,
  "Chest Pain Type": 0,
  "Blood Pressure": 140,
  "Cholesterol": 289,
  "Blood Sugar": 0,
```



```
"ECG": 0,  
"Heart Rate": 172,  
"Angina": 0,  
"ST": 0.0,  
"ST_Slope": 2  
}
```

And the received message will be a json data with the results of the prediction