Federated Learning in Multi-Center, Personalized Healthcare for COPD and Comorbidities: The RE-SAMPLE Platform

Jakob Lehmann[1][a], Gesa Wimberg[1][b], Serge Autexier[1][c], Alberto Acebes[2][d], Christos Kalloniatis[3][e], Costas Lamprinoudakis[4][f], Thrasyvoulos Giannakopoulos[4][g], Andreas Menegatos[4][h], Agni Delvinioti[5][i], Giulio Pagliari[5][j], Nicoletta di Giorgi[5][k], Jarno Raid[6][l], Danae Lekka[7][m], Aristodemos Pnevmatikakis[7][n], Sofoklis Kyriazakos[7][o], Konstantina Kostopoulou[7] and Monique Tabak[8][p]

[1]*Deutsches Forschungszentrum für Künstliche Intelligenz (DFKI), Enrique-Schmidt-Str. 5, 28359 Bremen, Germany*

[2]*Atos IT Solutions and Services Iberia, S.L. Calle de Albarracín, 25. 28037 Madrid, Spain*

[3]*Department of Cultural Technology and Communication, University of the Aegean, University Hill, 81100 Mytilene, Greece*

[4]*Department of Digital Systems, University of Piraeus, 150 Androutsou St., Piraeus 18532, Greece*

[5]*Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Largo Agostino Gemelli, 8, 00168 Rome, Italy*

[6]*Tartu Ülikooli Kliinikum, Ludvig Puusepa 8, 50406 Tartu, Estonia*

[7]*Innovation Sprint, Clos Chapelle-aux-Champs 30, Bte. 1.30.30 1200 Brussels, Belgium*

[8]*University of Twente, Drienerlolaan 5, 7522 NB Enschede, Netherlands*

{*jakob.lehmann, gesa.wimberg*}*@dfki.de*

Keywords: Federated Learning, Interpretable Machine Learning, Chronic Obstructive Pulmonary Disease, Personalized Care, Real-World Data.

Abstract: Federated learning is becoming more and more popular, also in healthcare applications. The platform, developed within a multidisciplinary consortium, is enabling privacy-preserving training of machine learning models generating predictions for patients with chronic obstructive pulmonary disease and comorbidities. Moreover, data synchronization and monitoring is made possible using the HL7 FHIR standard. The platform provides two front ends; a patient facing smartphone app and a healthcare professional facing dashboard that is used inside three different hospitals in Italy, Estonia and the Netherlands. The overall architecture and implementation into practice is shown in this paper.

[a] https://orcid.org/0009-0000-2331-0640
[b] https://orcid.org/0000-0002-0694-2942
[c] https://orcid.org/0000-0002-0769-0732
[d] https://orcid.org/0000-0002-0840-2915
[e] https://orcid.org/0000-0002-8844-2596
[f] https://orcid.org/0000-0003-3101-5347
[g] https://orcid.org/0000-0002-3453-1892
[h] https://orcid.org/0000-0002-2469-5535
[i] https://orcid.org/0000-0002-2402-9444
[j] https://orcid.org/0000-0001-8481-1529
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[n] https://orcid.org/0000-0002-9623-6354
[o] https://orcid.org/0000-0002-8841-6558
[p] https://orcid.org/0000-0001-5082-1112

1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnoea, cough, expectoration, exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction (Agustí et al., 2023). COPD is one of the three leading causes of death worldwide (Patel, 2024) and is one of the high-impact diseases with an increasing prevalence, mortality and morbidity, with a high burden of disease because of deterioration of symptoms and highly prevalent acute exacerbations. Around 65 million people live with moderate or severe COPD (PRASAD, 2020).

Many patients with COPD have comorbidities like

Lehmann, J., Wimberg, G., Autexier, S., Acebes, A., Kalloniatis, C., Lamprinoudakis, C., Giannakopoulos, T., Menegatos, A., Delvinioti, A., Pagliari, G., di Giorgi, N., Raid, J., Lekka, D., Pnevmatikakis, A., Kyriazakos, S., Kostopoulou, K. and Tabak, M.
Federated Learning in Multi-Center, Personalized Healthcare for COPD and Comorbidities: The RE-SAMPLE Platform.
DOI: 10.5220/0013149800003911
Paper published under CC license (CC BY-NC-ND 4.0)
In *Proceedings of the 18th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2025) - Volume 2: HEALTHINF*, pages 499-506
ISBN: 978-989-758-731-3; ISSN: 2184-4305
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diabetes mellitus or chronic heart failure that further increase patient burden, mortality and costs. Patients often struggle with the complex handling of the disease, especially if they have other comorbidities and therefore suffer from overlapping symptoms. Current disease management and monitoring of patients with COPD and comorbidities relies on information acquired during time-based scheduled visits when patients are usually stable, whereas the actual symptoms and changes during common daily life triggers are not quantified. As such disease management is a big challenge for Healthcare Professionals (HCPs) due to the complexity and heterogeneity of this multimorbidity and since they lack appropriate information (e.g. Real-World Data (RWD), like patient activity and symptom data, and environmental data) to predict exacerbations, tailor the disease management and treatment, and support self management.

EHealth technologies and smart tools, such as data platforms and home diagnostics allowing real-time, objective, and longitudinal monitoring at home, or virtual coaches offering coaching or personalized treatment suggestions, have a large potential to improve the health condition and quality of life of the patient and to relieve burden on HCPs, by for example preventing exacerbations. To develop eHealth technologies that offer functionalities based on Machine Learning (ML) or artificial intelligence, large datasets are necessary. However, knowledge and parameters that could be important for predicting exacerbations of COPD and comorbidities are distributed among different data sources and representations, including evidence from clinical studies, Electronic Health Records (EHRs) and RWD. To overcome the discrepancy of low resources for conducting a large study and the necessity for a large dataset, Federated Learning (FL) offers a promising solution. Smaller datasets from different hospitals can be used to train a global model with a higher robustness without transferring the sensitive medical patient data.

The RE-SAMPLE platform presented in this paper provides support for leveraging data of patients with COPD and comorbidities distributed in several places to support the HCP and patient in the management of the disease. The key contributions made by the RE-SAMPLE platform are:

1. RE-SAMPLE offers data storage, synchronisation and management of patients' data both from the hospital information systems, the patient app, RWD from wearables as well as weather and air quality RWD in order to improve patient monitoring and coaching.
2. The platform offers privacy-preserving federated learning of ML models to predict the risk of an upcoming COPD exacerbation and the quality of life of the patients.
3. The exacerbation risk and quality of life predictions and the influence of clinical, behavioural or environmental factors computed from the ML models are provided in a user interface to the clinicians at the collaborating hospitals to be used during shared decision-making.
4. The platform has been deployed in highly-secured hospital IT environments by adopting a privacy by design approach across all stages of the development life-cycle and taking into account all legal and technical requirements of the General Data Protection Regulation (GDPR).

This paper presents the technical development of the platform, describing the different components within the platform and their interplay. To this end the paper is organized as follows: Section 2 presents relevant related work on IT platforms for healthcare to provide ML-based support. Section 3 describes the architecture of the platform from a functional perspective along the data processing workflows of data ingestion, ML model training, ML model prediction and visualization for shared decision-making. Section 4 provides an insight on the privacy-by-design process of the platform development and introduced technical security and privacy measures. Section 5 provides an overview on how the platform has been deployed in production in three different hospital environments in different European countries and the challenges posed to connect to the very diverse local hospital information system environments. Section 6 concludes the paper and highlights future steps.

2 RELATED WORK

ML is used more and more in heathcare applications (Rahman et al., 2023), but there is still potential to improve the support from these systems regarding, e.g., collection and storage of data (Habehh and Gohel, 2021). So, the approach of RE-SAMPLE is particular, since we make use of clinical data from EHRs one the hand, and of RWD coming from an app, wearables and external environmental services on the other hand.

In the following, relevant applications and related projects are listed. The RETENTION project (Abdelaziz et al., 2018) has a cloud-based approach, they created a platform to support personalised interventions for patients with heart failure. It also supports ML model training and continuous monitoring of patients, but not with a federated infrastructure.

CrowdHEALTH is another example for a cloud-based approach to combine EHRs and other sources to obtain useful insights into outcomes of prevention strategies, health policies and efficiency of care (Kyriazis et al., 2019). However, the final platform was a set of different collections of data to be analysed on the cloud and had no FL approach. It thus required to extract the data from the hospitals to a central place, which hospitals are typically very reluctant to do.

One of the key aspects of the RE-SAMPLE platform is to provide close to real-time results to support the decision making during patient consultation. For example, there is an implemented system tested on multiple historical medical datasets (diabetes, heart diseases, breast cancer) (Hassan et al., 2020). However, this system does not support FL.

There are also projects with very similar objectives introducing a FL platform (Lampropoulos et al., 2021). This project focuses on patients with cancer and their healthcare providers, aiming to enhance the quality of life for patients by offering personalized intervention recommendations and support. Even if this also used different data sources, a difference to RE-SAMPLE is that the HCPs only had access to the data stored in the edge node, while in RE-SAMPLE the technical challenge was to allow both access to the data in the edge node as well as to data on the cloud which belongs to the disease self-management app used by the patients in the different hospital sites.

There are other works on predicting COPD exacerbations that do not use ML (Adibi et al., 2020). To our knowledge, there is no FL platform to predict COPD exacerbations.

However, there are deep learning approaches regarding COPD. One approach for prediction of COPD exacerbation is based on a dataset with 94 patients and frequent data (Nunavath et al., 2018). A Long Short-Term Memory (LSTM) is trained for classification with three classes (stable, significant deterioration, urgent need for follow up) achieving a good accuracy, but the prediction is only for a couple of days in advance. The model is more accurate for predicting the stable state. Moreover, LSTMs are used to study COPD disease progression based on the four GOLD standard levels (Tang et al., 2018). While extracting data from clinical notes, the irregular time visits in the data are handled.

3 ARCHITECTURE

A key idea of RE-SAMPLE is to enrich the patients' EHRs with RWD like weather and air quality data, answers to questionnaires and activity and sensor data.

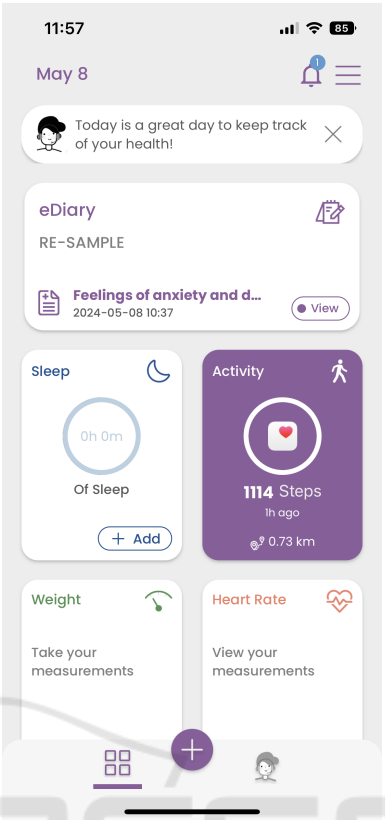

Figure 1: Patient smartphone app.

To this end, the patients are equipped with a wearable device capable of measuring activity data like the number of steps or the heart rate. Additionally, a smartphone app (see Figure 1) is used to fill-in questionnaires and to inform the patient. In contrast to clinical data, the RWD is collected continuously in-between the patients visits to the hospital. This allows the ML systems to take into account a more holistic picture of the patients' state. The data from both the wearable device and the patient smartphone app is synchronized to the centralized Healthentia cloud, while the clinical data remains at the hospital. Since different hospitals are involved, this means that the data is distributed. The platform architecture needs to facilitate data homogenization between these sources and combine it into a standardized data model — ensuring that the features as well as their encoding are the same between the hospitals, which may be using completely different software solutions and data representations internally. Further, datasets that are uniform across hospitals need to be created and preprocessed to allow for FL. RE-SAMPLE uses the Flower framework for the implementation of the FL (Beutel et al., 2020). Since sensitive patient data is involved, highest privacy standards need to be met resulting in a GDPR compliant privacy-by-design sys-

tem. To achieve this, the platform uses an edge computing architecture, with every pilot site running an edge node. These edge nodes run the components, which are docker containers, allowing for high portability and security. Each edge node is physically hosted in the hospitals' premises and is under the control of the pilot sites' ICT Departments. Due to the type of data available in each single node, only authorized personnel can have access to the VMs and perform installations or work on the datasets. In addition to the edge nodes, a single orchestrator node manages the FL and authorization process. The components of the RE-SAMPLE platform belong to one of the three parts:

- the **Health Data Hub** (HDH), consisting itself of four components which together allow for data ingestion and storage,
- the **ML components**, consisting of five edge node and one orchestrator node components, managing ML training and the production of ML results,
- the **Local Data Connector** (LDC), enabling the dashboard to display sensitive hospital data if accessed from within a secure hospital network or connection.

The architecture is visualized in Figure 4 on p..

3.1 Workflows

3.1.1 Data Ingestion

In RE-SAMPLE, patient data from the EHRs and RWD from Healthentia is ingested into a central storage component called the **Clinical Data Repository (CDR)**. It contains the entire patient data, including any ML results which are produced for the patient. The only data not in the CDR is the air quality and weather data, which is collected in a separate component and added on-demand to the patient data. The CDR is a standardized, FHIR-based (Bender and Sartipi, 2013) database storing data as interoperable resources. Built with Java and MariaDB, it runs in a separate docker container and provides a REST API for advanced searches, although external access is restricted in production. The HL7 FHIR **Implementation Guide (IG)** customizes the standard FHIR resources to meet project needs, using semantics to ensure data is correctly formatted. IGs are formal definitions for data exchange and, in this project, document and validate the use of the HL7 FHIR standard internally. The **Clinical Data Repository API (CDR-API)** is a RESTful API that follows the OpenAPI specification and handles data ingestion and export for the CDR, following predefined rules in the Implementation Guide. Built in Java, it validates and models the data using the RE-SAMPLE-model code library. The CDR-API is the entry-point for patient data into the CDR. Hospitals provide data stored in their EHRs directly to the CDR-API via scheduled periodic POST requests. The OpenAPI specification[1] was used to allow hospitals to easily produce clients which export their data to the CDR-API. Activity, sensor and questionnaire data from Healthentia is requested from Healthentias API with a dedicated component called the **Clinical Data Repository Synchronizer (CDR-SYNC)**. During patient creation in the CDR, it links the patient to their external Healthentia ID and syncs activity and questionnaire data via scheduled tasks. The CDR, IG, CDR-API and CDR-SYNC together form the **HDH**.

Air quality and weather data for the locations of all patients in the CDR are continuously collected by the **ML Environmental Data Manager**. In order to use the collected data for ML purposes, the **ML Data Manager** retrieves it periodically from the CDR-API and ML Environmental Data Manager and splits it into different training and inference datasets. The datasets have classification and regression targets and contain a varying number of features as input — depending on how many patient hospital visits are available in the hospitals EHRs.

3.1.2 ML Training

When the ML Data Manager refreshes the patient data from the CDR-API, it creates the new datasets for ML training as well as inference requests datasets, adding aggregated environmental data in the process. If it finds that new data has been added since the last synchronization, it triggers ML training. When ML training is triggered, any datasets that are not suitable for training (for example because of too few data-points or missing examples for a class in classification) are filtered out. The ML Data Manager informs the **ML Training Manager** of the suitable datasets with recent changes. The ML Training Manager then initiates both local and federated ML training for a predefined set of ML models for each training target. The process for local training is that the ML Training Manager requests the dataset from the ML Data Manager. It then runs missing value imputation, using a mean-matching scheme (Morris et al., 2014) wherever possible. The dataset is then normalized, ML models are iteratively fitted on it, performance metrics are calculated and if the metrics are above a threshold, the model is sent to the **ML Model Manager**.

[1] https://edge1-db.test.re-sample.eu/clinical-data-repository-api/swagger-ui/index.html#/

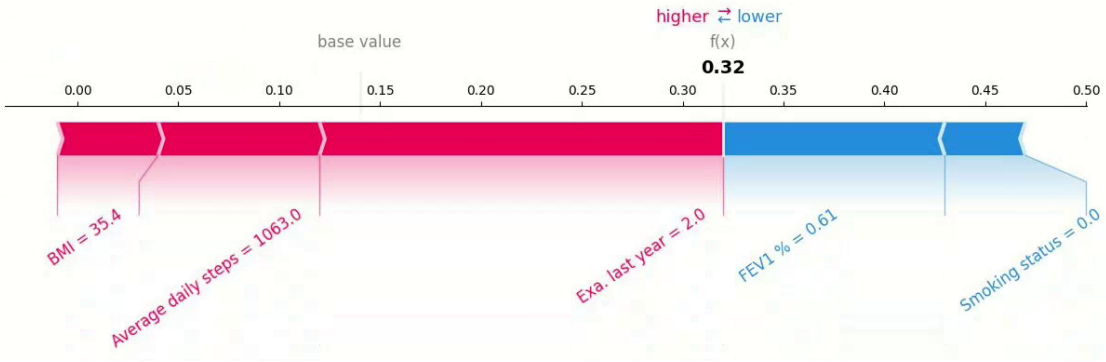

Figure 2: Prediction explanation.

3.1.3 ML Results

For federated training, the process is similar but also involves the **Federated Learning Coordination**, which is located in the orchestrator node at the secured coordinating central server outside of the hopistals. Instead of simply starting training like in the local case, the ML Training Manager submits a request to the Federated Learning Coordination to start training of a dataset. If other edge nodes also have this dataset available, the Federated Learning Coordination initiates federated training and starts the FL server. The ML Training Managers on all edge nodes periodically request what dataset and model should be trained next from the Federated Learning Coordination. If there is any to start, the ML Training Managers will each start a FL client and request and impute the dataset from their respective ML Data Managers like in the local case. What is different, however, is that the ML Data Manager will apply differential privacy (Dwork et al., 2014) to the dataset for additional privacy protection of the patients' data. The FL clients all fit their model on the dataset and send the parameters to the server who averages them and sends them back. This process continues for a specified number of training rounds. Finally, the FL clients calculate performance metrics with their own test data and send the jointly trained model to the ML Model Manager.

The **ML Results Manager** periodically retrieves inference requests for the latest patient data from the ML Data Manager to calculate updated ML results. ML results include predictions for every data target as well as accompanying SHAP values (Molnar, 2020) to explain it. In addition, counterfactual predictions are produced for classification targets that show what changes in the patient data could produce a different prediction outcome. For this, only the data values that are actually changeable are considered, such as, e.g., activity data or the body mass index. The ML Results Manager also calculates different simulated predictions, for which it changes a set of patient data in a predefined way in order to fully convey what effect these changes are predicted to have on the target variable value, visualized in Figure 3. All ML results are submitted to the CDR-API and stored in the HL7 FHIR CDR, where it can be retrieved for the user interface used by HCPs. Figure 5 shows how the predicted target values change over time within the dashboard.

In addition, Figure 2 shows the plot of SHAP values for the latest target value prediction, which indicates for all input variables with their current values how much these increased (blue values) or decreased (red values) the computation of the predicted score. This provides a mean for the HCPs to assess which and how values of that specific feature contributed to the prediction.

3.1.4 Use for Shared Decision-Making

The ML results contain a lot of information about the patients. As such, they are sensitive data from a privacy perspective that cannot be disclosed to external systems. To still be able to display them alongside the less sensitive activity and questionnaire data, the LDC was introduced. It is a software component used in hospital edge nodes to give the Healthentia web portal access to patient clinical data. This access is only available within the hospital's secure network, as data cannot leave the hospital due to strict pri-

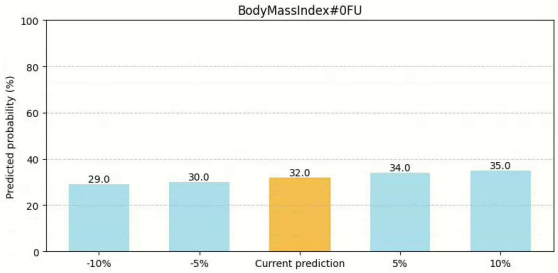

Figure 3: ML simulations.

vacy policies. The LDC allows the clinical dashboard to display hospital clinical data alongside Healthentia's data, formatting it for easy visualization in the Healthentia portal. It also retrieves ML results to be displayed in the dashboard.

4 RE-SAMPLE PLATFORM SECURITY AND PRIVACY

In order to ensure patient data security and privacy, the platform was designed using a privacy by design approach (Hes and Borking, 1995), meaning that privacy was taken into account across all stages of the development life-cycle to ensure that the sensitive medical data is protected. Furthermore, during the design phase all legal and technical requirements of the GDPR were considered. Indicatively, it was ensured that GDPR principles like the data protection (purpose limitation, data minimisation, accuracy, accountability), the lawfulness of processing, and the user consent, were fully satisfied. In order to accomplish this a gap analysis was performed on the platform to identify potential non compliance issues with the GDPR, and following that a data protection impact assessment was carried out to identify potential impact of a privacy violation incidents on the data subjects. Finally, a thorough risk analysis was conducted, in order to estimate the probability of occurrence and possible consequences of a security incident for the platform. Through the combination of the aforementioned procedures a list of both organisational and technical measures, such as patient anonymity via distinct IDs per component, authentication, application hardening, access control, and logging, were implemented to minimize security or privacy incidents.

One of the key aspects of this methodology was to identify the security domains, in order to ensure adequate measures for their communication. Three security domains were identified: the hospital network, the orchestrator node and external domains. The hospital network houses the majority of the components and is isolated in it's own docker network with only the CDR-API having a connection to the hospital information system, which supplies its data using a secured API call. The LDC exposes the data to the clinician dashboard only when a secure connection is established. The orchestrator node houses the federated learning coordination component for the joint training of the ML models and is secured by a keycloak[2] based authentication/authorization server. Before initiating a request a component must first authenticate using the OpenID Connect (OIDC) specification and then get an authorization token using OAuth 2.0. The token is then sent to an NGINX reverse proxy, that forwards the token to the keycloak instance that then allows access to the endpoint.

The platform's security scope ensures that the edge node operates within a secure hospital network, limiting physical access to aggregated data in the HDH. Within the edge node, components have restricted access to relevant data, with identifier mappings stored in a local database.

5 DEPLOYMENTS IN PRODUCTION

The platform is currently up and running in three collaborating European hospitals, where it is used during an interventional clinical study. The data used to train the machine learning models comprise retrospective data from approximately 1,000 patients and prospective data collected during the observational study from almost 200 patients. Hospitals typically store historical data in EHRs or study databases. In the RE-SAMPLE project, some hospitals have created data pipelines that automatically retrieve clinical data from internal hospital information systems. In one hospital, clinical data such as blood measurements and inpatient access information can be directly extracted from structured data sources, while spirometry measurements, six-minute walking test results, and other relevant details can be extracted from pseudonymized clinical reports via text mining. One hospital updated their internal system using forms to manually ingest the data by implementing new forms for the study data to send them to the edge node. The third hospital is working with HiX Digital Health Services[3] and has built a pipeline to automatically transform the data from the hospital information system into the correct uniform format to send the clinical data to the CDR-API. In all three collaborating hospitals, prospective patient data are dynamically collected following the common RE-SAMPLE data model, with scheduled daily updates that make it available to the data ingestion components of the RE-SAMPLE platform. The HCP facing dashboard is visualized in Figure 5, and the patient-facing smartphone app is shown in Figure 1.

[2]https://www.keycloak.org/

[3]https://www.chipsoft.com/en

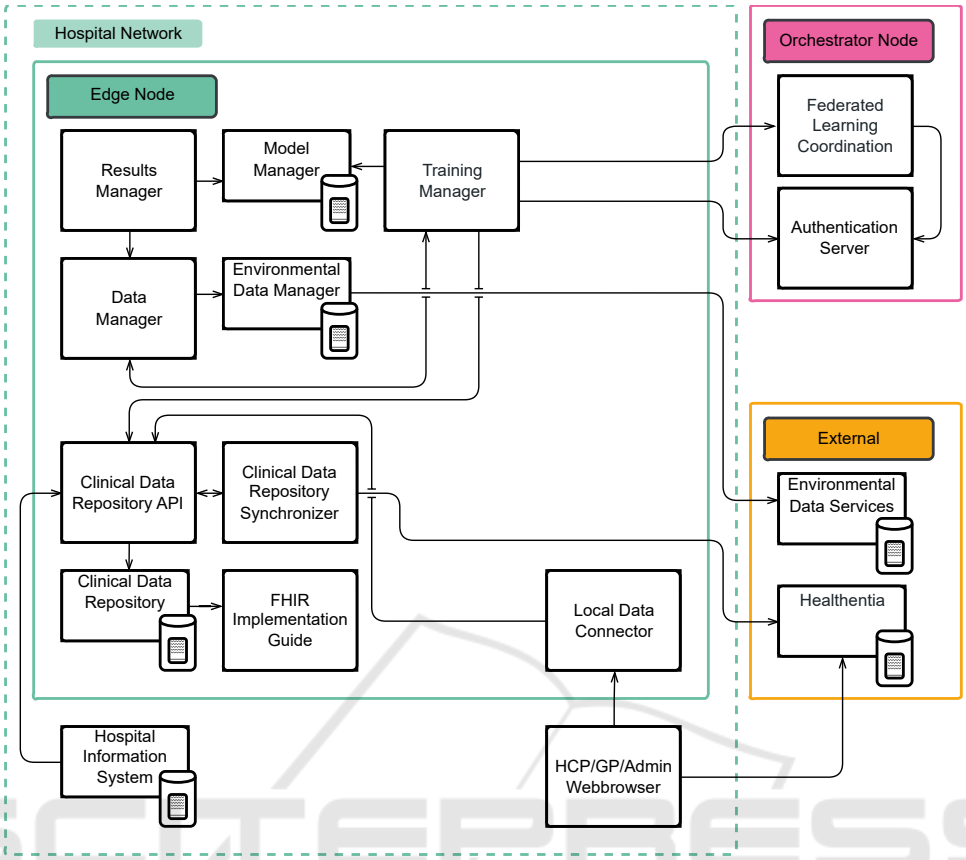

Figure 4: Architecture diagram.

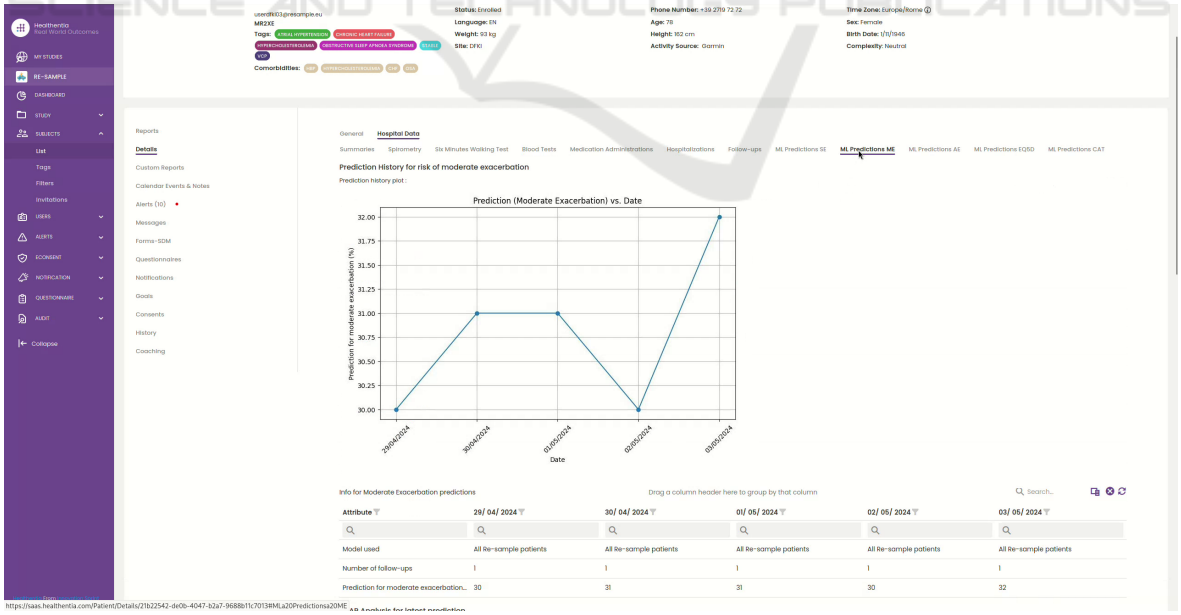

Figure 5: Screenshot of the clinical dashboard.

6 CONCLUSION

In this paper, we described the RE-SAMPLE platform that can be setup in multiple hospitals for federated ML model training and to generate personalized treatment suggestions for patients with COPD and comorbidities. It enables data storage, synchronisation and management for patient monitoring for use in shared-decision making for patients with COPD and comorbidities. We described the implemented architecture of the up-and-running system and the workflows.

To protect patient privacy, we implemented robust security measures and compliance with healthcare data protection regulations. Our federated learning approach ensures patient data remains secure within each hospital's environment. All components are open source.

Future work will include the analysis of the performance of the ML models – in particular comparing locally trained models to models trained by federated learning – and the importance of the predictors especially for COPD exacerbations.

ACKNOWLEDGEMENTS

This paper is part of a project that has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 965315.

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