



ONCORELIEF

**ENHANCING CANCER PATIENT'S WELL-BEING AND HEALTH STATUS
IMPROVEMENT FOLLOWING TREATMENT USING AI METHODS**

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Agenda

Project overview

Operation description

System architecture & key features

Data analytics & AI Engine

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Current status & next steps

Project overview

13 partners from 7 countries

- Belgium
- Cyprus
- Germany
- Greece
- Italy
- Portugal
- UK



Project overview - Vision

ONCORELIEF is a 36-month action that has leveraged, but also methodologically faced technical challenges related to the following key driving factors:

1. Improved cancer survival rate
2. Proliferation of smartphones
3. Increased importance of health-related quality of life (HRQOL),
4. Huge volumes of data from clinical, administrative, imaging and omics sources
5. Incoming flood of electronic patient reported outcome and experience measures (ePRO), patient internet activities, sensors and monitoring data and
6. Rapid advances in Artificial Intelligence (AI) and Big Data analytics.

Thus, a huge unprecedented opportunity was formed to create intelligent healthcare-patient services and tools to manage the health status and wellbeing of cancer patients at all levels.

Project overview

ONCORELIEF project aims to deliver a framework that consists of three main sub-systems:

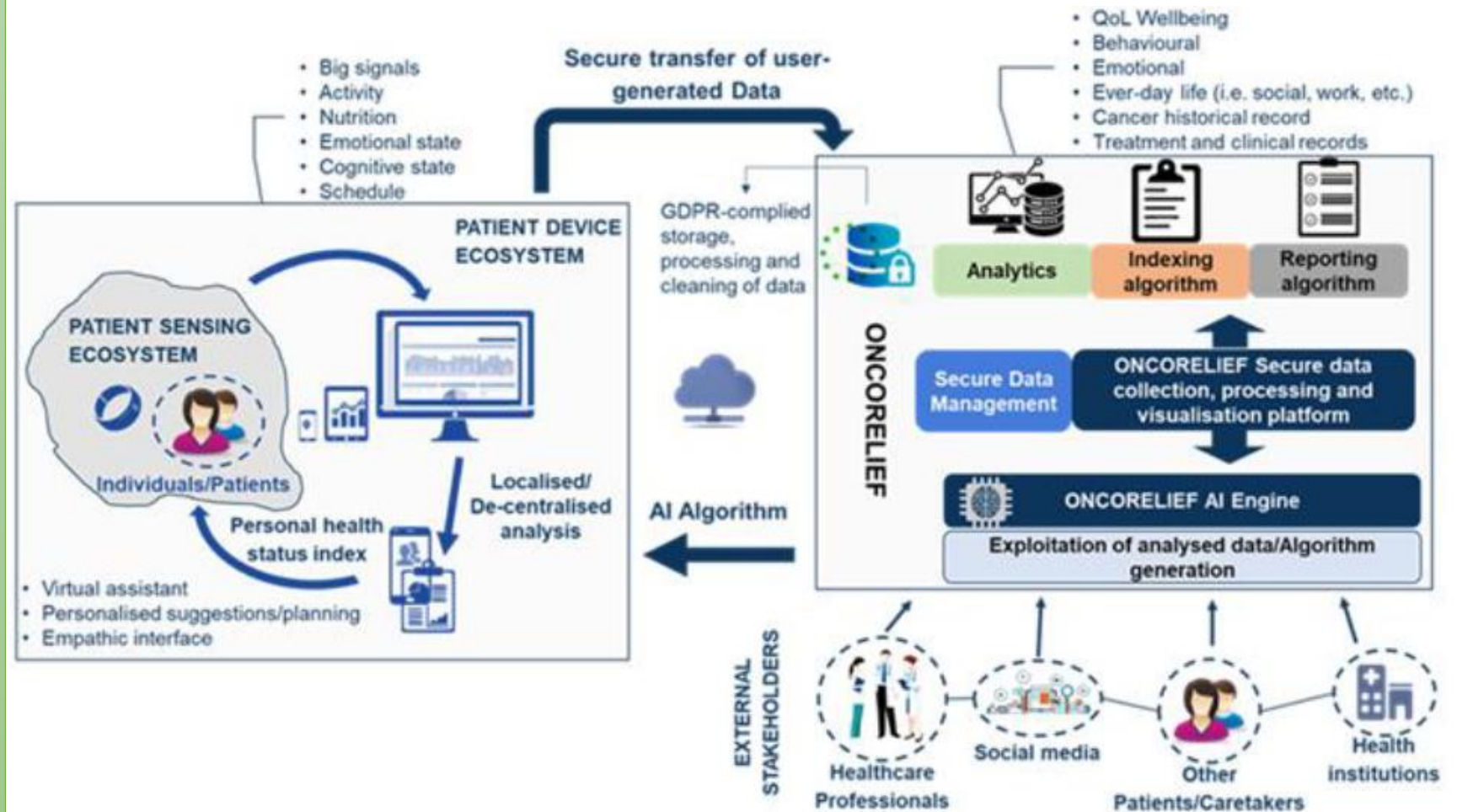
1. A **Back-end data platform** where data are securely collected from heterogeneous sources, anonymized, annotated and stored, etc.,
2. An **AI Engine** built on top of the Back-end platform, which consumes and analyses data, extracts important features, produces meaningful AI models and updates them accordingly, produces correlations, etc.,
3. A **downloadable application (ONCORELIEF Guardian Angel)** available for portable devices, connected both with the ONCORELIEF platform and the patients' sensing devices. It runs locally and uses models produced by the AI Engine to extract insights on the patient life and condition and make suggestions.
4. An **HCP Web app**, allowing the HCPs to monitor patient data as well as evaluate and decide on the proposed suggestions

Project overview

- The GA sends data back both for research-related reasons (another source of big data) and for computation offloading reasons (AI Engine not powerful enough on the mobile phone).
- Some of the models trained in the Back-end are uploaded to the GA application in order to locally process, streamline and analyze individual data, and to generate the **QoL (Quality of Life) index**, recommendations and warnings for the patients using the application.
- Extensive research has been performed in order to build a scientific formula, that calculates the QoL index that is based on measurements of vital signals from the patients' wearable devices, the patients' record as well as from the responses in specially designed questionnaires.

Project overview – high level architecture

- Detachment of design, development, execution and HPC empowered big data analysis processes
- Interoperability among all components involved and stakeholders, emphasis on security and privacy
- Standardized interfaces such as smart algorithms and AI elements of self-learning so that reusability of core system resources is supported
- Appropriate data models and communication protocols, allowing heterogeneous and sensitive information to be exchanged between the various components in a harmonic and secure way.



A simplified description: Patient

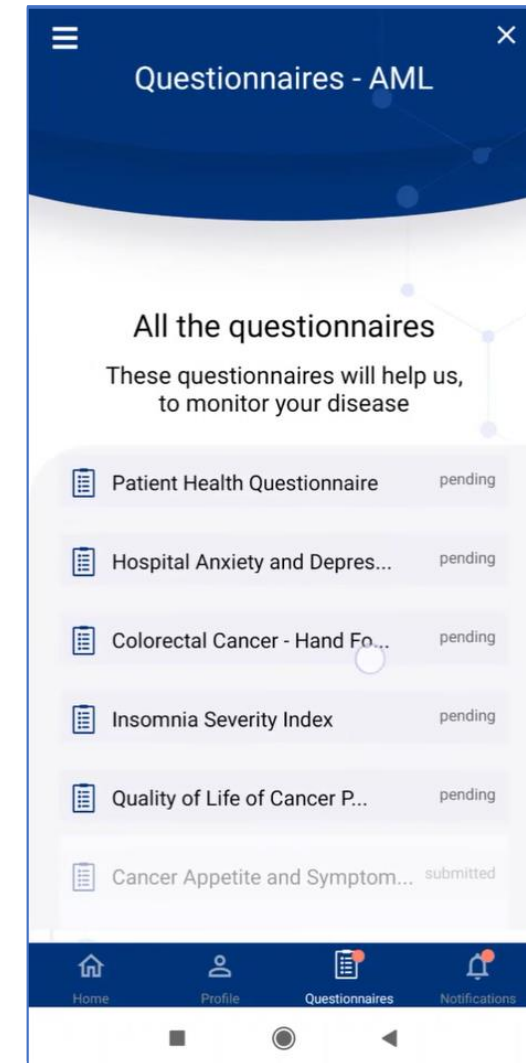


The patient:

- Gets enrolled by a clinical site and receives a wearable device that constantly monitors vital signs
- Downloads the Guardian Angel app, credentials are provided by the clinical sites
- At specific time intervals, answers to a set of Questionnaires applicable to her/his cancer type, through the GA app



SmartKo
device by
MCS Data Labs



A simplified description: ONCORELIEF Back-End



In the ONCORELIEF Back-End:

- The **QoL** index is calculated based on the Questionnaire responses, vital signs and other patient medical data
- The **AI Engine** proposes to the Healthcare Professional (HCP) **patient personalized suggestions**, specific to any reported undesirable conditions, for the cancer type of the patient
- The **suggestions are prioritized** based on the expected* positive impact on the QoL index

() based on the extended retrospective clinical data and the continuous retraining of the AI models*

A simplified description: Healthcare Professional



The Healthcare Professional (HCP):

- Uses the **ONCORELIEF HCP Web app** to monitor patient data
- Gets notified on the patient-specific suggestions proposed by the AI Engine
- Selects, modifies and proposes suggestions to the patient, personalizing them accordingly
- Receives alerts in cases of severe QoL index deteriorations

The screenshot displays the ONCORELIEF HCP Web app interface. The top navigation bar includes the ONCORELIEF logo and a breadcrumb trail: Dashboard > Patients > Patient > Questionnaire. A dark sidebar on the left contains navigation options for DASHBOARD and PATIENTS. The main content area is titled "Insomnia Severity Index" and contains three sections of questions, each with five radio button options: none, mild, moderate (selected), severe, and very severe.

1. Difficulty falling asleep

- none
- mild
- moderate
- severe
- very severe

2. Difficulty staying asleep

- none
- mild
- moderate
- severe
- very severe

3. Problems waking up too early

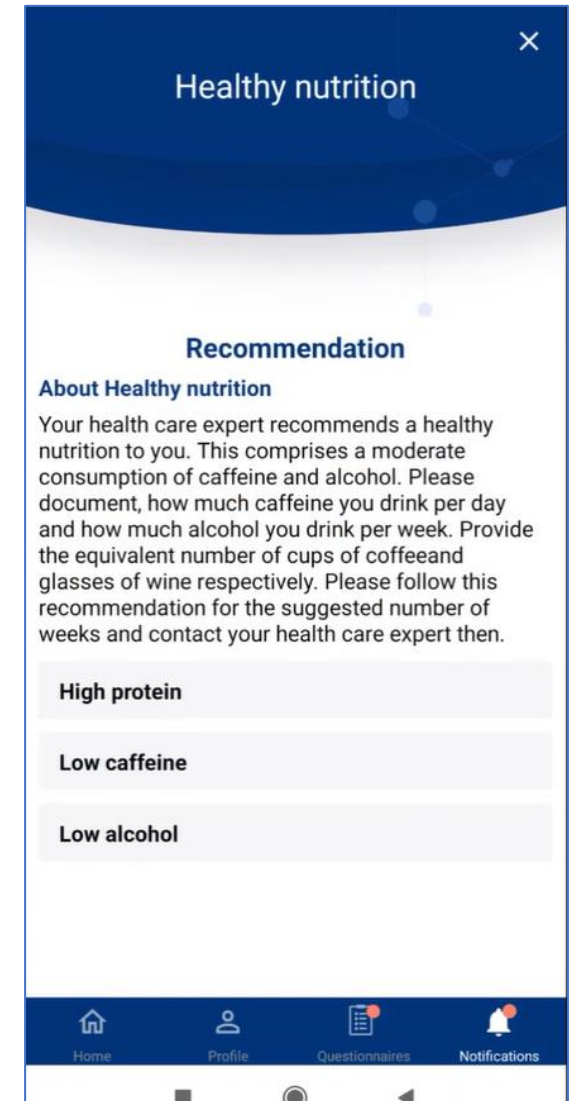
- none
- mild
- moderate
- severe
- very severe

A simplified description: Back to the Patient



The patient:

- Gets enrolled by a clinical site and receives a wearable device that constantly monitors vital signs
- Downloads the Guardian Angel app, credentials are provided by the clinical sites
- At specific time intervals, answers to a set of Questionnaires applicable to her/his cancer type, through the GA app
- Gets notified on the proposed suggestions
- May provide feedback on the suggestion. However the GA app cannot be used for communication with the HCP.

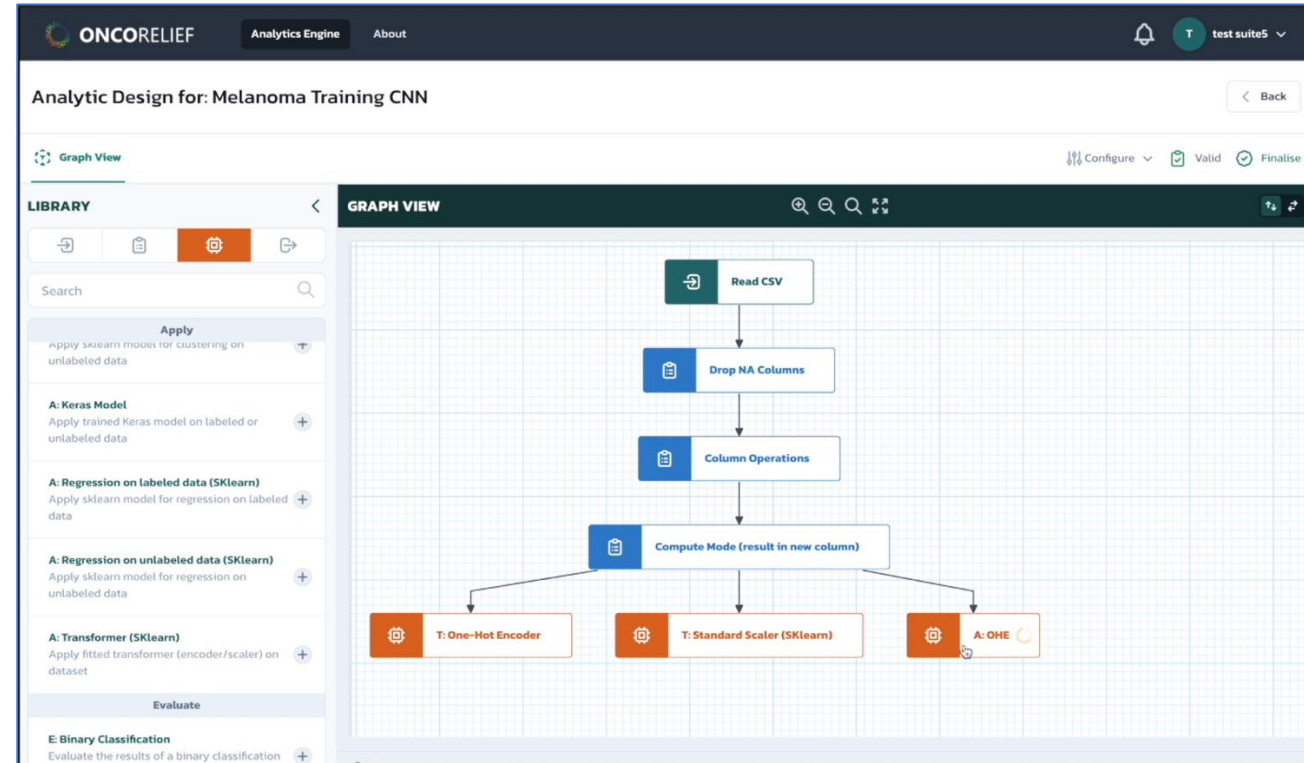


A simplified description: AI Researcher



The AI Researcher:

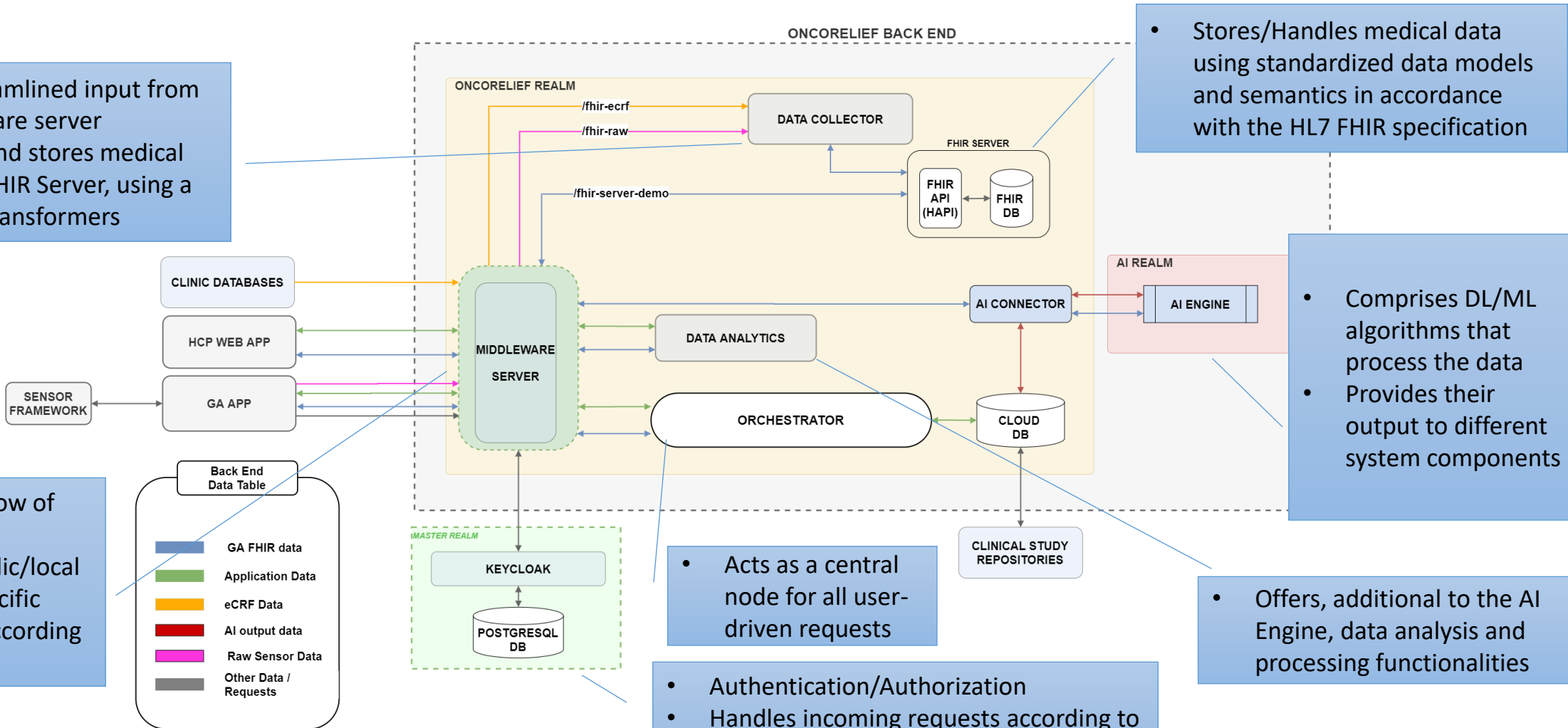
- Uses the Analytics Engine environment, developed from partner Suite5, to define and run AI workflows, for e.g. implementing a RNN on streaming vital signals data
- The environment allows the researcher to retrieve, process, experiment and analyse data and then export the obtained results and trained models back to the ONCORELIEF Platform



System Architecture

- Handles streamlined input from the Middleware server
- Transforms and stores medical data to the FHIR Server, using a set of FHIR Transformers

- Directs the flow of data
- Provides public/local access to specific endpoints, according to policies



- Stores/Handles medical data using standardized data models and semantics in accordance with the HL7 FHIR specification

- Comprises DL/ML algorithms that process the data
- Provides their output to different system components

- Acts as a central node for all user-driven requests

- Authentication/Authorization
- Handles incoming requests according to access rules, user groups and roles

- Offers, additional to the AI Engine, data analysis and processing functionalities

Sensor data & algorithms

SmartKo device by MCS Data Labs

Sensor data	Algorithms
Heartrate via photoplethysmography (PPG)	Heartrate variability (HRV)
Oxygen saturation (SpO2) via PPG	Stress tracker
Temperature (Skin, Environment)	Sleep tracker
1-channel-ECG (discrete measurement via fingerprint)	Respiratory rate
Barometer (air pressure)	
Hygrometer (air humidity)	
Air quality	
9 Axis IMU (step count)	

Key features

Interoperability

Back-end receives and stores medical data in FHIR format to ensure future interoperability

Localization

Currently available languages (English, German, Italian). Others can be easily supported.

Di-identification

- The Bank-end does not store patient identification data
- Backtracking can only be achieved with a specific key held by the clinical sites

Suggestion schema

A fully parametrized suggestion schema has been designed (lead: Fraunhofer) that allows for detailed, personalised suggestions

Key features

Patient monitoring

To facilitate clinical practice, all HCPs in the same clinic and for the same cancer type, can monitor a patient. But only designated HCPs can make suggestions.

Patient enrolment process & eCRF data transfer

- A flexible enrolment process has been designed, allowing the HCPs to upload patient data in stages
- Data is transferred in eCRF format, using an sFTP server deployed over a VPN tunnel

Questionnaires & Suggestions

- Definitions of Questionnaires and of Suggestions are not hard-coded
- Additions/modifications can be easily done through respective spreadsheets, in all supported languages
- They are automatically transformed into FHIR Resources

ONCORELIEF Data Model

According to the adopted ONCORELIEF Data Model, the data are collected from different data sources (Big Data), are transformed to FHIR format and stored to the Back-end storage. There are three different data sources:

1. Measurements from the wearable sensors
2. Data from questionnaires answered by the patients
3. Data from the medical record of the patient

The first case provides dynamic data (time dependent), while the last two provide static data (that could be updated when they change).

About 300 different patients, both for colorectal cancer (CRC) and Acute Myeloid Leukaemia (AML), are expected to provide the training data

Quality of Life (ONCORELIEF index)

- **Depends on**

- Physical aspects
- Psychological aspects
- Social aspects
- Spiritual aspects

- **Input**

Wearables	Questionnaires
Heart rate	PHQ9 (depression)
Respiration	HADS (anxiety and depression)
Temperature	HFS (Hand-foot syndrome)
Oxygen saturation	ISI (sleep quality)
...	...

- **Output**

- Quality of Life index (0 – 1000)
 - 901 – 1000: Very Good
 - 801 – 900: Good
 - 601 – 800: Faulty
 - 401 – 600: Poor
 - < 400: Very poor

Identified needs

AML	
Category	Included Needs
Distress	<ul style="list-style-type: none"> • Depression • Anxiety • Other needs
Psycho-physiological	<ul style="list-style-type: none"> • Sleep • Fatigue • Lack of sexual interest • Other needs
Physical symptoms	<ul style="list-style-type: none"> • Sore mouth • Hair loss • Weight loss • Other needs

CRC	
Category	Included Needs
Distress	<ul style="list-style-type: none"> • Depression • Anxiety • Other needs
Psycho-physiological	<ul style="list-style-type: none"> • Fatigue • Other needs
Physical symptoms	<ul style="list-style-type: none"> • Colitis • Appetite Loss • Peripheral neuropathy • Weight • Hand-Foot Syndrome • Other needs

QoL Index

- ONCORELIEF visualizes current health and WB with a personal **ONCORELIEF QoL Index, a complex scientifically calculated number (indicator) from 1 (low) to 1,000 (high)**.
- It is based on the specific person (body), cancer type and peculiarities (disease); health literacy and physical symptoms such as pain, etc. (symptoms); how they feel and overall mental health such as anxiety, depression, positive and emotional distress or negative affect, etc. (feelings); and how they live and work, including social capital, life satisfaction and socio-economic factors, exercise, nutrition and sleep (lifestyle).
- The ONCORELIEF QoL Index moves up or down in real-time, depending on how body, symptoms, feelings and lifestyle change.
- When tracked over time, it will offer a good indicator of how the person's health and wellbeing is evolving.

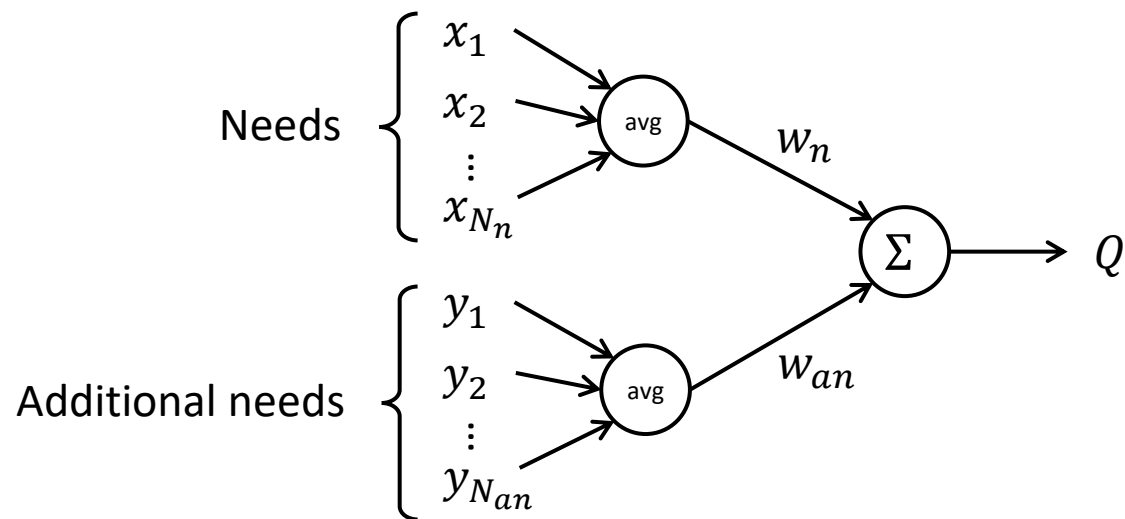
Quality of Life (ONCORELIEF index)

- Baseline QoL index

- $Q = w_n Q_n + w_{an} Q_{an}$, w_n : initially set to 80%, w_{an} : initially set to 20%

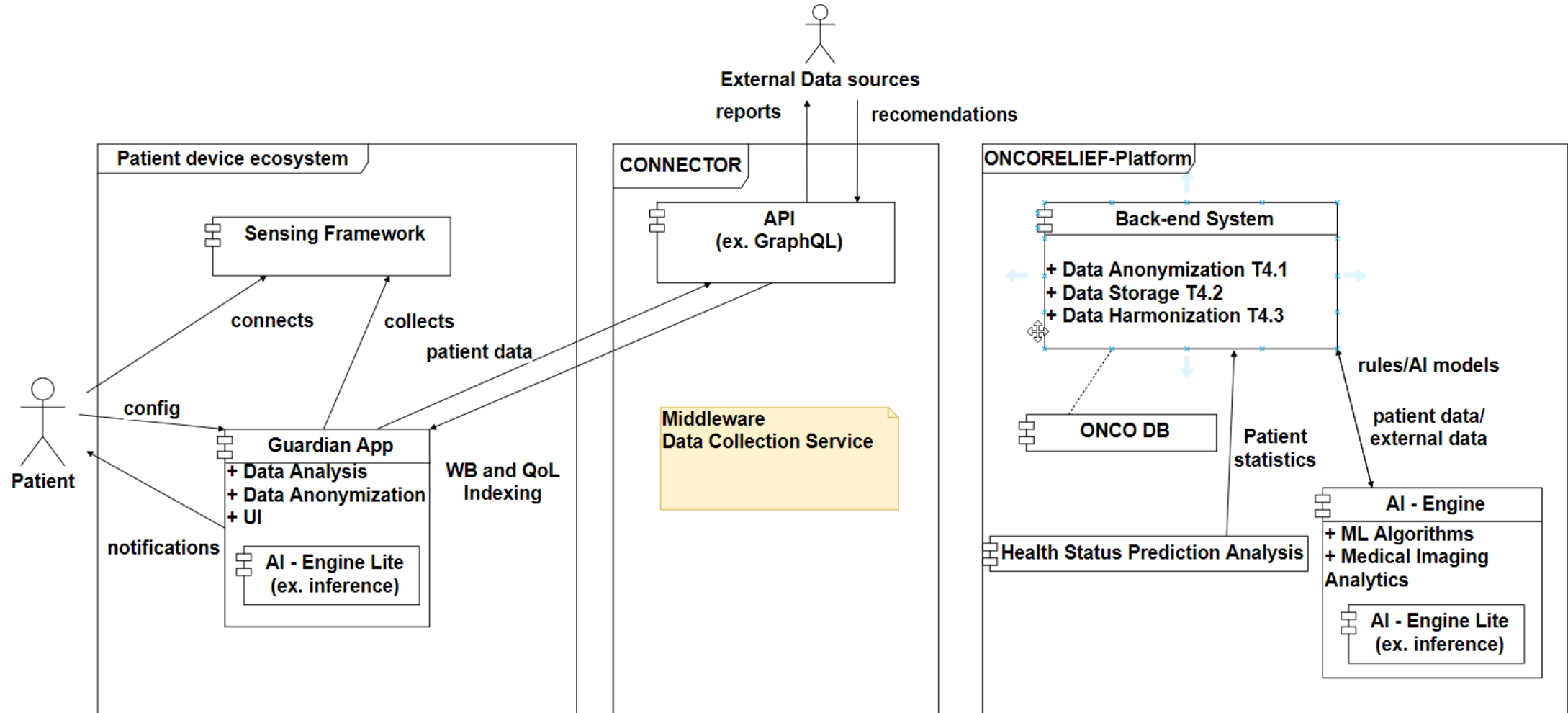
- $Q_n = \frac{1}{N_n} \sum_{i=1}^{N_n} x_i$, x_i : Needs

- $Q_{an} = \frac{1}{N_{an}} \sum_{i=1}^{N_{an}} y_i$, y_i : Additional needs



- The **baseline** QoL has been currently implemented based on questionnaire data

AI Engine



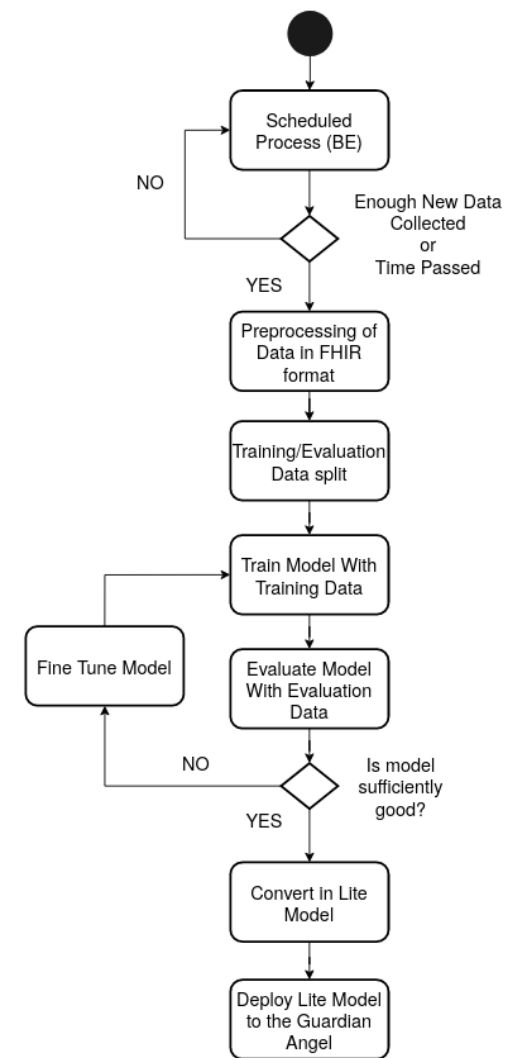
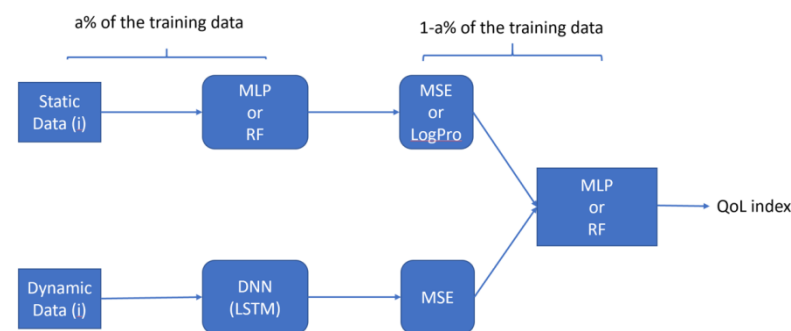
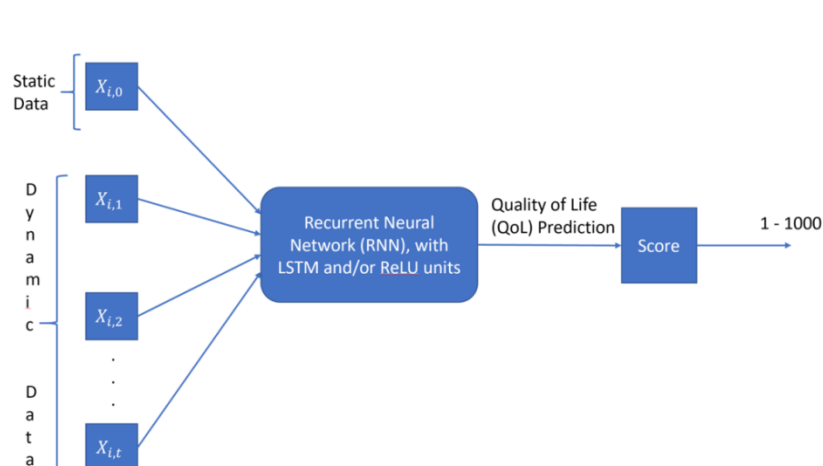
Building the AI Engine

- AI Engine
 - Off-Line
 - Data collection and preprocessing
 - Training set creation
 - Model training
 - Model evaluation
 - On-line
 - Input data transformation
 - Trained ML model
 - Output (WB, QoL index)

Proposed ML Algorithms and Architectures

- Next steps: Machine learning-based

- RNN architecture
 - Combines static and dynamic data
 - Uses recent historical data in a specified time window
- Ensemble learning architecture
 - Different models for static and dynamic data
 - Static: MLP, RF, etc.
 - Dynamic: LSTM
 - Combines the outputs of the two models
- Training using baseline QoL as ground truth
- Personalized to each patient



AI Engine - Services

- AI Engine allows to design and configure an analytics pipeline for selected ML/DL (baseline/pre-trained) algorithms.
- The expected input of the pipeline is explicitly defined and may range from batch data stored in storage areas to near real-time data directly sent to trigger the analytics execution.
- The desired output can be provided in two different ways:
 - (a) as a visualization that can be sent to the HCP,
 - (b) as raw data that can be retrieved from or published to another component.
 -
- The Services Bundle in the AI Engine in the Back-End platform consists of:
 - **The Analytics Configurator** (provides a user interface that guides the creation of complete data analysis pipelines)
 - **The Analytics Execution Service** (executing data analytics jobs)
 - **The Visualization & Reporting Engine** (gives the ability to visually gain insights from specific health data elements)

The Pilot Study

- Study Design by IRST IRCCS, Meldola and Universitätsmedizin Mainz.

Objectives:

Primary

To investigate feasibility of ONCORELIEF system and use by:

- 1) Patient and healthcare professional (HCP) satisfaction with regard to the ONCORELIEF System (MAUQ Questionnaire)
- 2) To assess engagement of patients with ONCORELIEF (e.g. % patients recruited, answering regularly etc.)

Secondary

- 1) To describe patients' Quality of Life (EORTC QLQ C30 Questionnaire)
- 2) To describe patients' well-being (OR Index)

Methodology:

Prospective, interventional, non-pharmacological pilot study designed to evaluate the feasibility of the ONCORELIEF system in real-life clinical settings.

Pre-Pilot (feedback and issues to improve system) and Pilot Phase (75 AML and 150 CRC patients, each participant engaged for 6 months)

Use of ONCORELIEF system

By patients: GA APP (asked to complete questionnaires every 4 weeks), SWD (collects sensor data)

By HCP /doctors: Web APP (can check questionnaires and WB Index, can send suggestions)

Selection Criteria

The main focus of ONCORELIEF has been placed on **two different types of cancer**. The **selection criteria** have been:

- a) **high incidence**, thus covering a wider need in the general patient ecosystem,
- b) **avoid low survival rate**, thus allowing applicability for an improved level of wellbeing, quality of life and health-status, especially for Pilot and model training purposes
- c) **adequate time for “before” and “after” treatment**, therefore leveraging the balance between data availability and life expectancy,
- d) **adequate amount of data for analysis** , therefore enabling substantially diverse datasets that would be adequate for training the models
- e) **adequate biologic diversity** to broaden applicability beyond the scope of the Pilots
- f) **cross-gender**, thus focusing on a wider patient audience without gender discrimination or limitation.

Based on the above, **ONCORELIEF** project and its Pilots will focus on **Acute Myeloid Leukaemia (AML)** and **Colorectal cancer (CRC)**.

The Pilot Study

Preparatory work before Pilot Study start, included

1. **Determine patient needs** (at post-treatment stage) in order to choose the appropriate questionnaires that ask the right questions
2. **Find and select questionnaires** that are both validated and available in the three languages (English, Italian, German)
3. **Design study and write study protocol** (for both clinics): objectives, procedures, methodology
4. **Submit ethical application**, to the authorities in Italy and in Germany. Address issues raised by the ethical committees concerning: Medical devices laws (EU- MDR - Medical Device Regulations), data security, benefits and burden for patients.
5. **Register with clinical studies registries** (e.g. WHO; in Germany via the DRKS)
6. **Set up Data Sharing Agreement** (see GDPR) for all project partners to sign
7. **Train HCPs** on devices and how to engage patients with this tool.

Selection of Patient Need Questionnaires

Cancer Type	Patient Need	Questionnaire
AML	Anxiety	HADS (Hospital Anxiety and Depression Scale)
AML	Depression	PHQ-9 (Patient Health Questionnaire-9)
AML	Fatigue	BFI (Brief Fatigue Inventory)
AML	Hair loss	<i>No validated questionnaire available</i>
AML	Lack of sexual interest	EORTC-SHQ-C22
AML	Sleep Problems	ISI (Insomnia severity index)
AML	Sore Mouth	EORTC-SHQ-OH15
AML	Weight loss	Part of EORTC-QLQ-C30
CRC	Anxiety	HADS
CRC	Depression	PHQ-9
CRC	Fatigue	BFI
CRC	Appetite Loss	Part of EORTC-QLQ-C30
CRC	Colitis	EORTC-QLQ-CR29
CRC	Hand-foot syndrome	Part of EORTC-QLQ-CIPN20*
CRC	Peripheral Neuropathy	EORTC-QLQ-CIPN20*
CRC	Weight changes	Part of EORTC-QLQ-C30

*testing phase III – in development

In addition: Well-Being with Questionnaire WHO-5

The Pilot Study

Procedures:

- Eligibility: Inclusion and Exclusion Criteria
- Patient Recruitment

Informed Consent!

- Patient Registration (in eCRF plus entering data from medical records)

Pseudonymization is done in the clinic and data is collected, stored and transferred with a username/ code only. The clinical sites are responsible to assign each patient a username; user accounts and an initial password will be created and given to each patient by the clinical sites staff. When a patient logs in for the first time, they will be requested to change the password. The relationship between username and actual patient name, remains within the clinical sites. A unique identifier code will be assigned to each patient through the eCRF.

- Baseline Procedures and Assessment, e.g. demographics, EORTC- QLQ-C30
- Assessment during Pilot Phase, e.g. physical examination, re-newed App training for patients
- End of intervention assessment, e.g. physical examination, satisfaction (MAUQ), QoL (EORTC-QLQ-C30)

The Pilot Study: First results

First feedback

- From patients recruited during the Pre-Phase:
 - Good use of the GA APP, give suggestions how to improve usability of questionnaires.
- From doctors monitoring via the HCP web app:
 - good overview, like to see the variation of the WB- index

Pilot phase will start in July

Current status & next steps

Current status

- Pre-pilot phase has been completed, initial feedback from patients & HCPs has been collected
- A first set of 120 wearable devices has been sent to the clinical sites for the Pilot phase
- Android and iOS versions of the Guardian Angel application have been deployed
- System verification completed, initial patient data gathered

Next steps

- Final ONCORELIEF platform expected to be delivered within 2022
- Updated versions of ML/DL algorithms are also scheduled
- First evaluation and impact analysis is expected at early 2023
- Pilot will be concluded in June 2023

An exploitation note

- The ONCORELIEF Platform has intentionally been designed in the most generic way
- With minor modifications it can support similar projects and clinical studies



THANK YOU!

ACKNOWLEDGEMENTS

We would like to thank all our colleagues of the project partners.



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