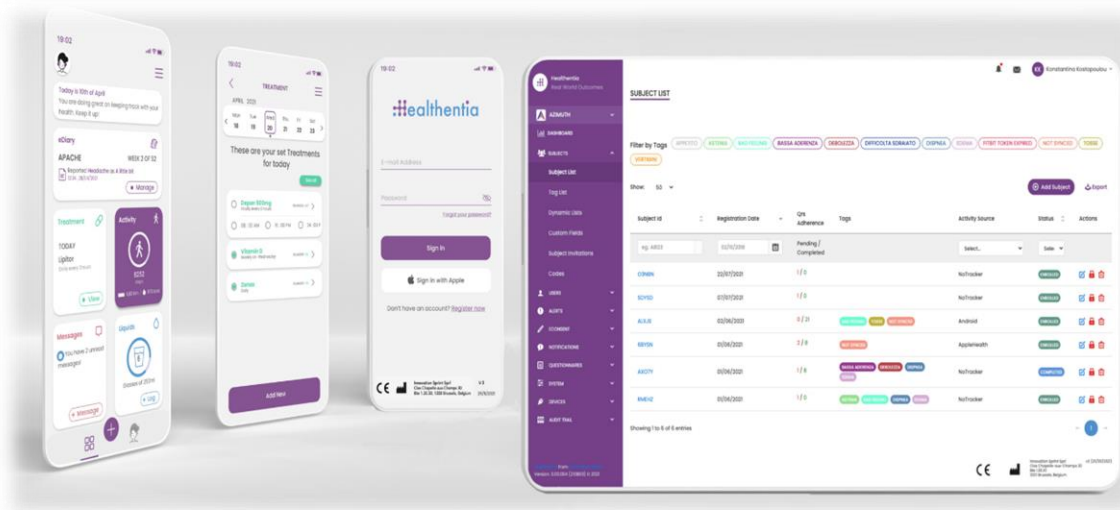




STUDY PORTAL



INVESTIGATOR MANUAL

HEALTHENTIA v3.6

DATE OF ISSUE: 05-03-2024



Innovation Sprint Sprl
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1200 Brussels, Belgium

v3 (25/05/2021)

INFORMATION

Healthentia consists of a collection of modules. Several modules are medical software covered by the CE mark (Class I per rule 12 of Annex IX of Directive 93/42/EEC):

- **Virtual Coaching:** It allows the user (subject/patient) to interact with an embodied conversational coach for informative and motivational purposes.
- **eDiary:** The e-Diary enables the presentation of any reported outcomes of the patient, in the form of a list, grouped by day or outcome (symptom). In this way, patients can have anytime access to their electronic Diary and see the progress of their reported outcomes.
- **Physical activity:** The physical activity widget gives an overview on the steps walked.
- **Sleep:** The sleep widget gives an overview on the sleep duration.
- **Liquid consumption:** The liquid consumption widget gives an overview on the water consumed.
- **Nutrition:** The nutrition widget offers the ability to see and edit the consumption of different food categories of interest.
- **Weight:** The weight widget offers the ability to add manually and through a digital scale, measure and view the weight.

For more information, please visit: <https://healthentia.com>

For any privacy-related questions or requests, you can contact: dpo@healthentia.com

For general questions, you can contact: info@healthentia.com

Report of a serious incident

For any serious incident that has occurred in relation to the Healthentia Medical Device App, you can contact the manufacturer (Innovation Sprint Sprl) at: support@healthentia.com and the authority having jurisdiction in your locale.

Technical support

Healthentia support service is offered at a best-effort level.

For any technical support queries, you can contact: support@healthentia.com

Our support team will reply to you within 1 working day.

Paper-version of IFU

If you would like a paper version of the instructions for use, please contact the manufacturer at the following e-mail address: info@healthentia.com.

It will be delivered within 7 calendar days after receiving the request.

Intended use & user

Intended Use: The intended use of the device is: Software intended for monitoring non-vital parameters to support decision-making and virtual coaching of patients during clinical trials or under a medical or well-being treatment context.

User: Principal Investigators (PI) of clinical studies and their patients, as well as patients using it as a medical or well-being device.

DISCLAIMER

The user is responsible of the final assessment of the diagnosis and treatment decided for the patient.

Healthentia is providing information to support diagnostic and therapeutic decision, but the overall clinical context should be taken into consideration before taking any decision.

Contra-indications

- Any physical or cognitive condition that, in clinical judgment, would prevent the patient from using Healthentia, e.g., dementia.
- The device is not intended to replace the care of a health care professional, including prescription, diagnosis, or treatment. The device should not be used during pregnancy.
- Healthentia has not been tested on the pediatric population. Therefore, Healthentia is intended for adult use only (>18 years old) and does not cover use by children.
- Consult periodically the Alerts dashboard as it may influence the follow-up of your patients.

Warnings

- Healthentia is not monitored in real-time by healthcare personnel; it is intended for non-emergency communication only. In case of an emergency, contact your care unit or the emergency number by phone.
- In some special cases, the self-care advice and instructions provided by Healthentia may not be applicable to your situation.
- If you have questions about your care, symptoms, and management, contact your healthcare team.
- The device is not intended to replace the care of a healthcare professional, including prescription, diagnosis, or treatment.
- Telemonitoring does not replace regular check-ups with your doctor. Consult your doctor in case of severe and persistent symptoms.
- In combination with Healthentia, use only measuring devices for which the technical performances (accuracy, precision) have been verified by your healthcare provider as it may affect the outcome of your monitoring.
- Verify the consistency of your clinical data and the good transfer of them to your healthcare provider as the quality of the diagnosis and treatment is partially based on this information.

MINIMUM REQUIREMENTS

Supported hardware

Any personal computer that is using the supported Operating System (OS) and browser – see below- is a supported hardware device.

Operating system/browser requirements

Healthentia Portal requires a stable Internet connection and a compatible device (laptop, desktop, etc). The operating systems supported are:

- Microsoft Windows: version 8.1 and above
- MacOS: version 10.15 and above
- Linux: LTS distributions released after 2019

This device will need an up-to-date internet browser in order to consult the web application. It is suggested using one of the following browsers that were each tested:

- Google Chrome: version 93 and above
- Mozilla Firefox: version 88 and above
- Safari: version 12 and above
- Microsoft Edge: version 93 and above

Specific issues that come in at Innovation Sprint from the users (post-market surveillance) are analyzed and when a systematic error on one browser is detected, this is added to the backlog and prioritized for the correct version.

Integration with other devices

Healthentia App is compatible with other devices. The supported devices intended for use together with Healthentia are:

- Garmin trackers and watches via the Garmin API (Android & iOS): Fenix 5 pro, Fenix 6 pro, Forerunner 945, Vivoactive 4, Vivosmart 4, Venu 2S,
- Fitbit trackers and watches via the Fitbit API (Android & iOS): Versa, Inspire 2
- iHealth devices via Bluetooth (Android & iOS): Connected Blood Pressure Monitor iHealth Track (KN-550BT), Smart body composition scale iHealth Fit (HS2S), Smart Pulse Oximeter - iHealth Air (POM3)
- Polar belt via the Polar API (Android & iOS): H9

In combination with Healthentia, use only measuring devices prescribed by your healthcare provider as it may affect the outcome of your monitoring.

Healthentia is not intended to monitor vital parameters. For the avoidance of doubt, such parameters are highlighted in the application, so that users are informed about them. Furthermore, there is no guarantee of the reliability of the data shown and the user should always refer to the display of the measurement device (e.g., activity tracker).

Training

No training is required to use the device safely.

SECURITY & PERFORMANCE

Security

Innovation Sprint is committed to protecting the security of data subject's information and takes reasonable precautions to protect it, including protection against unauthorised access, necessary to run the software as intended. In this context, Innovation Sprint regularly evaluates and reviews technologies, facilities, procedures and potential risks to maintain the security and privacy of users' data, paying particular attention to role-based access and logging of health data access. Moreover, any potential changes to software applications, provided services and/or hardware systems are properly justified, evaluated and registered based on international best practices and standards.

- Avoid using public wi-fi networks to connect to Healthentia when you are about to add and/or manage health data and/or your profile details.
- Do not use jailbroken devices.
- Passwords should be at least eight (8) characters long, contain characters from three of the following four groups: Lowercase letters, Uppercase letters, Numbers (0-9), Special characters.
- Never store your passwords on your devices.
- Change your passwords at least every six months.
- Install an anti-malware program on your devices and update it regularly.
- Make sure that each e-mail you register in Healthentia corresponds to you.
- Ignore and delete messages of doubtful origin and do not follow links that include and refer to websites.
- Do not reveal by phone, e-mail, Internet form, or social media, confidential information such as your username, password.
- Always use the most up-to-date versions of your device operating system and Healthentia App.
- The user is suggested to keep the Bluetooth setting in "not discoverable" (transmission disabled) and switch to "discoverable" mode only when he/she wants to use it.
- The user should avoid storing critical information (account credentials) on his/her Bluetooth-enabled devices.
- If the user is going to connect with a device via Bluetooth, it is strongly suggested to activate this connection in a safe place.

Performance

Provide objective inputs for healthcare professionals to support diagnosis and patient management; Highlight evolution of physiological parameters by trends analysis of the patient's inputs; Increase patient's adherence to treatment.

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DOCUMENT HISTORY

Date	Author	Description
6/12/2018	Konstantina Kostopoulou	ToC
14/3/2019	Konstantina Kostopoulou	Healthentia version 1
14/5/2019	Konstantina Kostopoulou	Healthentia version 1 -upd
27/4/2020	Sofoklis Kyriazakos	Healthentia version 2
25/5/2021	Konstantina Kostopoulou	Healthentia version 3
3/12/2021	Konstantina Kostopoulou	Healthentia version 3.1
10/08/2022	Konstantina Kostopoulou	Healthentia version 3.2
1/09/2022	Konstantina Kostopoulou	Healthentia version 3.3
29/09/2023	Konstantina Kostopoulou	Healthentia version 3.4

1 GETTING STARTED

HEALTHENTIA can be used both by individuals and by sponsors of clinical trials. Individuals can report and monitor their outcomes (e.g. symptoms) and activity and receive automatic-generated questionnaires for wellbeing. Aggregated data provided after users' consent, can be processed for conducting non-profit research studies. Clinical trial sponsors can operate HEALTHENTIA to collect ePROM/ePREMs under the appropriate regulatory framework (e.g. Good Clinical Practice) to carry out study protocols, often by the use of a PaaS instance of the platform. Individuals, depending on their consent information, may receive invitation to participate in research studies.

This manual is targeting Organization Admins, Study Admin, Investigators and other authorized personnel of the Study Portal.

1.1 PORTAL USER ROLES & PERMISSIONS

Portal User Roles & permissions

1.2 LOGIN/ REGISTER AS A PORTAL USER

To login user should go to the login page, which is available in <https://saas.healthentia.com> for the SaaS version, or a specified URL for the PaaS version.

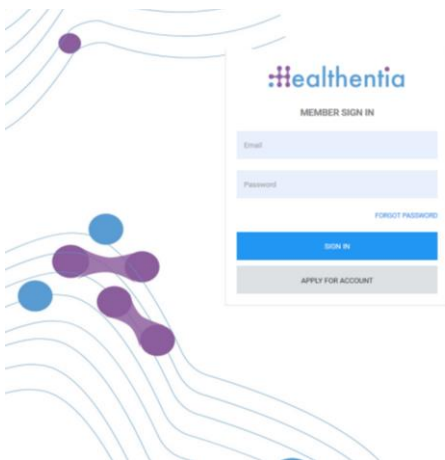


Figure 1: Login page



Figure 2 - Registration page

Users receive an invitation from an Organization Admin to register their account and enter in the portal in the allocated study with an allocated role.

2 STUDY MANAGEMENT

2.1 STUDY OVERVIEW

After log in you are directed to the Study Overview Page – My Studies, which has a list of your available studies and some overall statistics. You can access your Studies, edit them or create a new one.

MY STUDIES

Overall
18 studies
785 participants

Tracked Activity
95218 days
256 subjects

Adherence
6172 events from 376 participants
15216/16141 answered questionnaires

Last week's activity
6 subjects with reported events
1 participants

Show: 10

Create Study Export Clear Filters

Icon	Name	Organization	Codename	Disease	Patients No	Status	Alerts	Actions
	Monoclonal Antibodies	ORG_1	MoAbs	Remote Covid19 Therapy Monitoring	0	ONGOING	0	
	Virtual Ward	ORG_1	VIRTUALWAR	Ovarian Cancer	3	ONGOING	0	
	VITO Demo Study	ORG_18	VITO_Demo	Observational	7	ONGOING	3	
	Digital Check-up	ORG_17	DIG CHECK	Health Assessment	9	ONGOING	7	
	IPF Vaccine Study	ORG_6	IPFVaccine	IPF	69	ONGOING	90	
	iHelp	ORG_16	iHelp	Pancreatic Cancer	3	ONGOING	0	
	Beia	ORG_12	BEIA		4	ONGOING	0	
	KEYRUS Demo	ORG_11	Keyrus		11	ONGOING	10	
	imec Demo	ORG_10	imec	Health Monitoring	1	ONGOING	0	
	Med-ex Demo	ORG_9	Med-ex	Physical Activity Monitoring	1	ONGOING	0	

Showing 1 to 10 of 18 entries

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1200 Brussels Belgium v1.01.00.0011

Figure 3 - Study Overview

2.2 SETTING UP A NEW STUDY

From this first page, you have the option to create a new study. Depending on the type of study, investigator provides different information. In Figure 4 one can see the available configurations for the study per se but also the mobile App. There is a selection of available widgets to select for the new study and configure the data sources but also several fields to fill in like Name, Code, logo, Languages, therapeutic area, duration and consents.

Healthentia
Real World Outcomes

Symptom Tracker

DASHBOARD

SUBJECTS

USERS

ALERTS

ECONSENT

MESSAGES

NOTIFICATIONS

QUESTIONNAIRES

SYSTEM

DEVICES

AUDIT TRAIL

🔔 ✉️ KK Konstantina Kostopoulou

CREATE STUDY

GENERAL

Account Settings

Name: * Therapeutic Area: Codename: *

Protocol: Duration in Months: Start Date: End Date:

Primary Language: * Add More Languages:

Study Logo:

Additional Services

Video-Chat Multicenter Interactive Map

MOBILE CONFIGURATION

Study Information Page: Study Logo on App:

Pop-up for Study's terms & Privacy ?

Short Term's Description:

Terms of Use URL:

Privacy Policy URL:

Available Consents

General Terms Allowing Reporting Contacted by doctor in case of need

Additional App Widgets

Treatment Reminder Two-Factor Authentication Liquid consumption Sleep Widget

Activity Widget (Available Integrations)

Fitbit Sync Garmin Sync Apple Health Sync Android Sync

SUBJECT DETAIL PAGE CONFIGURATION

<input type="checkbox"/> First/Last Name	<input type="checkbox"/> Fiscal Number	<input type="checkbox"/> Study Dates	<input type="checkbox"/> Severity
<input type="checkbox"/> Managed Fitbit	<input type="checkbox"/> Tracker Description	<input type="checkbox"/> Mobile Description	<input type="checkbox"/> Therapeutic Area
<input checked="" type="checkbox"/> Subject Id	<input checked="" type="checkbox"/> Email	<input checked="" type="checkbox"/> Phone Number	<input checked="" type="checkbox"/> Status
<input checked="" type="checkbox"/> Time Zone	<input checked="" type="checkbox"/> Language	<input checked="" type="checkbox"/> Gender	<input checked="" type="checkbox"/> Weight
<input checked="" type="checkbox"/> Height	<input checked="" type="checkbox"/> Birth Date	<input checked="" type="checkbox"/> Tags	<input checked="" type="checkbox"/> Notes

Innovation Sprint Spot
One, Chausseée aux Charpentiers 30
Boulevard 1000
1200 Brussels, Belgium v1 (2018/02/21)

Figure 4 - Create New Study

3 DASHBOARD

The user dashboard contains information of the selected study in tabs, e.g. Interactive map, Study Overview, Measured Activities Overview and Outcomes Overview. This is a customizable set of dashboard tabs; they depend on the Outcomes that each trial collects. The map is connected to a Location question, Measured activity requires a connection the mobile sensors (or fitbit, Garmin, etc) and the reported outcomes tab has a self-service mechanisms for questions asked in the questionnaire to be seen in two types of graphs

3.1 INTERACTIVE MAP

At the configuration of the study, the Study Admin can select to enable the interactive map if there are questions regarding location. Portal users can select parameters through several filters and have an overview of subject outcomes at a geographical level, as presented in Figure 5.

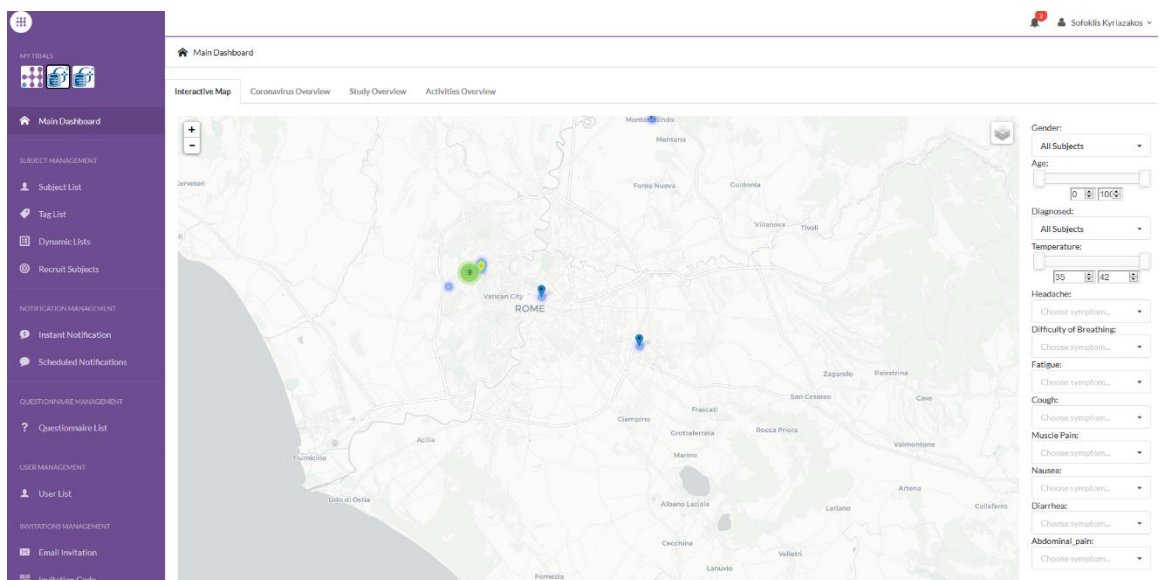


Figure 5: Interactive Map

3.2 BI

Further to the Interactive map, there are other tabs in the Dashboard that can be configured with study Overview statics, like registrations and protocol adherence – Figure 6.

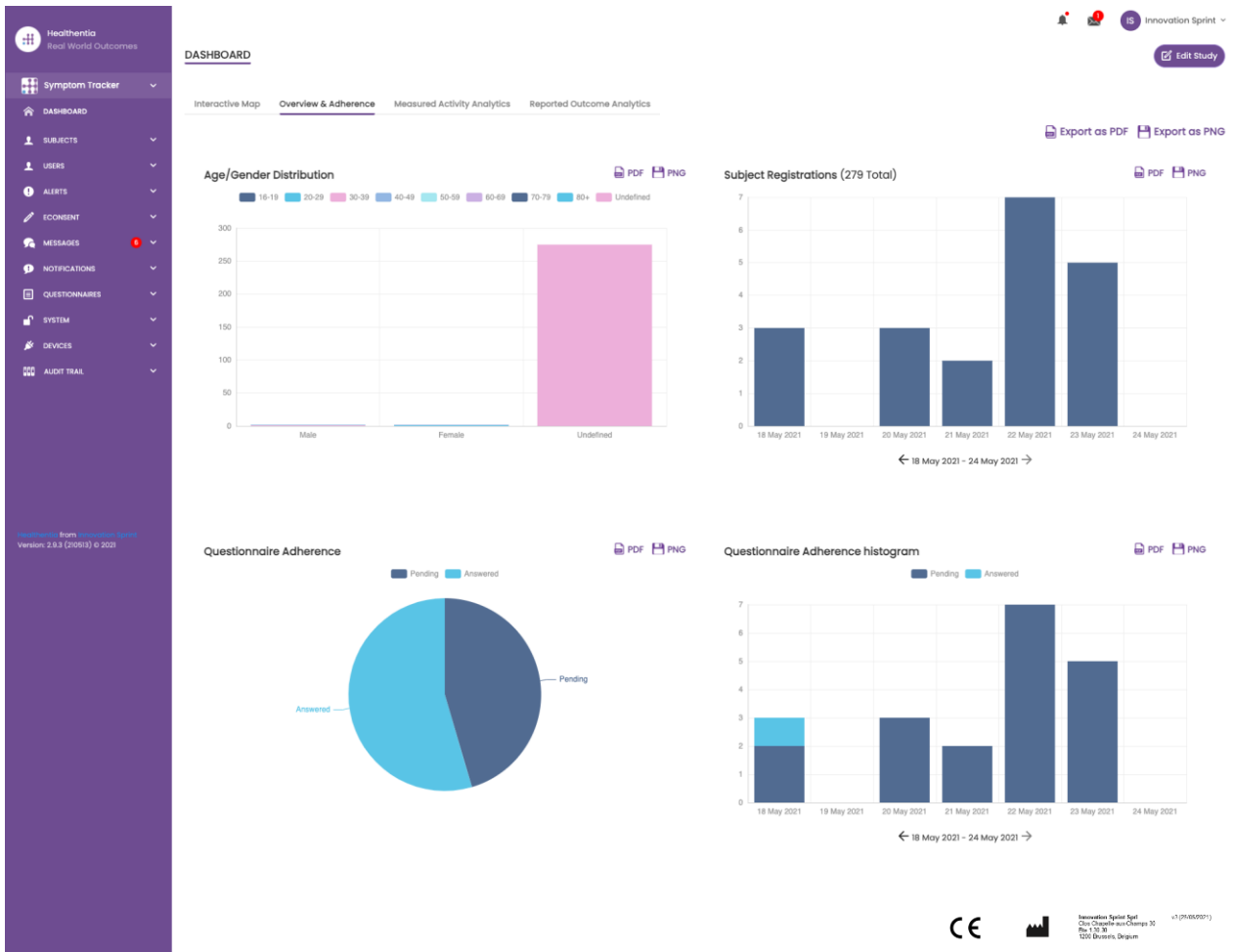


Figure 6: Study registration and compliance overview

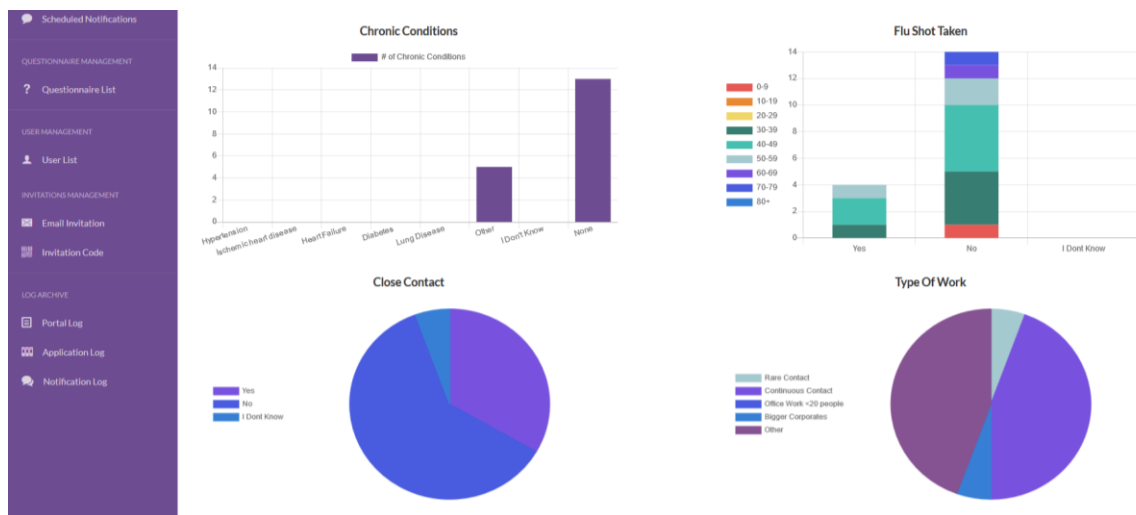


Figure 7: Study statistics overview

Healthentia
Real World Outcomes

Symptom Tracker

- DASHBOARD
- SUBJECTS
- USERS
- ALERTS
- ECONSENT
- MESSAGES
- NOTIFICATIONS
- QUESTIONNAIRES
- SYSTEM
- DEVICES
- AUDIT TRAIL

DASHBOARD

Interactive Map Overview & Adherence **Measured Activity Analytics** Reported Outcome Analytics

Innovation Sprint

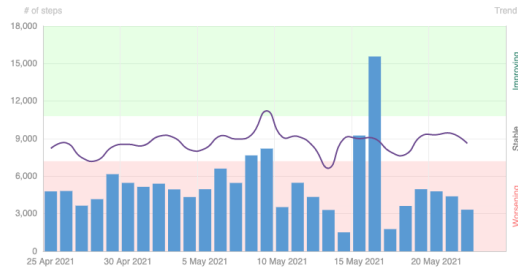
Edit Study

Export as PDF Export as PNG

Physical activity in Average

PDF PNG

Steps 30-days interval 25 Apr 2021 - 24 May 2021



Average Active time (minutes)

PDF PNG

30-days interval 25 Apr 2021 - 24 May 2021

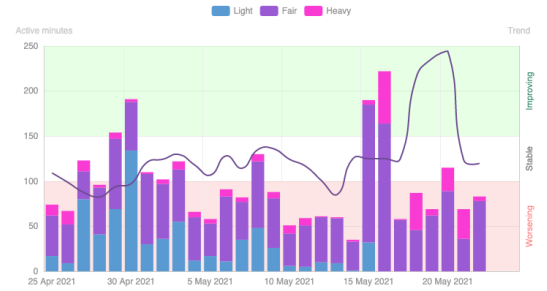


Figure 8: Measured Activity overview

4 SUBJECTS

4.1 ADD A SUBJECT

Subjects are either imported via an integration with an EDC into Healthentia as inactive subjects that are activated once they have logged in to Healthentia, they can be manually added by the button on the Subject List or invited through the system from the Subject Invitations. The email used for the invitation will be recognized by the system to allow them, at registration on the App to enter to the specific Study. **Not using the same email will not enroll the Subject in the correct Study.**

The screenshot displays the 'SUBJECT INVITATION' page. On the left is a navigation menu with options like 'Interface', 'DASHBOARD', 'SUBJECTS', 'Subject List', 'Tag List', 'Dynamic Lists', 'Custom Fields', 'Subject Invitations', 'Codes', 'USERS', 'ALERTS', 'ECONSENT', 'NOTIFICATIONS', 'QUESTIONNAIRES', 'SYSTEM', 'DEVICES', and 'AUDIT TRAIL'. The main area shows a table of invitations with columns for Email, Invited On (Browser Time), Role, Joined On (Browser Time), and Invited By. A modal window titled 'Invite Subject' is open, containing fields for 'Email', 'Phone Number: (Required only for eConsent)', and 'Invitation Code:'. A 'Send Email' button is also present.

Email	Invited On (Browser Time)	Role	Joined On (Browser Time)	Invited By
330d5182-7e49-4d6d-a7a4-81aac6a78e5a@healthentia.com	2021/05/07, 16:15:48	Subject	07/05/2021, 18:13:50	9f714f3f-0c02-4cbf-aa89-e7d75d83adc3@healthentia.com
ff524ee-cf6a-4321-adf3-4aadae35bf08@healthentia.com	2021/05/07, 16:15:04	Subject	11/05/2021, 17:03:03	9f714f3f-0c02-4cbf-aa89-e7d75d83adc3@healthentia.com
4ff2da93-2c3f-4a9e-9996-c28be8f83fbc@healthentia.com	2021/05/07, 16:14:30	Subject	07/05/2021, 16:27:41	9f714f3f-0c02-4cbf-aa89-e7d75d83adc3@healthentia.com

Figure 9 - Invite Subjects

Similarly, to the Email invitation above, the investigator can invite patients by providing them a code. Subjects can enter this code at the registration, even if they have not received an email. Once they register, they are automatically connected to that specific study only. They can be massively generated to use one per subject and or one can be used for all the subjects for the Study as seen in Figure 10

The screenshot displays the 'INVITATION CODES' page. The navigation menu is similar to the previous figure. The main area shows a table of invitation codes with columns for Active, Created On (Browser Time), Code, Used Slots, Email Only, Document, and Action. A modal window titled 'Generate Invitation Code(s)' is open, containing a 'No. of Codes' input field and a 'Generate' button.

Active	Created On (Browser Time)	Code	Used Slots	Email Only	Document	Action
✓	14/01/2021, 12:44:42	Interface	0/50	YES	Unavailable	🗑️
✓	20/10/2020, 11:03:52	FUGN4N	0/1	NO	-	🗑️
✓	20/10/2020, 11:03:52	WMESEH	0/1	NO	-	🗑️
✗	20/10/2020, 11:02:09	YUEBAZ	0/1	NO	-	🗑️

Figure 10 - Invitation Codes

4.2 SUBJECT RECORD

In the Subject record, the portal user that has permissions to view or edit the patient details and view ePRO related data and measured activity can have access to the different tabs of information coming from different sources. They can even have the ability to complete questionnaires for them.

Figure 11 - Subject Details

4.3 SUBJECT LIST

The subject's list gathers in a table all patients assigned in the specific study. The list table gives an overview of important elements like dates, Questionnaire adherence, tags, activity status and more.

Sr.No	Email	Subject id	Registration Date	Qrs Adherence	Tags	Activity Source	Status	Actions
1	f1f524ee-cf6a-4321-adf3-4aadae35bf08@healthentia.com	15096001	11/05/2021	0 / 6	PSYCHOLOGICAL SUPPORT	NoTracker	ENROLLED	[Icons]
2	330d5182-7e49-4d6d-a7a4-81aac8a78e5a@healthentia.com	19254317	07/05/2021	0 / 3	DOSE 1 COVIDVAX NOT SYNCED	Android	ENROLLED	[Icons]
3	4f12da93-2c3f-4a9e-9996-c28be8f83fbc@healthentia.com	12296802	07/05/2021	0 / 7	PSYCHOLOGICAL SUPPORT NOT SYNCED	AppleHealth	ENROLLED	[Icons]
4	9b37ed2a-3b49-444d-8a94-6e26e7c8ddef@healthentia.com	24329179	07/05/2021	0 / 12	HIVSRQ SYMPTOM PSYCHIATRIC SUPPORT NOT SYNCED	AppleHealth	ENROLLED	[Icons]
5	0b0ed1cb-c8ee-4568-85ee-dd729f69df33@healthentia.com	9524489	30/04/2021	0 / 7	FEEDBACK DOSE 1 COVIDVAX NOT SYNCED	AppleHealth	ENROLLED	[Icons]
6	dd1ed84d-20b3-4481-a743-bda58102c22d@healthentia.com	12718649	17/04/2021	1 / 0		NoTracker	ENROLLED	[Icons]

Figure 12 Subject list

4.4 TAGS & DYNAMIC ALERTS

In the section of Tags, we list all the tags available in the study as seen in Figure 13 to be used for grouping the patients in their entry in the system or depending on their answers in the questionnaires. These tags can be then attached to an Alert seen in Figure 14. All Alerts are featured in a table as seen in Figure 15. As in all sections of the portal all data are exportable to an excel file.

The screenshot shows the 'Tag Management' interface. At the top, there is a breadcrumb 'Home / Tag' and an 'Add Tag' button. Below this, there is a 'Show: 10' dropdown and an 'Export data to excel' button. The main content is a table with the following data:

Title	Created On	Status	Actions
e.g. Chronic	Created On	--Select--	Search, Filter
Acute	10/09/2018	INACTIVE	Edit, Delete
Chronic	08/09/2018	INACTIVE	Edit, Delete
Congenital	13/10/2018	ACTIVE	Edit, Delete
Diagnosed	08/09/2018	ACTIVE	Edit, Delete
language - DE	22/10/2018	ACTIVE	Edit, Delete
language - EN	22/10/2018	ACTIVE	Edit, Delete
Vertigo	15/11/2018	ACTIVE	Edit, Delete

At the bottom of the table, it says 'Showing 1 to 7 of 7 entries' and a pagination control showing '1'.

Figure 13 Tags List

CREATE DYNAMIC ALERT

Name: * Status:

Portal Alert Message: (You can use [Shortid] to include recipient's Short id in your message)

Push Notification Message:

Email List: (Enter emails separated by spaces or commas)

Email Message: (You can use [Shortid] to include recipient's Short id in your message)

API Endpoint to Call: API Alert Codename:

Tags to Apply:

Figure 14 - Create New Alert

Title	Web Alert	Push Alert	Email Alert	API Call	Apply Tag	Status	Actions
COVID-19 POSITIVE	✓	✗	✗	✗	✓	ACTIVE	✉ 🗑
DOSE 1 COVIDVax	✗	✗	✗	✗	✓	ACTIVE	✉ 🗑
DOSE 2 COVIDVax	✗	✗	✗	✗	✓	ACTIVE	✉ 🗑
FEEDBACK	✓	✗	✗	✗	✓	ACTIVE	✉ 🗑
Frailty Alert	✓	✗	✗	✗	✓	ACTIVE	✉ 🗑
HIGH COVID risk	✓	✓	✗	✗	✓	ACTIVE	✉ 🗑
HIVSRQ symptom	✓	✗	✗	✗	✓	ACTIVE	✉ 🗑
Low Adherence	✓	✓	✗	✗	✓	ACTIVE	✉ 🗑
LOW COVID risk	✓	✓	✗	✗	✓	ACTIVE	✉ 🗑
Psychiatric support	✓	✗	✗	✗	✓	ACTIVE	✉ 🗑

Figure 15 - Dynamic Alerts List

4.5 ALERTS DASHBOARD

The Alerts are shown in a separate Dashboard where the portal user has an overview of what tags are allocated and whether a patients requires an immediate action or has low adherence in his reporting of questionnaires.

Triggered On (Browser Time)	Subject Id	Alert Message	Tag	Manager
21/04/2021, 14:21:27	20575866	Patient 20575866 needs psychological support	PSYCHOLOGICAL SUPPORT	Giulia Micheli
20/04/2021, 16:30:02	14455901	Subject 14455901 has «Questionario sulla Salute - EQ-5D-3L» as pending		Giulia Micheli
18/04/2021, 16:30:01	04588190	Subject 04588190 has «Questionario sulla Salute - EQ-5D-3L» as pending		Giulia Micheli
18/04/2021, 13:15:19	14455901	Patient 14455901 is identified as FRAIL	PAZIENTE FRAGILE	Giulia Micheli
18/04/2021, 13:12:09	14455901	Subject 14455901 has an HIVSRQ symptom alert	HIVSRQ SYMPTOM	Giulia Micheli
17/04/2021, 19:19:56	03806999	Patient 03806999 needs psychological support	PSYCHOLOGICAL SUPPORT	Giulia Micheli
17/04/2021, 16:30:02	03806999	Subject 03806999 has «Questionario sulla Salute - EQ-5D-3L» as pending		Subject answered the questionnaire.
15/04/2021, 16:30:01	15929649	Subject 15929649 has «Questionario sulla Salute - EQ-5D-3L» as pending		Giulia Micheli
10/04/2021, 09:10:41	11294295	Patient 11294295 needs psychological support	PSYCHOLOGICAL SUPPORT	Cristina Seguiti

Figure 16 - Alerts Dashboard

4.6 DYNAMIC LISTS

The Dynamic lists are used to group patients in a dynamic way. We create grouping requirements and patients are added automatically in a list when they meet the criteria. The attributes of patients that can be used as criteria for filtering the patient list are status, screening, termination or treatment switch date and even using tags that are explained below. As in all sections of the portal all data are exportable to an excel file, as presented in Figure 17.

DYNAMIC LISTS Add Dynamic List

Show: 10 Export

Sr.No	Title	Description	Created On	Status	Actions
	<input type="text" value="e.g. Subjects"/>	<input type="text" value="e.g. Description"/>	<input type="text" value="Created On"/>	<input type="text" value="--Select--"/>	<input type="button" value="Search"/> <input type="button" value="Close"/>
1	test		05/03/2021	ACTIVE	<input type="button" value="Edit"/> <input type="button" value="Delete"/>

Showing 1 to 1 of 1 entries 1

Figure 17 Dynamic List table

Dynamic List Detail (Edit Mode)

Home / Dynamic List / Edit

Query Title: Status:

Query Description:

Query Criteria

Patient Attributes

Status: Gender: Screening Date: Study Completion Date:

Weight(kg): Height(cm): Day of treatment switch:

Treatment A: Treatment B:

Filter Patient By Tags:

Figure 18 - Dynamic list details

5 NOTIFICATIONS

5.1 NOTIFICATION LOG

In the section of Notifications, we can see all communication sent by the system to patients, we can create instant notifications or scheduled. All notifications are listed by date in the Notification List and you have an overlook of the content of these notifications and if their type. As in all sections of the portal all data are exportable to an excel file, as presented in Figure 19.

NOTIFICATION LOG

Show: 10 Export Clear Search Filters

Description	Type	Content	Recipients	Sent On (User Time)	Sent On (Your Time)
<input type="text" value="e.g. Monthly Reminder"/>	<input type="text" value="-- Select --"/>			<input type="text" value="24/05/2021"/>	<input type="text" value="24/05/2021"/>
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	24/05/2021, 14:24:09	24/05/2021, 15:24:09
Severity Alert	Severity Alert	View Content	View Recipients (1)	24/05/2021, 13:05:33	24/05/2021, 14:05:33
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	24/05/2021, 09:30:07	24/05/2021, 10:30:07
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	24/05/2021, 09:00:01	24/05/2021, 10:00:01
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	24/05/2021, 08:01:05	24/05/2021, 09:01:05
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	23/05/2021, 21:30:14	23/05/2021, 22:30:14
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	23/05/2021, 09:30:06	23/05/2021, 10:30:06
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	23/05/2021, 09:00:15	23/05/2021, 10:00:15
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	23/05/2021, 08:01:29	23/05/2021, 09:01:29
Treatment Reminder	Treatment Reminder	View Content	View Recipients (1)	22/05/2021, 21:30:12	22/05/2021, 22:30:12

Showing 1 to 10 of 6,261 entries 1 2 3 4 5 ... 627

Figure 19 - Notification Log

5.2 INSTANT NOTIFICATIONS

Instant Notifications are the ad hoc messages that the investigator can send to a patient that hold a simple message or accompany a questionnaire. You can select individual recipients for the notification from the full subject list or filter by using tags or Dynamic Lists as seen in Figure 20.

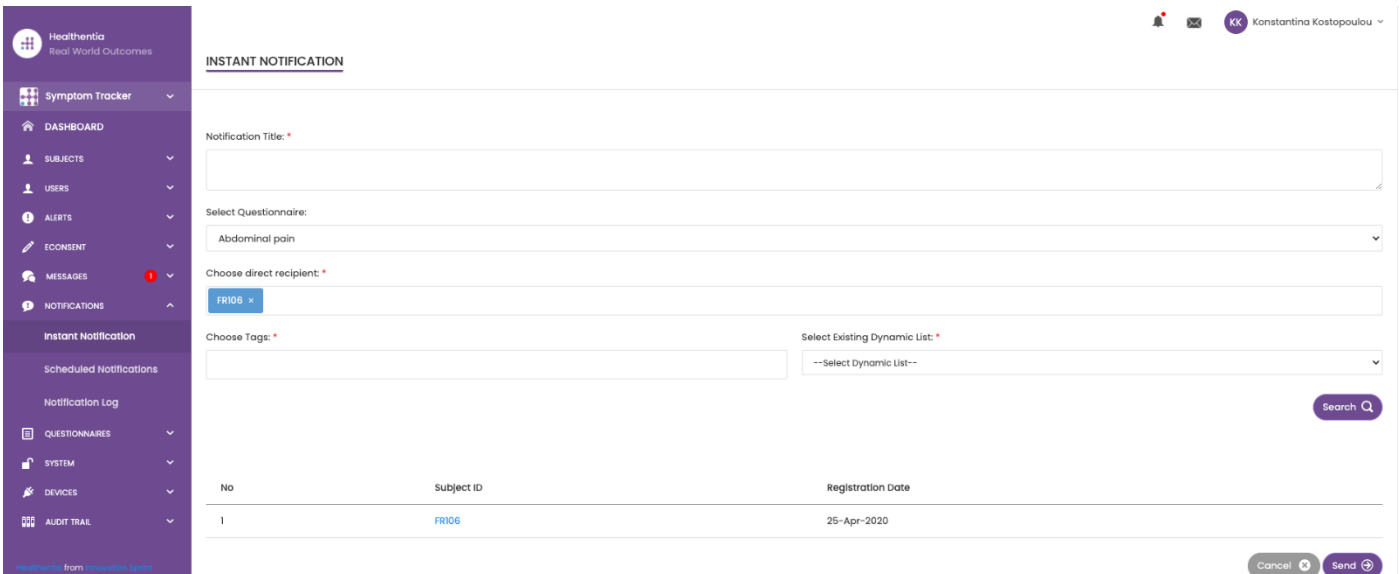


Figure 20 - Instant Notification

5.3 SCHEDULED NOTIFICATIONS

Scheduled notifications are the ones that are created in the beginning of the study and are used to schedule the questionnaires to be sent to a group of recipients based on a filtering by tags or dynamic lists or to the whole list.

The scheduling of a notification can be done based on a regular Date with a Daily, weekly or Monthly interval sent once at a specific time or recurring. The system also allows the coordinator to send notifications based on the protocol’s specific dates and X days before or after these days. You can see the Notifications List at Figure 21 and the New Scheduling Notification at Figure 21

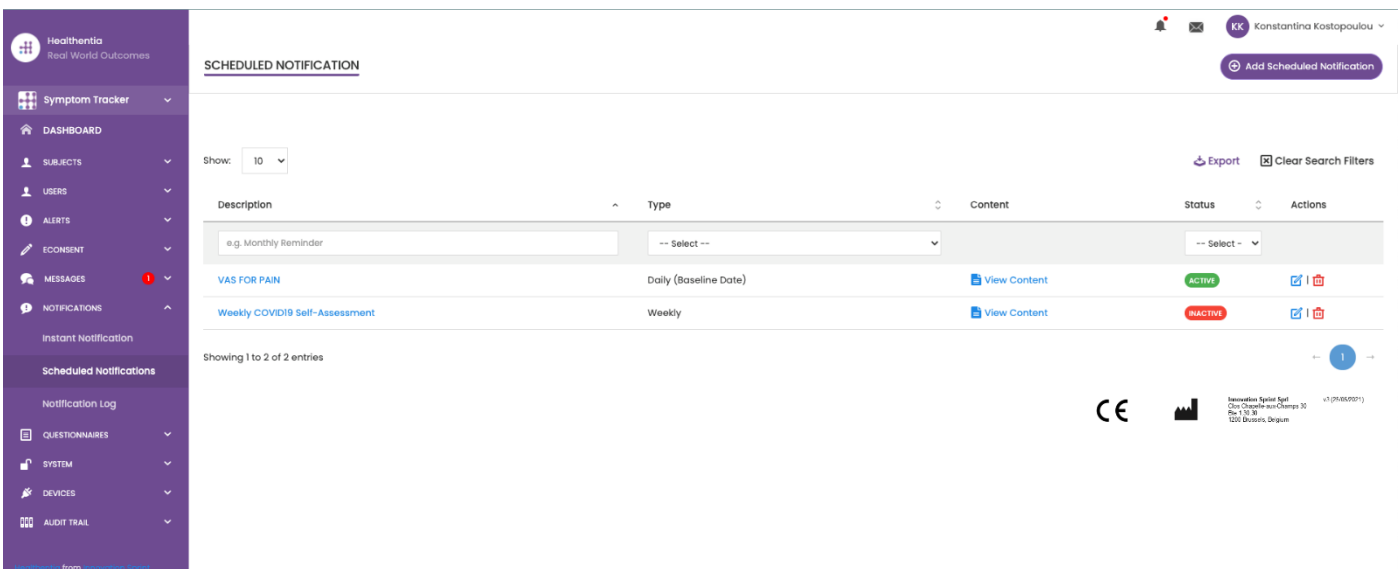


Figure 21 - Scheduled Notifications

Healthentia
Real World Outcomes

Symptom Tracker

DASHBOARD

SUBJECTS

USERS

ALERTS

ECONSENT

MESSAGES

NOTIFICATIONS

QUESTIONNAIRES

SYSTEM

DEVICES

AUDIT TRAIL

EDIT SCHEDULED NOTIFICATION

Description: * VAS FOR PAIN Status: Active

Schedule Type:
 Regular By Baseline Date

Frequency: Daily by Baseline Date End repeat: After Repeat these many times: 10

Recipient Tags: George

Questionnaires: Muscle Pain

Message (Individual Notification):

Schedule Type:
 Regular By Baseline Date

Frequency: Daily End repeat: Never

Cancel Edit

CE [Logo] v1 (25/08/2017)
Amsterdam, Eindhoven, Groningen, Maastricht, Nijmegen, Radboud, Rotterdam, Utrecht, Vrije Universiteit Amsterdam, Zuydam

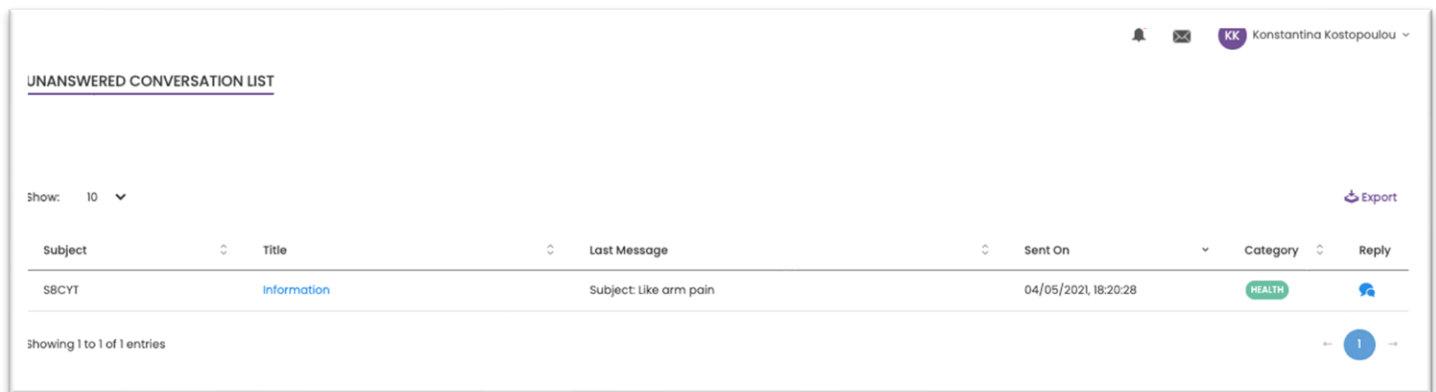
Figure 22 - New Scheduled Notification

6 MESSAGES-TELECONSULTATION

6.1 MESSAGE INBOX

End-users of the mobile app if the feature is enabled they can send a Message to the Investigator/study assistant and start a conversation. If needed the investigator can start a teleconsultation video link that will be valid for 15 minutes. See inbox in Figure 23 and the conversation in Figure 24.

Figure 24.



The screenshot displays a web interface for a message inbox. At the top right, there are notification icons and a user profile for 'Konstantina Kostopoulou'. The main heading is 'UNANSWERED CONVERSATION LIST'. Below this, there is a 'Show: 10' dropdown menu and an 'Export' button. The inbox contains one entry with the following details:

Subject	Title	Last Message	Sent On	Category	Reply
SBCYT	Information	Subject: Like arm pain	04/05/2021, 18:20:28	HEALTH	

At the bottom left, it says 'Showing 1 to 1 of 1 entries'. At the bottom right, there is a pagination control showing '1'.

Figure 23 - Message Inbox

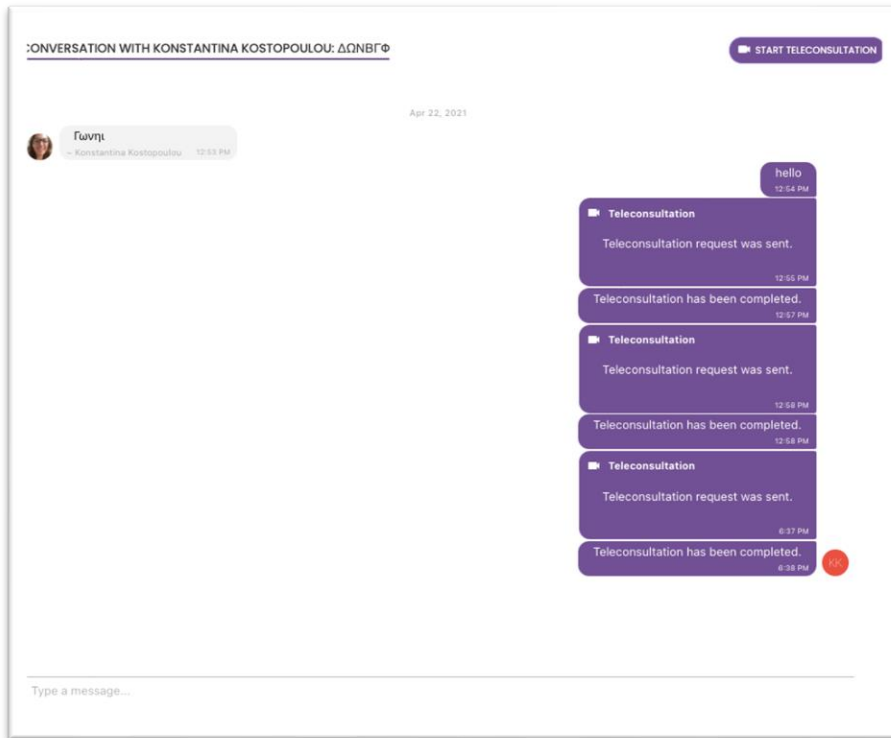


Figure 24 - Message conversation

6.2 TELECONSULTATION

If needed, the investigator can start a teleconsultation video link that will be valid for 15 minutes, as shown in the Figure below.

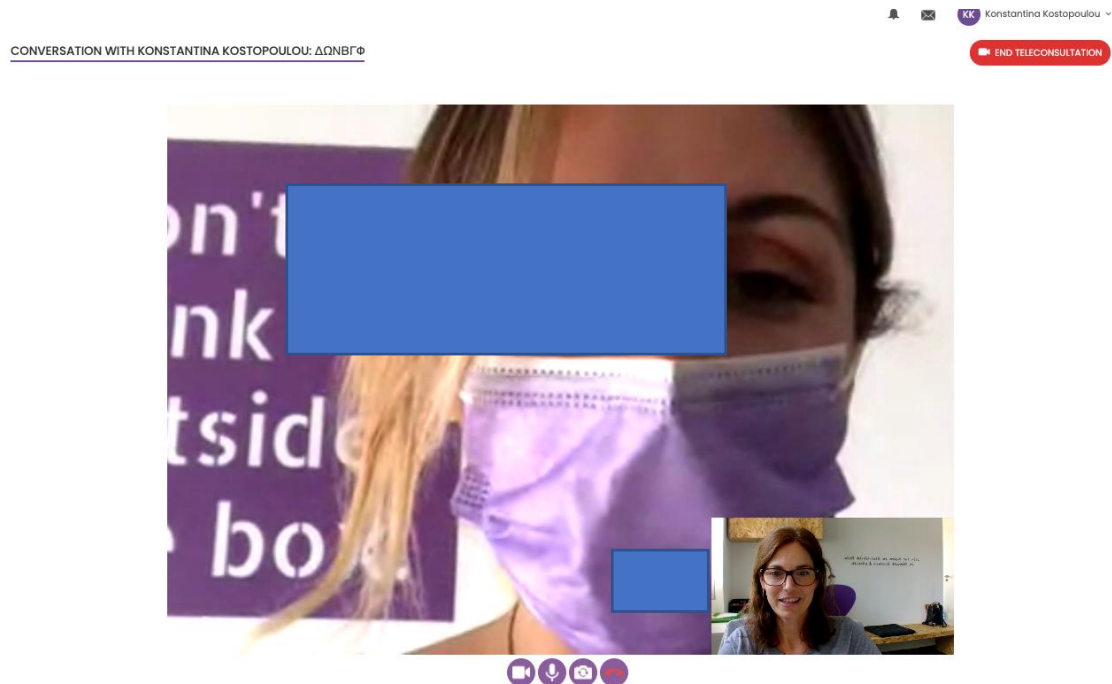


Figure 25 – Teleconsultation

7 E-CONSENT

7.1 E-CONSENT

If the trial has an active eConsent, the eConsent is triggered by the Healthentia app after the user has registered and agreed with the Terms of the Healthentia application. Each eConsent form must have a unique Version and a unique Title in the context of this study or site (in case of multicenter trials). When creating or editing an eConsent form, users with the appropriate permission shall be able to: (1) add a plain text field to write the "Terms" of the eConsent Form; (2) add a plain text field to write the "Introduction" of the eConsent form; (3) upload a url from a video streaming provider to the eConsent form; and (4) define a Status. An eConsent setup has three status: "draft", "active" and "inactive". While in "draft" mode, the eConsent is editable. Once the investigator changes its status to "active", the eConsent is locked and no longer editable. The "inactive" status is given to eConsent forms that are no longer active but that have been signed at least by one study participant. See Figure 26 and Figure 27.

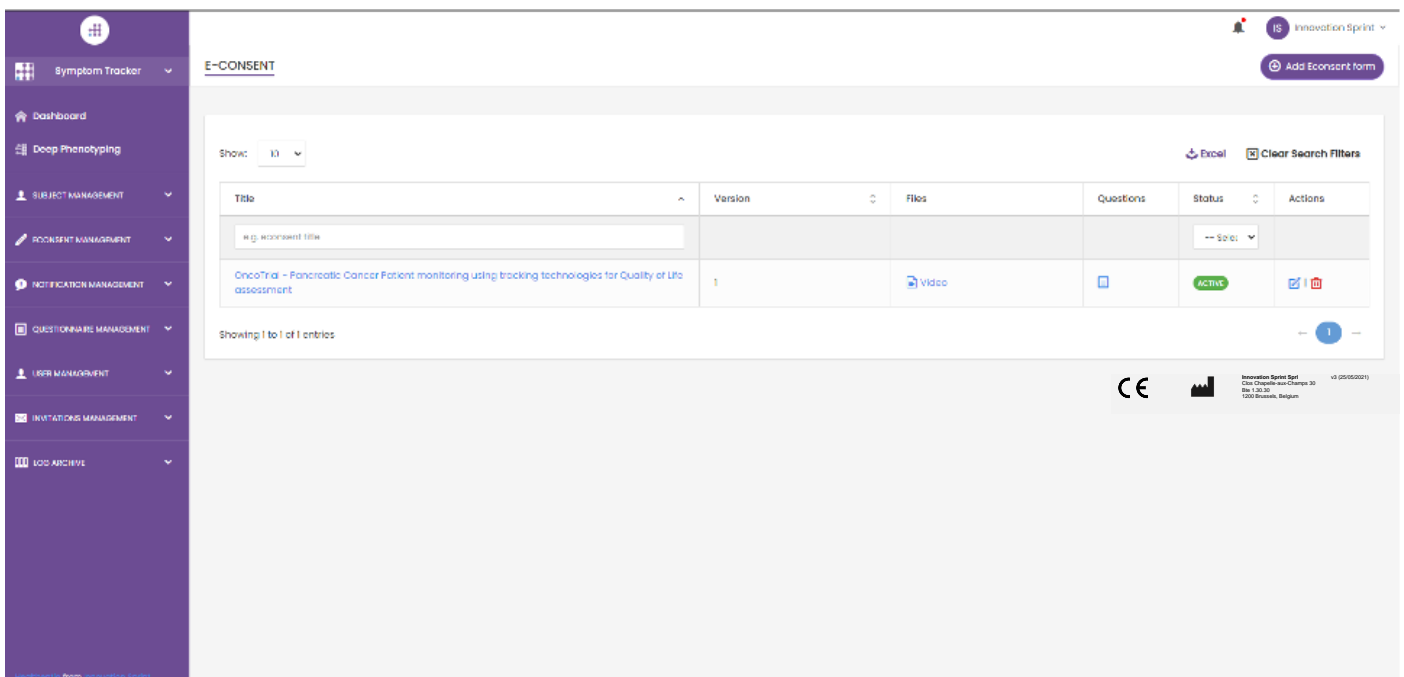


Figure 26 - eConsent list

Figure 27 - eConsent configuration

The process of signing an eConsent form can only be completed after a mobile app user has verified his identity providing a code received via email or mobile phone. Once the participant has signed the eConsent, a pdf document is created with the name, date and signature of the participant on top of the Terms plain text. The pdf document created after the participant signed the eConsent is saved in the Healthentia Patient documents with type "consent". Once the participant has signed the eConsent, the tag of the eConsent in the subject list changes from "not started" to "requires signature".

ID	Email	Subject ID	Consent Info	Version	Consent Date	Comprehension	Status	File
1	0007766-0470-4092-8611-03644880@healthentia.com	40749	OVERVIEW - PAPERLESS	1			Needs	
222	0001108-0430-0806-8611-07646102@healthentia.com	40749	OVERVIEW		10/7/2020		Completed	
2	0200786-0412-4777-0424-03644880@healthentia.com	40749	OVERVIEW - PAPERLESS	1			Needs	
3	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
4	0200066-0401-4250-8611-03232058@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
5	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
6	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
7	0724336-0420-4260-0420-03644880@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
8	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
9	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
10	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
11	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
12	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
13	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
14	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	
15	0001807-0970-4136-4638-06520026@healthentia.com	07600	OVERVIEW - PAPERLESS	1			Needs	

Figure 28 - eConsent PDF list

8 QUESTIONNAIRES

8.1 QUESTIONNAIRE LIST

The portal allows the study coordinators to create a questionnaire with different question types but also allows the questionnaire to be uploaded from a specified excel file. These questionnaires are then sent to the patient through a notification. In the Questionnaire management one can see the list of available questionnaires in the study and the number of questions that each has as well as their status and date created. As in all sections of the portal all questionnaires can be exportable to an excel file.

Title	Codename	Kind	No. of Questions	Types	Created On	Status	Actions
e.g. Diabetic Questionnaire	e.g. Q_MUSCLES	-- Selec	e.g.11	e.g. Initial	02/10	--Select	Q I
Abdominal pain	ISPRINT_ABDPAIN	Simple	1	ADD-EVENT-LIST	26/03/2020	ACTIVE	I I
Add or take photo		Simple	1	ADD-EVENT-LIST	24/04/2020	ACTIVE	I I
Body temperature	ISPRINT_FEVER	Simple	1	ADD-EVENT-LIST	18/03/2020	ACTIVE	I I
Cough	ISPRINT_COUGH	Simple	2	ADD-EVENT-LIST	18/03/2020	ACTIVE	I I
Diarrhea	ISPRINT_DIARRHEA	Simple	1	ADD-EVENT-LIST	26/03/2020	ACTIVE	I I
Difficulty of breathing	ISPRINT_DBREATH	Simple	1	ADD-EVENT-LIST	26/03/2020	ACTIVE	I I
eConsent comprehension Assessment	eCONSENT	Simple	2	ECONSENT QUESTIONNAIRE	16/02/2021	ACTIVE	I I
Emotional State		Simple	1	ADD-EVENT-LIST	06/05/2020	ACTIVE	I I
Fatigue	ISPRINT_FATIGUE	Simple	1	ADD-EVENT-LIST	18/03/2020	ACTIVE	I I
Headache	ISPRINT_HEADACHE	Simple	1	ADD-EVENT-LIST	26/03/2020	ACTIVE	I I
Initial Questionnaire	ISPRINT_COVID19	Simple	11	INITIAL	16/03/2020	ACTIVE	I I

Figure 29 Questionnaire Management

When creating a new one you define the title and questionnaire type (select from a list created by the admin) and upload a characteristic image for it if you want it to be shown on the app and start adding the questions one by one. In the question options you can choose from a variety of UI controls like if the question is a single, multiple, entry text or slider bar as presented in Figure 30.

VIEW QUESTIONNAIRE

Title (EN): Title (IT): Codename:

Types: Status:

Upload Image: Color: Description:

No file chosen

QUESTION LIST

No	Code	Question	UI Control	Routing	Actions
1	COUGH	Do you have a cough?	Single Choice	<input type="button" value="Options Routing"/>	<input type="button" value="Edit"/> <input type="button" value="Delete"/>
2	COUGH_TYPE	Define your cough type:	Single Choice	<input type="button" value="Options Routing"/>	<input type="button" value="Edit"/> <input type="button" value="Delete"/>

Figure 30 - Simple Questionnaire Details

VIEW COMPOSITE QUESTIONNAIRE

Title (IT): Codename:

Types: Status:

Upload Image: Color: Description:

No file chosen

QUESTIONNAIRE ROUTING

- Send Questionnaire: IF All the following conditions are met:
 - AND
 - THEN: Send Questionnaire: Continue:
 - Send Questionnaire: Continue:
 - Send Questionnaire: End Questionnaire
- ELSE: New Condition: IF All the following conditions are met:
 - AND
 - THEN: Send Questionnaire: Continue:
 - Send Questionnaire: End Questionnaire
 - ELSE: New Condition: IF All the following conditions are met:
 - AND
 - THEN: Send Questionnaire: Continue:
 - Send Questionnaire: End Questionnaire
 - ELSE: Send Questionnaire: End Questionnaire

innovation sprint team
Clara Chagnon - Jean-Charles St
1050 Brussels, Belgium

Figure 31 - Composite Questionnaire

9 USERS

9.1 ROLES & PERMISSIONS

This section is used by the admin to create the main roles and their permissions in the portal sections. Permissions can be configured for viewing, editing and delete, as depicted in Figure 32.

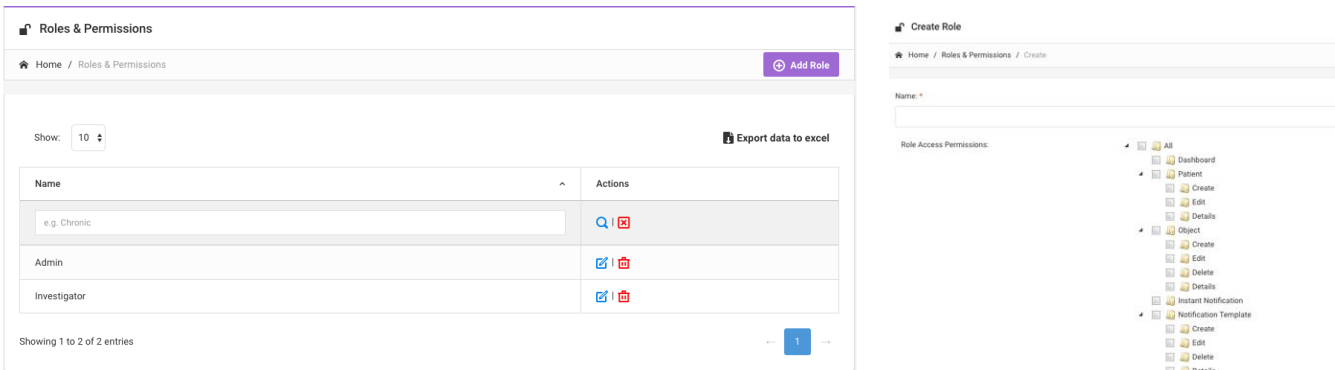


Figure 32 Role Management and Add new Role

9.2 USER LIST

In the users list you can find all the portal users that are assigned in the study. The study admin can create or invite new users or assign existing ones to a specific study with a permission role. The user provides the email of an investigator that triggers an auto generated email to that email. Upon receipt, investigators need to confirm the email and follow a registration. This list can be then exported to an excel, as depicted in Figure 33.

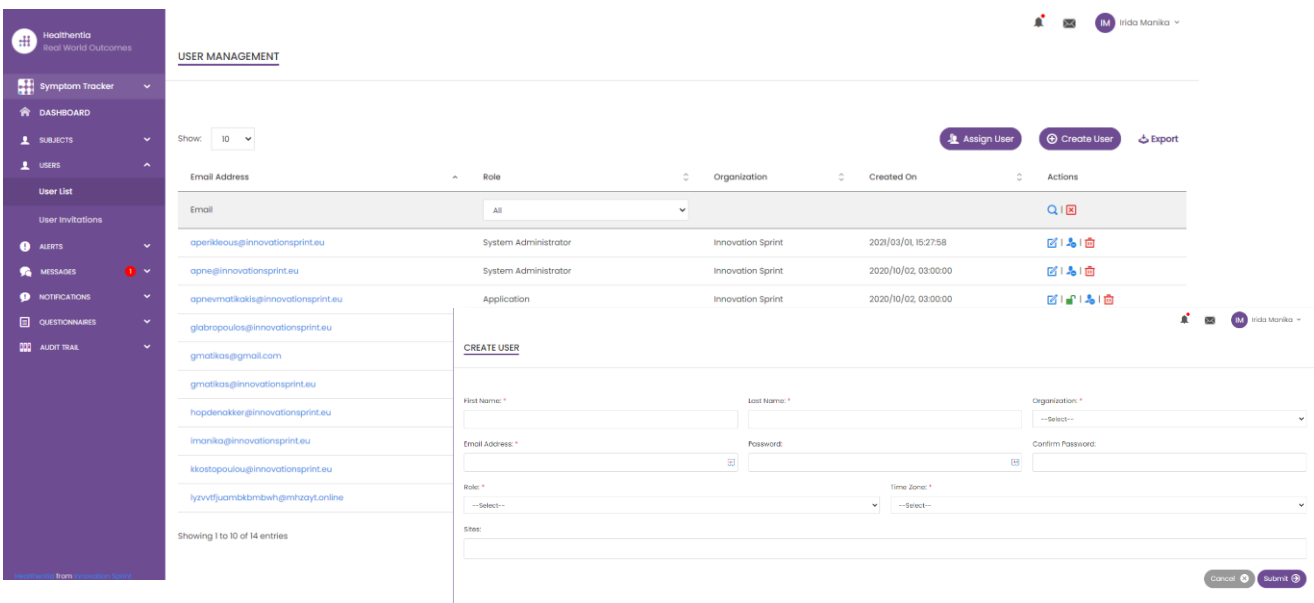


Figure 33 User Management and User Creation

10 AI MODULE

10.1 DEEP PHENOTYPING

Further to the currently supported features of Healthentia, i.e. collecting data from patients and making it available to an EDC for further statistical evaluation, the wealth of information collected is used in real time by the Healthentia AI/ML module to create clusters of patients' phenotypes and provide useful insights for clinical endpoints. Based on the patients' vector data, we create behavioural phenotype models and we cluster patients' profiles into them. Using the clustering mechanism, we can characterise patients' habits and detect deviations from them to generate alarms. The clustering of patients into behavioural phenotypes creates a valuable content to associate them with drug efficacy and support the self-configured adaptive trials. Finally, AI/ML algorithms can train models to predict outcomes, e.g. VAS, QoL, bleedings, falls, before the patients report them, by feeding the system with the automatically collected vectors.

10.2 PREDICTION SERVICES

The deep phenotyping process described in the previous section, enables a number of forecasting services, among them the ability to predict study endpoints, or behavioural biomarkers. In Figure 34, one can see how activity patterns are recognized and characterized, while the system is able to provide predictions or alarms.

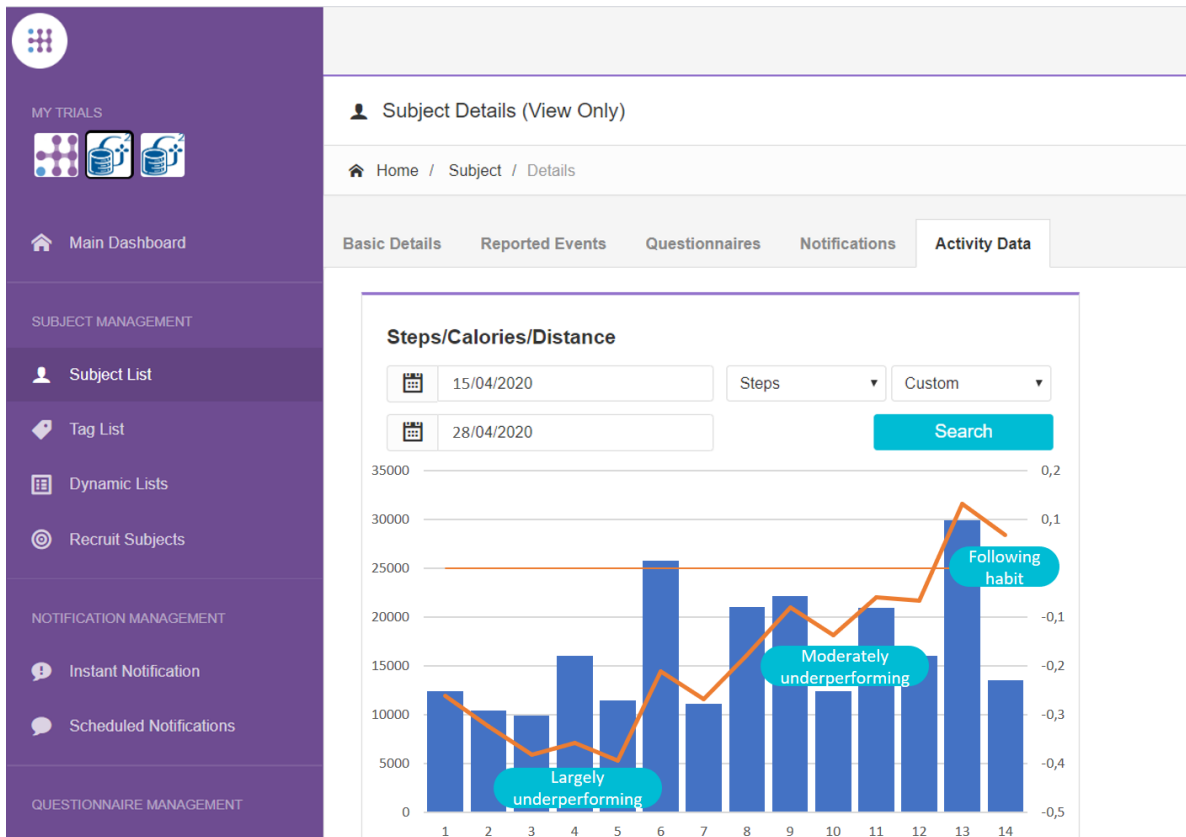


Figure 34: Activity patterns for specific subject

Further to the patten detections, the system uses AI/ML algorithms to break down the distribution of several behavioral biomarkers and evaluate their prediction capacity; see Figure 35 and Figure 36.

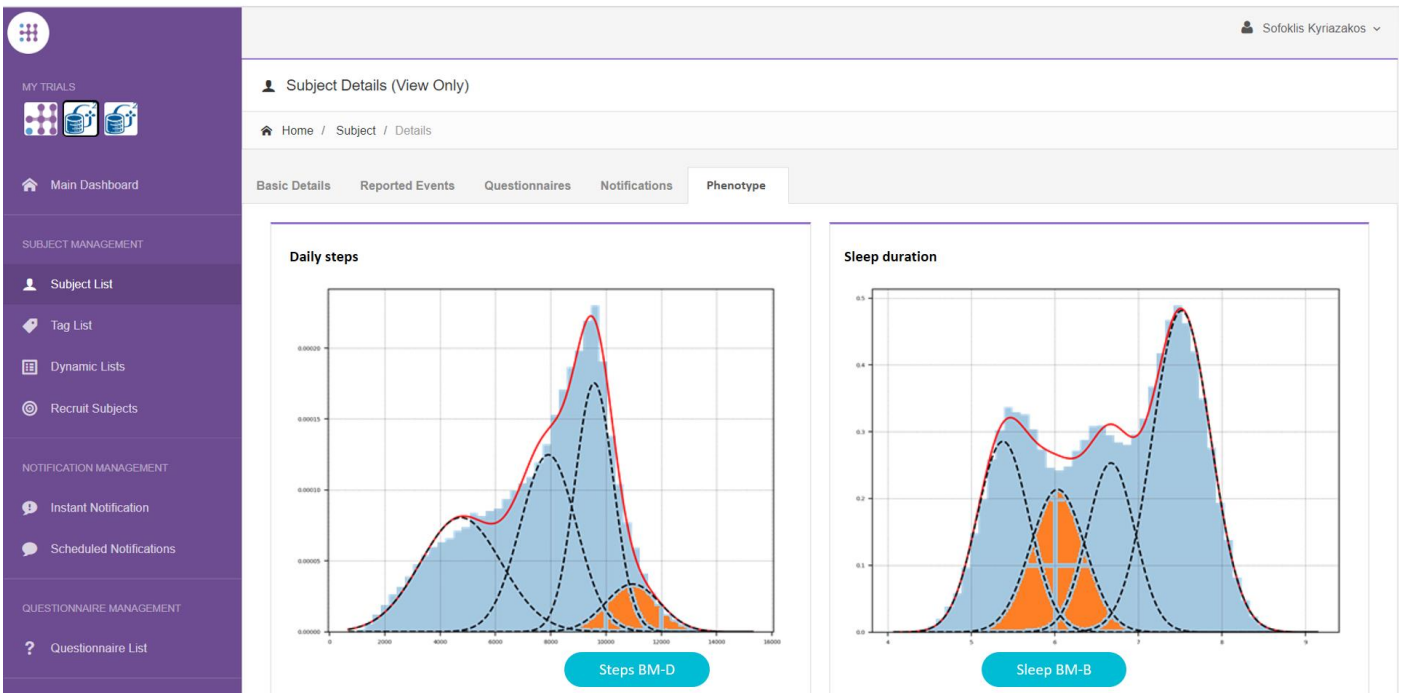


Figure 35: Distribution of activity biomarkers

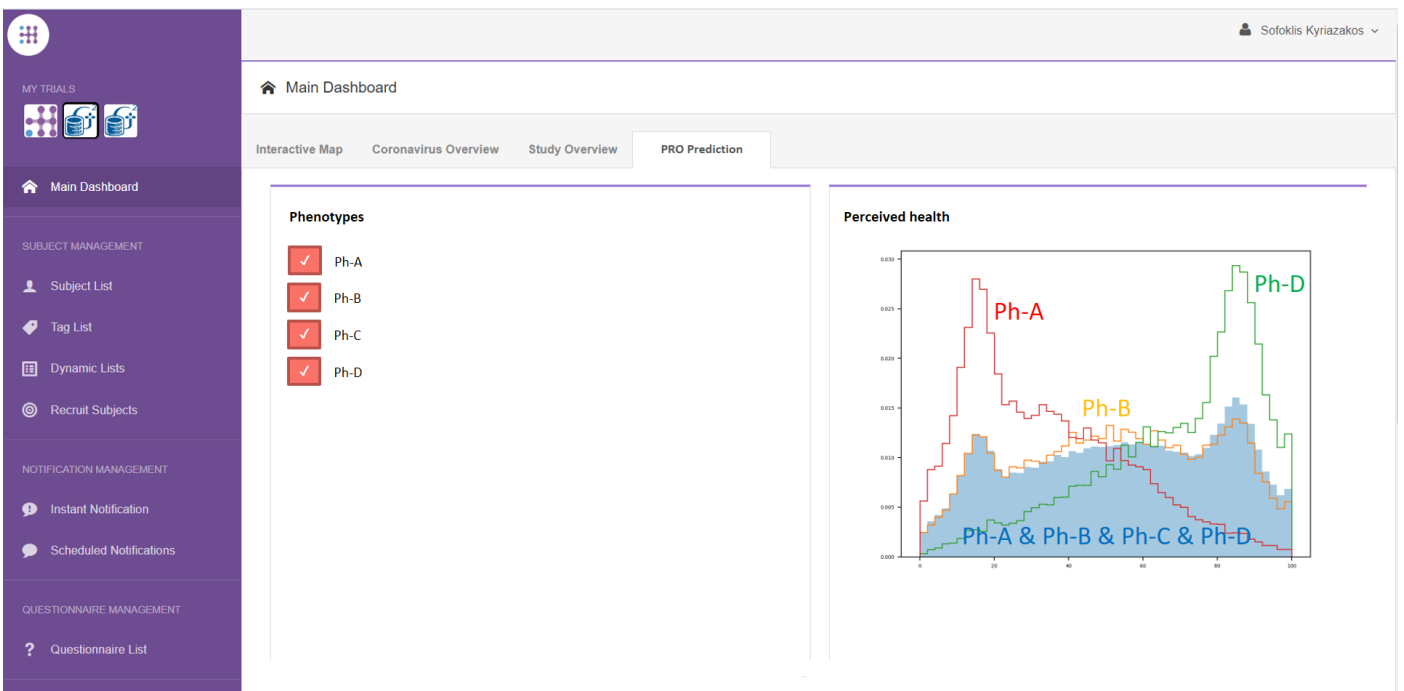


Figure 36: Prediction capabilities of behavioral phenotypes

11 AUDIT TRAIL

11.1 PORTAL LOG

In the section of Log Management all actions that users do from viewing to editing or deleting. The log list of actions can be filtered by date from the top of the page, while each column on the table allows the search for a specific result. You can also sort by alphabetic or numeric order per column. When viewing the log details you can get more information on the reported action. As in all sections of the portal all data are exportable to an excel file.

The screenshot displays the 'PORTAL LOG' section of the Healthentia portal. On the left is a navigation sidebar with options like Symptom Tracker, Dashboard, Subjects, Alerts, Incident, Messages, Notifications, Questionnaires, System, Devices, and Audit Trail. The main area shows a table of log entries with columns for Email, Role, and Description. A 'Log Details' modal is open, showing fields for Email (palak@evincedev.com), Role (Admin), Action Performed (View Details of Patient), Time Stamp (05/12/2018 10:11:01), and a detailed Description of the action.

Email	Role	Description
gmatikas@innovationsprint.eu	System Administrator	Logout by: gmatikas@innovationsprint.eu on 19/05/2021 18:31:40.
gmatikas@innovationsprint.eu	System Administrator	View Details of Subject Id:5C9AA by: gmatikas@innovationsprint.eu on 19/05/2021 18:34:17.
gmatikas@innovationsprint.eu	System Administrator	View List of Subject by: gmatikas@innovationsprint.eu on 19/05/2021 18:34:15.
gmatikas@innovationsprint.eu	System Administrator	View List of Subject by: gmatikas@innovationsprint.eu on 19/05/2021 18:34:14.

Figure 37 Log Management & Details

11.2 APPLICATION LOG

The application log, provides information about the actions of the subjects, e.g. their participation in questionnaires, as shown in Figure 38

The screenshot shows the 'Application Log' section. The left sidebar includes options like My Trials, Main Dashboard, Subject Management, Notification Management, Questionnaire Management, and User Management. The main area displays a table of application log entries with columns for Subject ID, Description, Log Type, and Timestamp. The entries list various symptoms and assessments such as 'Initial COVID-19 Assessment', 'Abdominal pain', 'Diarrhea', 'Nausea', 'Muscle Pain', 'Headache', 'Fatigue', 'Difficulty of breathing', 'Cough', and 'Oxygen saturation'.

Subject ID	Description	Log Type	Timestamp
6CEFC	Initial COVID-19 Assessment	Questionnaire	27/04/2020, 17:36:24
HTAXF	Abdominal pain	Questionnaire	27/04/2020, 15:08:36
HTAXF	Diarrhea	Questionnaire	27/04/2020, 15:08:30
HTAXF	Nausea	Questionnaire	27/04/2020, 15:08:24
HTAXF	Muscle Pain	Questionnaire	27/04/2020, 15:08:19
HTAXF	Headache	Questionnaire	27/04/2020, 15:08:04
HTAXF	Fatigue	Questionnaire	27/04/2020, 15:07:51
HTAXF	Difficulty of breathing	Questionnaire	27/04/2020, 15:07:39
HTAXF	Cough	Questionnaire	27/04/2020, 15:07:31
HTAXF	Oxygen saturation	Questionnaire	27/04/2020, 15:07:23

Figure 38 Application Log Details