Fondazione Monasterio
la ricerca che cura

InteropEHRate
EHR in people's hands across Europe

INTEROPEHRATE SOLUTIONS FOR HEALTH RESEARCH DATA-SHARING

STEFANO DALMIANI

HEAD ICT AREA

MONASTERIO FOUNDATION RESEARCH HOSPITALS - FTGM

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 826106

SCENARIO 3 - HEALTH RESEARCH STUDY

- **Sharing/donate health data**

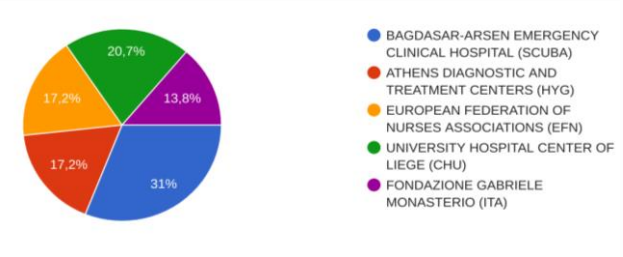
- ***Support the effort spent for patient selection and data collection***

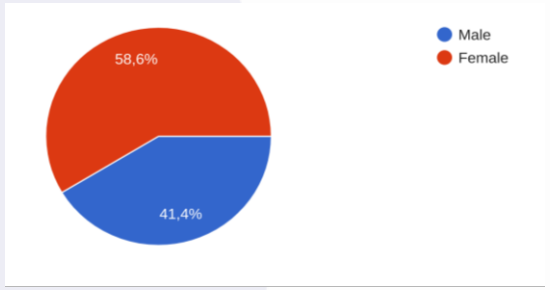
A population of patients have a collection of clinical data related to their status and clinical condition.

A Research Organization defines a research protocol with an associated selection criteria and clinical dataset

FINAL USERS - RESEARCHERS FOCUS GROUPS

- **The researchers focus group was formed by professionals performing clinical research in different settings, such as pulmonology, cardiology, gynaecology, neurosurgery and cardiac surgery:**
  - *GABRIELE MONASTERIO TUSCANY FOUNDATION (FTGM).*
  - *BAGDASAR-ARSEN EMERGENCY CLINICAL HOSPITAL (SCUBA).*
  - *ATHENS DIAGNOSTIC AND TREATMENT CENTERS (HYG).*
  - *UNIVERSITY HOSPITAL CENTER OF LIEGE (CHU).*
- **3 cycles - 4 focus groups of (22+29+29) researchers**
- **Analyzed different types of health research, e.g.:**
  - *Epidemiological studies (Retrospective, Retrospective+Prospective)*
  - *Experimental trials of drugs/devices/etc., cohorts studies (Prospective, Retrospective+Prospective)*



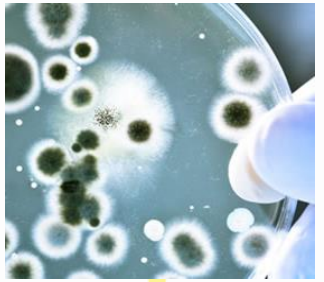


RESEARCHERS FOCUS GROUPS - REQUIREMENTS

- **Want the ability to reach a patient trough the smartphones or direct contact**
  - *send personal/general final results of the study*
- **Want to receive statistical information about the matching rate of inclusion/exclusion criteria of studies and patient approval rate**
  - *Also to evaluate cohorts sizes*
- **Want to manage Patient Localization (current or preferred)**
  - *Not necessary to know the location*
- **Want to maintain the reference of the author/producer (HCP, Hospital, patient, caregiver, etc) for collected data**

RESEARCHERS FOCUS GROUP: RESPONSE

- **Most researchers like very much the idea of getting their data directly from patients.**
  - *especially if these data are certified by hospitals, avoiding manual data entry by the patients.*
  - *they fear that elderly patients would not adhere to this solution.*
- **They like the possibility of allowing patients to apply for a research study using a personal app**
  - *This represent an effective way of increasing, in a simple manner, the number of participants in the study.*
- **Some Epidemiological studies do not need to manage a local population**
  - *They work with large anonymous cohorts of patients*
- **Experimental trials need a population with a real follow-up**
  - *consider important to perform studies on a local population, suitable for performing instrumental control examinations at regular intervals with direct contacts with the patients*



SCENARIO 3 - HEALTH RESEARCH STUDY

Patients:

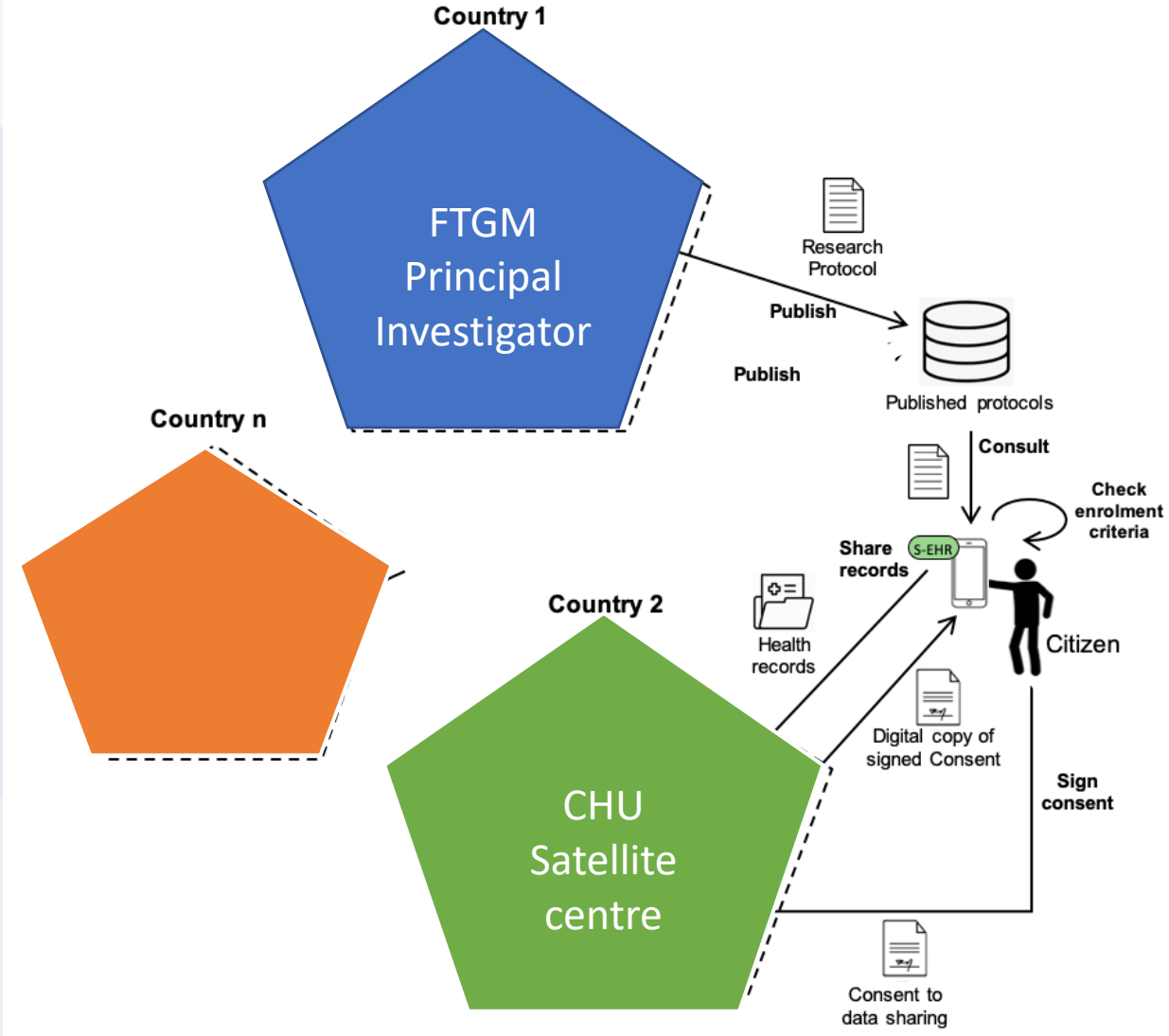
- *Get involved in studies related to their conditions*
- *Worried by potential data misuse associated with data sharing*

Researchers:

- *Retrospective studies*
- *Prospective studies*
- *Cohort selection (criteria) and management*
- *Consent management*
- *Participation withdrawals*
- *Exit criteria*

OPEN RESEARCH NETWORK

- *constituted by **patients** and a group of **research organizations** (Hospitals, Universities, Research Centres, Institutes) that **exploit a common IT infrastructure**, **Data Protection policies**, etc.*
- *allows the participating **researchers** to **enrol citizens** in their research studies (described by specific research protocols) and **collect** health data for the studies **directly** from the enrolled **citizens**.*
- ***Researchers share** a **common set of vocabularies**, specified in the InteropEHRate profiles, used to **refer to any health data** required by the research studies performed on the InteropEHRate Open Research Network*



DEMONSTRATOR: CLINICAL RESEARCH PROTOCOL

INTERopehrate VALidation – INTERVAL Study: observational, pilot study on the feasibility and ease of use of the InteroEHRate (Interoperable EHRs at user edge) tools

- INTERVAL is a prospective, multicenter (cross border), observational study.

- Primary objective
  - *Patients who have installed and populated a S-EHR within the InteropEHRate project will be asked, via mobile app notification, to share some of their clinical data for the aims of the INTERVAL study.*
  - *Among S-EHR app users, only those fulfilling pre-specified inclusion criteria will be contacted via mobile app and asked to sign the informed consent for participating in the study.*

- Secondary objectives
  - *#1: The relative amount of patients with data available on arterial blood pressure and anti-hypertensive medications and possible side-effects (patient questionnaire) will be calculated. The prevalence of reported side-effects will be assessed and the association between each side-effect and disease/patients characteristics will be investigated.*
  - *#2: Anonymized data collected by the investigators will be decrypted and compared to source data from patients S-EHR app. A pre-specified threshold of >99.5% for data consistency will be considered as indicative of adequate accuracy.*

INTERVAL CLINICAL RESEARCH PROTOCOL

- ***Inclusion criteria***

  1) age > 18 years at the moment of recruitment

  2) history of hypertension and therapy with anti-hypertensive drugs

  3) Ability to understand study instructions

  4) ability to provide informed consent.

- ***Exclusion criteria***

  1) Denial or inability to provide informed consent.

  2) Diagnosis of dementia or cognitive decline that makes him/her unable to understand study information

INTERVAL CLINICAL RESEARCH PROTOCOL

- the following data were retrieved from patients' S-EHR app:
  - *age and gender;*
  - *year of hypertension diagnosis;*
  - *latest blood pressure measurement;*
  - *latest creatinine value (last year max);*
  - *latest echocardiogram, including left ventricular ejection fraction and interventricular septum thickness;*
    - Report and DICOM file (anonimized)
  - *latest ECG*
    - Report and DICOM/pdf file (anonimized)
  - *concurrent medications*

Fondazione CNR/Regione Toscana per la Ricerca Medica e di Sanità Pubblica
(L. R.T. n. 85/2009)

Version N°1.0 12/10/2020

Case Report Form

Patient ID: ITA_907_____

Section 1: Patient general data

Surname, initial		Name, initial	
		Allergies	
Gender	[] M [] F	Date of birth (DD/MM/YYYY)	

Section 2: Disease related data

Year of hypertension diagnosis	
blood pressure measurement SYS/DIA (mmHg/mmHg)	
Latest creatinine (mg/dL)	
Current Medications	
EKG report signal	
Echocardiogram report and video	
Latest left ventricular ejection fraction (%)	
Latest interventricular septum thickness (mm)	

INTERVAL CLINICAL RESEARCH PROTOCOL

patients were asked to fill a questionnaire focused on the perceived side effects of antihypertensive medications

Section 3: Questionnaire on side effects

Patient ID: **ITA_907_** _____

(the patients selects the drug from the list of current/past antihypertensive drugs)

Repeat for each current/past antihypertensive drugs associated to adverse effects:

Name of the DRUG	
1. Type of symptom(s)	a. Cutaneous symptoms (please describe)
	b. Nausea
	c. Constipation
	d. Palpitation
	e. Cough
	f. Swollen feet or legs
	g. Cold hands or feet
	h. Cramps
	i. Persistent dry cough
	j. Frequent urination
	k. Decreased sexual desire
	l. Other (please specify)
2. How long the adverse event last?	< 1 day
	1 day to 1 week
	1 week to 1 month
	> 1 month
3. Did you withdraw the drug?	Yes NO
4. Did the adverse reaction require specific treatment?	Yes NO

INTERVAL CLINICAL RESEARCH PROTOCOL CRF

Section 4: Feasibility assessment

PATIENT SATISFACTION QUESTIONNAIRE OF INTEROPEHRATE PROJECT

Patient Code: ITA_907_____ Date: ___/___/_____

Preliminary Questions

Age: _____

Sex: _____

Educational level:

No studies ☐
Some School ☐
Graduate ☐
Postgraduate ☐

Urban zone (rural/urban): _____

Profession (if retired, previously exercised): _____

_____

Do you routinely use apps of your smartphone/tablet in your daily life (excluded messages and phone calls)?

Yes No

Do you have wifi/xDSL/3g/4g connection in your home?

Yes No

What satisfaction level do you have about the clinical staff explanation or instructions manual for use and maintenance of the system?

☐Very dissatisfied ☐Dissatisfied ☐Satisfied ☐Very Satisfied

How would you rate the ease of use of the platform?

☐ Very difficult ☐Difficult ☐Easy ☐Very easy

What satisfaction level do you have about the received clinical care provided by the use of the platform?

☐Very dissatisfied ☐Dissatisfied ☐Satisfied ☐Very Satisfied

If you had any technical problem, were you satisfied with the solution of it?

☐Very dissatisfied ☐Dissatisfied ☐Satisfied ☐Very Satisfied

How would you rate the mobile device operation?

☐ Very unsafe ☐ Bit unsafe ☐Fairly safe ☐Very safe

Has the INTEROPEHRATE System helped you to understand better your disease?

☐Strongly disagree ☐Disagree ☐Agree ☐Strongly Agree

Has the INTEROPEHRATE System allowed you to have more autonomy to access to hospitals or care Centres?

☐Strongly disagree ☐Disagree ☐Agree ☐Strongly Agree ☐

Do you consider that INTEROPEHRATE system has a major role in communicating with foreign healthcare provider?

☐Strongly disagree ☐Disagree ☐Agree ☐Strongly Agree ☐

The INTEROPEHRATE System has had a positive impact in the way that you live with your disease.

☐Strongly disagree ☐Disagree

Do you consider that your family/caregivers have been benefited from your use of the INTEROPEHRATE system by a lower possibility of psychological or physical burden that can cause the disease?

☐Strongly disagree ☐Disagree ☐Agree ☐Strongly Agree

Please, mark from 1 to 4 your satisfaction level about the INTEROPEHRATE system.

1 2 3 4
|_____|_____|_____|

Where value 1 is considered as *"Very* dissatisfied" and 4 as *"Very satisfied".*

Would you recommend other people to use the INTEROPEHRATE System?

1 2 3 4
|_____|_____|_____|

Where value 1 is considered as *"Never"* and 4 as *"Certain".*

INTERVAL CLINICAL RESEARCH PROTOCOL - RDD

- **Research Definition Document, downloaded by each smartphone**
- **RDD contains an accurate and structured description of:**
  - *Study aim and description, represented in the Natural Language of the Patient*
  - *Selection criteria (inclusion and exclusion)*
  - *Exit criteria*
  - *Starting and ending dates*
  - *Requested data and anonimization/pseudonimization constraints*
    - Patient questionnaires represented in the Natural Language of the Patient
  - *Prinicipal investigator and reference reseach centres*
    - Multiple research centres supported, selectable by the patient
  - *Information document (consent) for the patient in different languages:*
  - **Enable the smartphone to show the proper version according to the patient's spoken language**

INTERVAL CLINICAL RESEARCH PROTOCOL - RDD

- **Powerful selection/exclusion criteria: capable to include many diseases classified in different vocabulary without specifying the whole list of codes**
- **ICD9: 401 Essential hypertension**
  - *Specific code 401.0 Malignant essential hypertension convert*
  - *Specific code 401.1 Benign essential hypertension convert*
  - *Specific code 401.9 Unspecified essential hypertension*
- **ICD10:**
  - *I10 Essential (primary) hypertension*
  - *I15 Secondary hypertension*
    - I15.0 Renovascular hypertension
    - I15.1 Hypertension secondary to other renal disorders
    - I15.2 Hypertension secondary to endocrine disorders
    - I15.8 Other secondary hypertension
    - I15.9 Secondary hypertension, unspecified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INTERVAL CLINICAL RESEARCH PROTOCOL - RDD

- **Powerful data requirements description: includes a range of drugs classified in multiple vocabulary without specifying the whole list of codes**
- **ATC : ANTIHYPERTENSIVES – C02***
  - *C02A Antiadrenergic agents, centrally acting*
  - *C02B Antiadrenergic agents, ganglion-blocking*
  - *C02C Antiadrenergic agents, peripherally acting*
  - *C02D Arteriolar smooth muscle, agents acting on*
  - *C02K Other antihypertensives*
  - *C02L Antihypertensives and diuretics in combination*
  - *C02N Combinations of antihypertensives in ATC gr. C02*
- **C02* +C03* + C05* + C09* = 90 drug classes**


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INTERVAL CLINICAL RESEARCH PROTOCOL - RDD

- **RDD specifies data selection and extraction from S-EHR: fulfil GDPR minimization principles, request and process only the minimum set of data to pursue the study objective**
- **Implement minimal data requirements with a HL7 FHIR extension**
  - *Date of birth and gender extracted from Person Resource*
  - *Any other Person data remains in the patient's phone*

Name	Flags	Card.	Type
Person	TU		DomainResource
identifier		0..*	Identifier
name	Σ	0..*	HumanName
telecom	Σ	0..*	ContactPoint
gender	Σ	0..1	code
birthDate	Σ	0..1	date
address		0..*	Address
photo		0..1	Attachment
managingOrganization	Σ	0..1	Reference(Organization)
active	?! Σ	0..1	boolean
link		0..*	BackboneElement
target		1..1	Reference(Patient | Practitioner | RelatedPerson | Person)
assurance		0..1	code

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Thank you!

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HEALTH RESEARCH DATA-SHARING RESULTS SUMMARY

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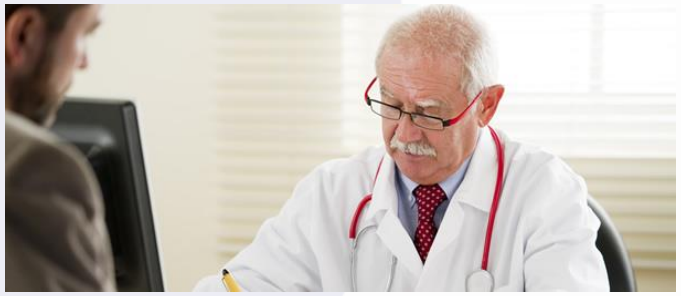
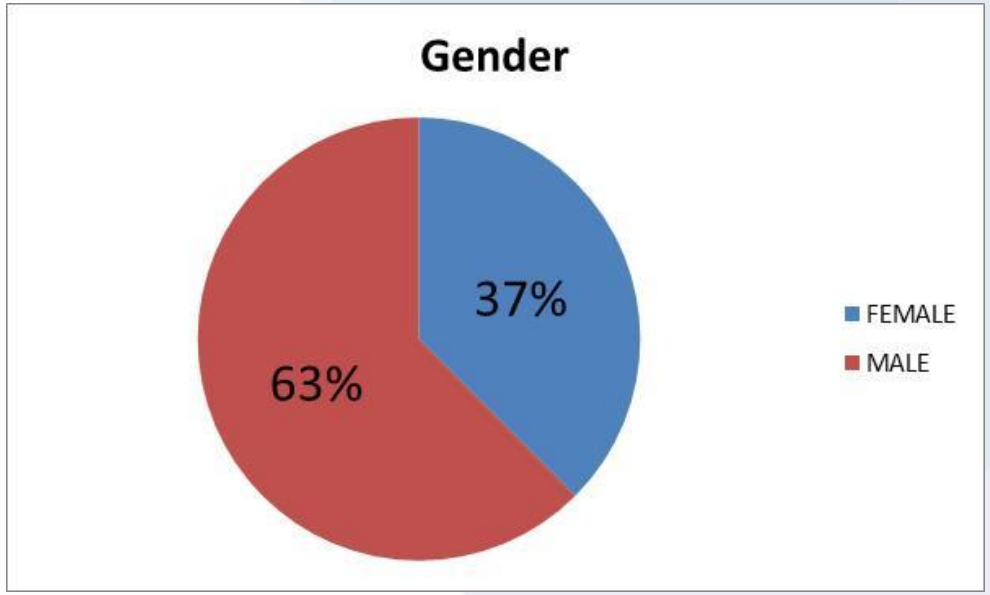
PILOT RESULTS

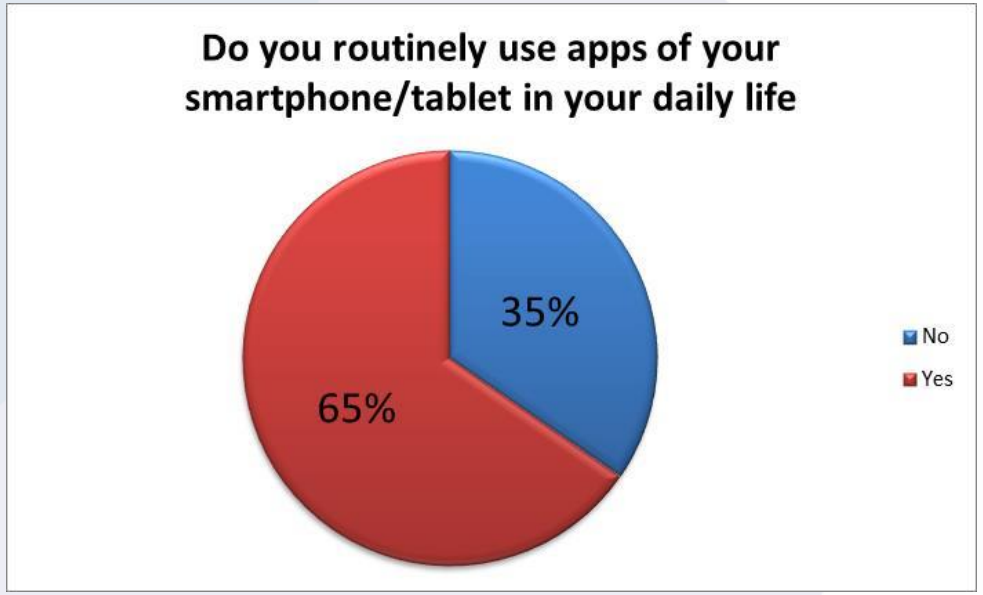
- **Activities: june 2022 - september 2022**
- **Participants:**
  - Patients/persons (& family informal Caregivers) : 32 people in experimental group + 6 people in control group (application of defined cohort selection criteria)
  - Indirect involvement (data production): Healthcare Professionals involved in data collection for Pilot 1 and 2
  - Researchers: 4 CHU researchers + 4 FTGM researchers (nurses and cardiologists) + 1 P.I. FTGM
- **Collected images and signals**



INTERVAL RESULTS - PATIENTS

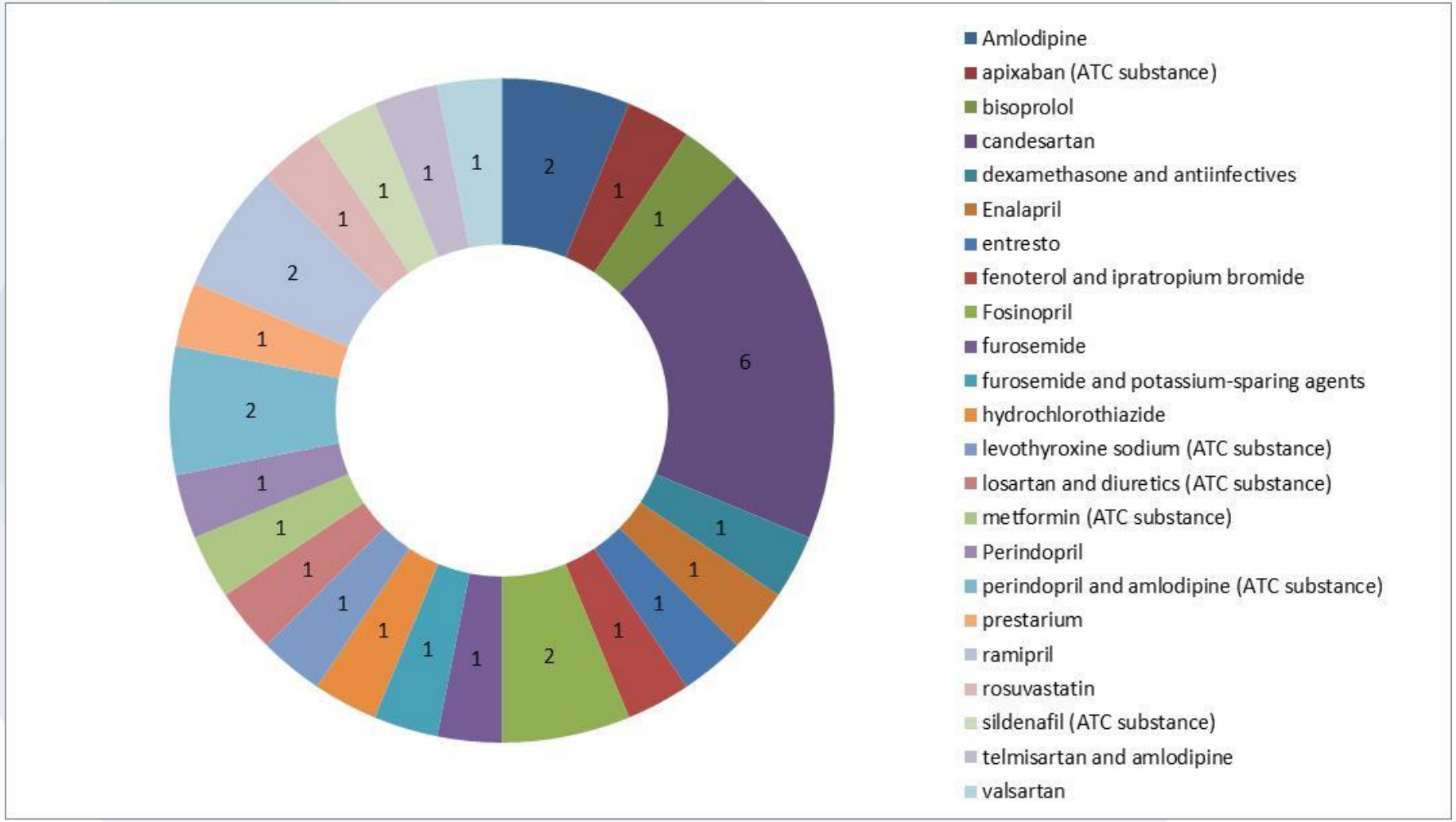
- **Age: 42y to 88y**
- **Average value 62 y**





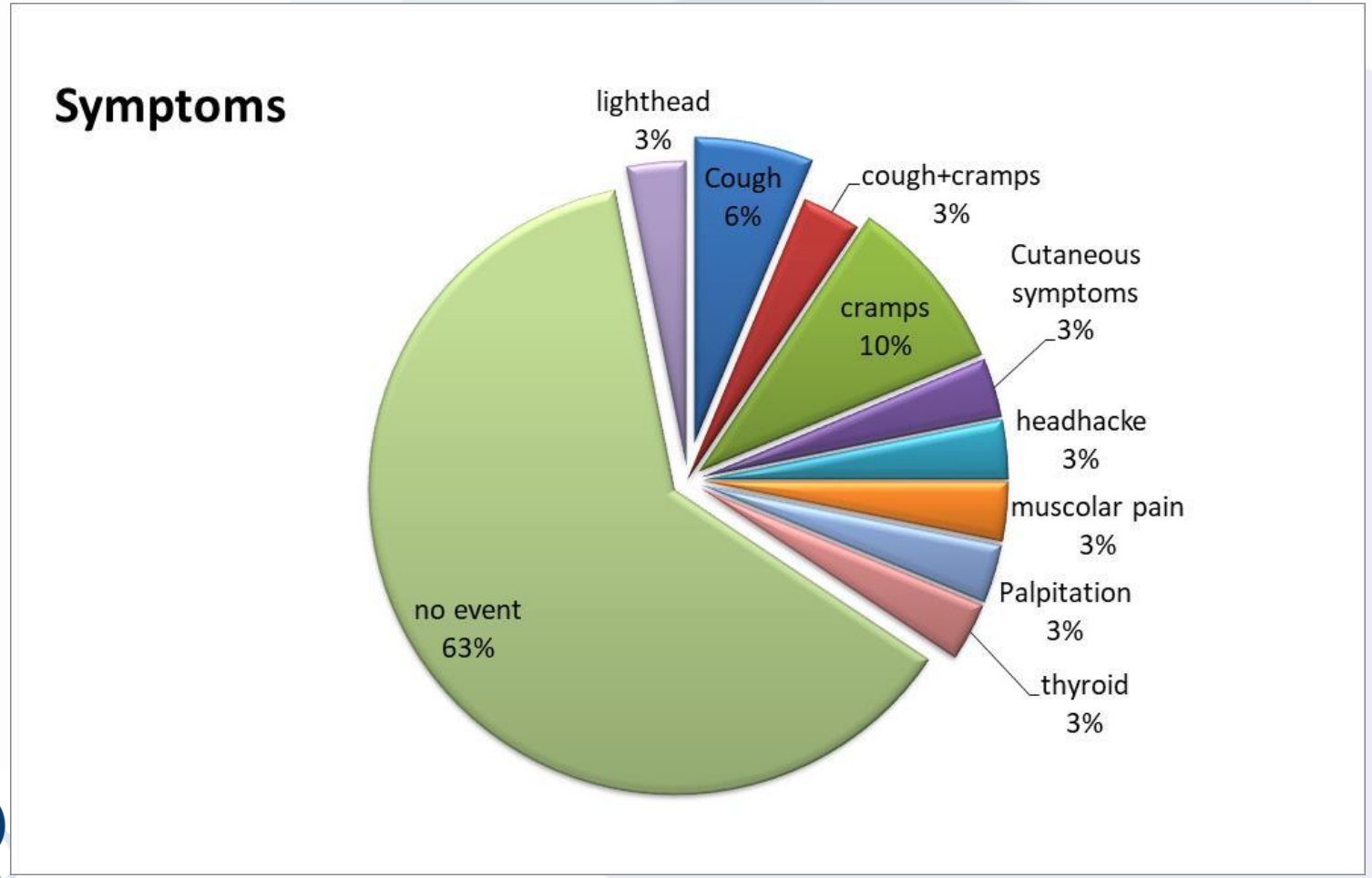
INTERVAL RESULTS - DRUGS

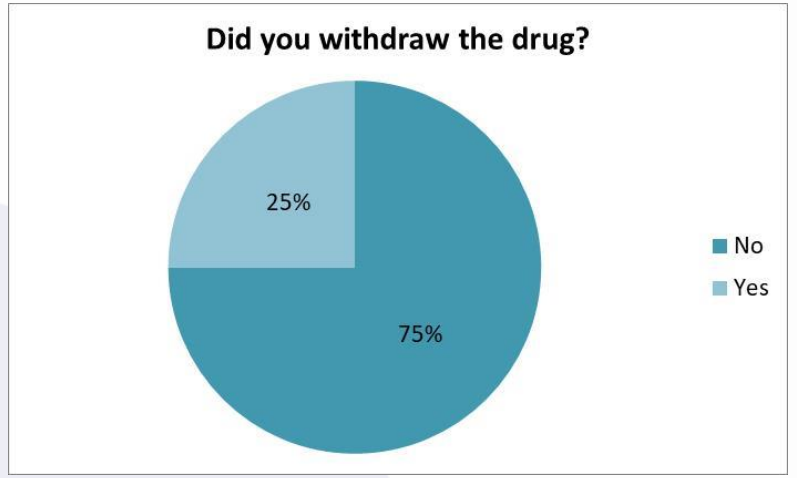
- **23 different drugs and ATC codes**

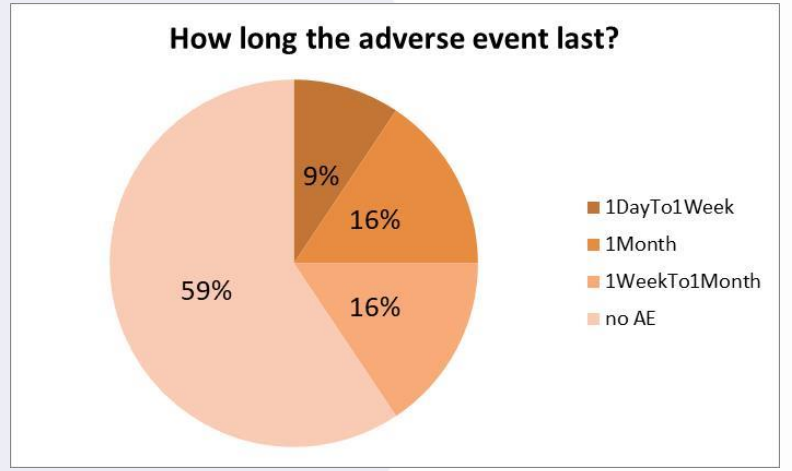


INTERVAL RESULTS – ADVERSE EVENT

- **15 patient / 32 reported brief adverse effects**

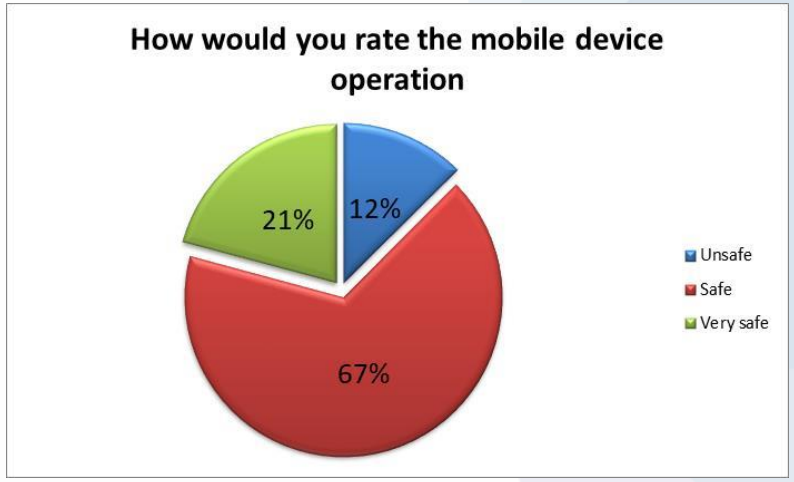


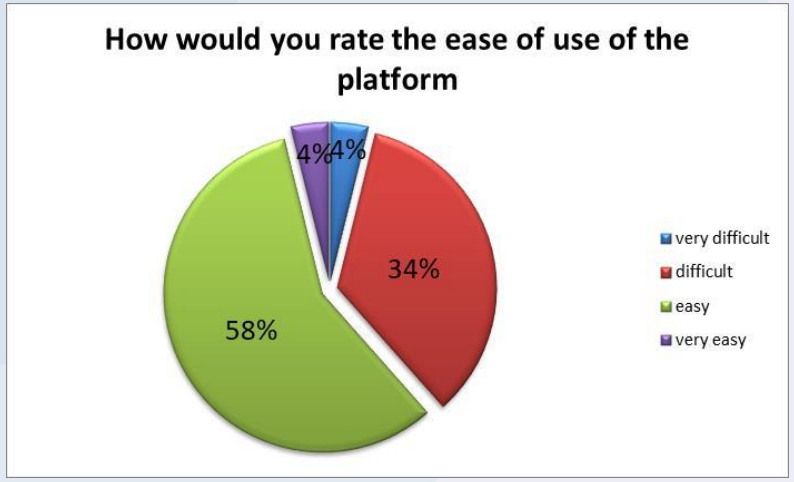


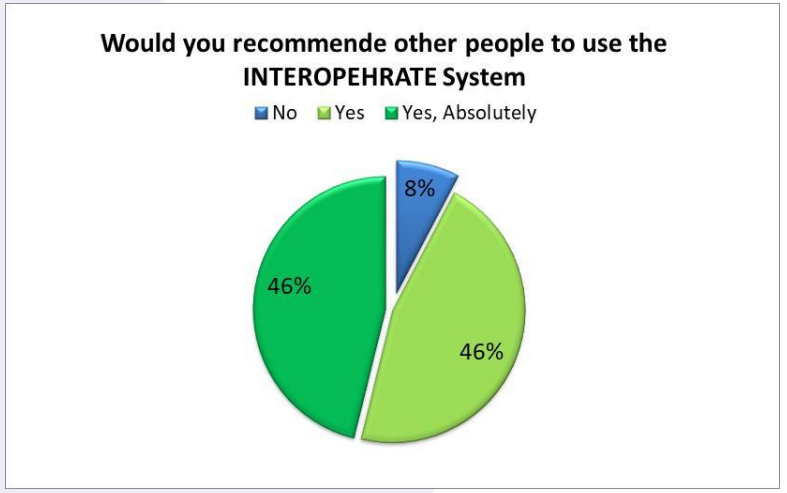


INTERVAL RESULTS

- **Used INTERVAL and PSSUQ questionnaires to collect users' feedbacks.**
- **Patients' feedback (INTERVAL questionnaire) : good response**







- **Researchers' feedback (PSSUQ): good response**

CONCLUSIONS

- **InteropEHRate represents an ambitious way to collect data directly from the patient and their smartphone, while preserving personal data protection, security and integrity**

- **Connected to dataspaces initiatives (personal dataspace)**
  - *EHDS European Health DataSpace secondary use (session 3+4 this afternoon)*

- **Real world evidences collected directly from the patient**
  - *Proof of concept*

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