

1. The HEARTFAID Scenarios

1.1 The validation sites

Three validation sites have been foreseen for the HEARTFAID platform (HFP) and these sites will test the functionalities of the HFP in all of the typical environments served for the support of the heart failure (HF) patient: home, the general practitioner (GP)'s office, the specialized cardiology hospital (both outpatient and inpatient services).

1.1.1 Profile of the first validation site

The first validation site will be located in Krakow under the supervision of Jagiellonian University. Jagiellonian University is the oldest and most prestigious university in Poland (founded in 1364) and the second oldest in the Central Europe. It is a member of the Utrecht Network, the Coimbra Group and the SYLFF Institutions' Network. It has the biggest number of publications per academic teacher and the biggest number of quotations per academic teacher (the Philadelphia list) in Poland. Jagiellonian University pursues a programme of international cooperation with academic centres abroad involving staff and student exchange schemes, joint research projects, participation in international conferences, networks, university programmes and projects and cooperation with international organizations.

The structure of the Jagiellonian University includes thirteen faculties (with about 42.000 students), three of which form the Medical College (Faculties of Medicine, Pharmacy and Health Protection). The Faculty of Medicine is currently the biggest organizational unit of Jagiellonian University. The Faculty's scientific activities cover a wide range of basic and clinical research in all fields of medicine.

In HEARTFAID project, Jagiellonian University is represented by I Cardiac Department headed by Prof. Kalina Kawecka-Jaszcz. I Cardiac Department is a full-profile unit offering extensive diagnostic and therapeutic services covering the entire scope of cardiology, including the management of ischaemic heart disease (conservative and interventional), hypertension, arrhythmias, heart failure, myocarditis as well as valvular and congenital heart disease. The Department includes inpatient unit (Clinical Unit - 35 beds and Intensive Care Unit – 7 beds) with a total of 1500 hospitalizations per year, as well as outpatient facilities - Cardiology Clinic, Hypertension Clinic and Cardiologic Rehabilitation Day Hospital. The personnel of the Department consists of c. 70 persons, including over 20 physicians. The activity of the Department includes interventional cardiology procedures: pacemaker implantations, RF ablations, cardioverter-defibrillator implantations, coronary angiography procedures, percutaneous coronary interventions, including primary PCI and peripheral arteriography (carotid, renal and lower extremities).

The clinical activity of the Department goes in parallel with its research activity (documented by a number of abstracts presented at national and international scientific meetings and a consistent number of publications in peer reviewed journals) and with clinical teaching of Medical Faculty students as well as postgraduate teaching of physicians specializing in internal medicine, cardiology and hypertensiology.

1.1.2 Profile of the second validation site

The second validation site will be located in the Cardiovascular Disease Unit, in Catanzaro under the supervision of University of "Magna Graecia". The University in Catanzaro was founded in 1982 as a branch of the University of Reggio Calabria,

which is in the same region, in Calabria. In January 1998, University of "Magna Græcia" was officially established.

The Campus has three Faculties, forty degree courses and numerous specialization schools. The Department of Clinical and Experimental Medicine includes the majority of clinical and biological research units. The Department promotes and carries out research activities in cooperation with the academic research and with other private and public organizations and much of the work consists of translating basic laboratory work into medical and clinical applications.

From March 2006 the Catanzaro University Hospital is located in a new building: "Campus Germaneto". The new hospital provides 52000 square meters of surface, with large hospitalization areas, numerous laboratories and out-patient's departments, a surgery complex with a very advanced structures: a recovery room for post-surgery therapy, a sophisticated imaging diagnostic system (Pet/CT, NMR, nuclear imaging, etc.), with several medical instruments for a full cost of 52 thousands of euros, an informatic network that permits to optimize diagnosis and therapy timing.

130 physicians, 450 medical and administrative operators and 90 university researchers and professors are working in the new University Hospital and the structure is serving several thousands of in- and out-patients.

Actually, Cardiovascular Disease Unit (CDU) is deeply involved in the diagnosis and management of patients with several cardiovascular diseases as essential hypertension, coronary artery disease, valvular disease, cardiomyopathy and congestive heart failure. It's an operative unit that includes one full professor of internal medicine, one confirmed researcher in geriatrics, two PHD fellows, three cardiologists, and about 13 young physicians in the post graduate schools of internal medicine and geriatrics. CDU has 6 beds for ordinary admissions, two day-hospital seats, and several cardiovascular instrumental means (Echocardiograph VIVID7/VIVID 7 PRO for vascular and cardiologic studies, Hokanson plethysmographes EC 5R to measure the flow changes during increasing doses of vasoactive substance to test endothelial function, SphygmoCor to evaluate arterial stiffness, 24-h Holter ECG monitoring, cardiopulmonary stress test on treadmill, 24-h ambulatory blood pressure monitoring, etc.).

In CDU a lot of clinical trials are going on, regarding heart failure, arterial hypertension, etc. (Aloft, Gissi-HF, Gissi-AF, Cardiosis, Scout, Allay, etc.).

CDU is involved in many national and international research projects (MIUR, SOPHIA Study, etc.) about clinical and pharmacogenomic topics in arterial hypertension, insulin-resistance and diabetes, heart failure, etc.

In addition, in the last years our work has been focusing in genetic and molecular biology related to pathophysiology of cardiovascular diseases. In fact CDU collaborates with a molecular biology laboratory; in particular experiments on endothelial cells are performed to analyze the NO pathway that is involved in cardiovascular disease pathogenesis, moreover also genetic polymorphisms of genes involved in cardiovascular diseases are studied, knowing the genetic background of patients.

In conclusions, we have acquired a specific competence for phenotypic characterization of cardiovascular patients identifying the target-organ damage related to cardiovascular risk factors, utilizing appropriate instrumental and laboratory means.

1.1.3 Profile of the third validation site

The third validation site will be located in Milan under the joint supervision of University of Milan - Bicocca and Istituto Auxologico Italiano. This will take place at

San Luca Hospital, a clinical care and research Institution led by the Istituto Auxologico Italiano and appointed to the University of Milan - Bicocca.

1.1.3.1 Istituto Auxologico Italiano

The **Istituto Auxologico Italiano** is a non-profit foundation for biomedical research. In 1963 the Italian government granted it legal status as an istituto di ricovero e cura a carattere scientifico (IRCCS), or research hospital. Its official recognition as such has been confirmed and extended in subsequent years.

The nationally renowned clinics making up the Istituto Auxologico Italiano are highly specialized facilities where experimental and clinical research is integrated with top rate health care. They are also testing grounds for original models of health service organization and management, including telemedicine systems and approaches based on virtual environments.

The initial focus was on growth disorders, chiefly pituitary dwarfism subsequently expanding its scientific and clinical operations to various aspects of human development, from conception through adulthood, by studying disorders and degenerative processes from the standpoint of prevention, diagnosis, treatment and rehabilitation, with a special emphasis on growth, endocrine and metabolic disorders, cardiovascular diseases and the neurosciences. In particular a strong interest was developed towards medical and molecular genetics of these diseases.

The clinical activity is based on a few hospital with a total of 514 beds, serving patients on an inpatient, day hospital and outpatient basis. Experimental and clinical research is conducted at 18 laboratories whose activities are integrated with the patient care units.

Our investigations fall within the three main spheres of research that are established in the foundation's by-laws: 1) auxological, endocrinological and metabolic research, dealing with metabolic issues, mostly in relation to obesity and diabetes; 2) research in the field of neurosciences, focussing on cerebrovascular diseases, particularly the prevention, diagnosis and treatment of strokes, neuroendocrinology, neurodegenerative diseases, and the cytogenetics and molecular genetics of certain neurological disorders, and on rehabilitation for neurology patients, linked with research institutes in the United States and Europe; 3) cardiovascular research, focussing on the pathophysiology of nervous control of the circulation in various disorders (like atherosclerosis, arterial hypertension, myocardial infarction, heart failure and autoimmune vasculitis), the development of non-invasive techniques for cardiovascular diagnosis, clinical cardiovascular pharmacology, and the genetic and immunological aspects of cardiovascular diseases. An important and innovative field of research is cardiovascular rehabilitation after heart attack and heart failure and remote telemonitoring of patients with hypertension and chronic heart failure. The cardiology unit has 55 beds, including intensive care, hemodynamics lab, electrophysiology, rehabilitation unit, outpatient services, and is located in central Milan, offering its services to a large city area, and being approached by thousands of patients each year. The cardiology department staff includes around 25 doctors and 30 nurses, plus administrative and secretarial staff involved in support activities.

1.1.3.2 The University of Milan - Bicocca

Milan and its surroundings area, as well as being the most populous region in Italy, is generally recognized as the economic heart of Lombardy. It is therefore, not by chance that the city is called "one of the four driving engines of Europe". During the 20th century, Northern Milan was Italy's most important industrial center thanks to its heavy metal and mechanical industries. Since the crisis in heavy industries, the economy of the area has radically changed and now revolves almost entirely around innovation and technology based activities.

The University of Milan - Bicocca is situated in an area called Bicocca, on the northern outskirts of Milan. The University stands on what was once the industrial site of the internationally known Pirelli tyre company. The University is part of a new urban center, in which others are taking part as well: the CNR (National Research Council), Pneumatici Pirelli, multinational company offices, the new headquarters of the Pirelli Group, the Arcimboldi Theatre, a sports center and shops.

The University of Milan - Bicocca was officially created in 1998, but did not at that time have an officially nominated teaching staff. Groups of professors and researchers from the same scientific fields chose to come and participate in the project. They were driven by their enthusiasm for the new, and by the chance to broaden academic horizons without having their work undermined by traditional education methods. From the start, this very fertile climate became a unique training ground, which offered something new, even for the most traditional disciplines.

The University of Milan - Bicocca has a campus which is open to everyone, not only students. It has at its disposal large open spaces, large lecture rooms, study areas, equipped laboratories, specialized libraries, and a well equipped central library. Its facilities include University student services, University sports Center, Handicap assistance, University surgery, Dining hall, Bank, European Mobility Center, Halls of residence. It can accommodate 1.100 people, and also acts as a reference point for meeting and seminars organized by local economic and social foundations.

Notwithstanding its short history, University of Milan - Bicocca has a significant role in the international scientific community. This becomes quite evident especially if one takes into account that most of the researchers and scientists at Bicocca began or carried out long periods of research at other universities, principally the University of Milan (called "Statale") and Politecnico of Milan.

The University of Milan - Bicocca quickly embraced European research and training programmes. As far as educational programmes are concerned; from the outset the University began to participate in the Socrates Programme encouraging students and staff of the benefits, as well as developing the possibility of having common curricula with other universities. The rate of participation of researchers in international research projects (whether alone or under national research Institutes like INFN and INFN) is very high, and is accompanied by a very fertile production of papers published in specialized international journals, and by the organization of International PHD research programmes in collaboration with foreign universities. Thanks to European Union financing and to University support, students are becoming more and more mobile. They are now graduating and being awarded PHD degrees in European and foreign universities.

The University of Milan - Bicocca has twenty-one departments for the various scientific areas. The departments promote research at the University, and organise the research doctorate programmes.

This University also has four Research and Technology Transfer Centres of Excellence.

The Department of Clinical Medicine and Prevention is highly specialized in research in different fields of Internal Medicine, and in particular in the cardiological area, focussing on Hypertension and heart failure. The teaching hospitals appointed to this University, such as the San Luca Hospital in Milan, are heavily involved both in research and in clinical activities, and offer support to a number of European research programs, such as HEARTFAID.

1.2 Functional organization of the HEARTFAID Platform

The organization of the HEARTFAID technological platform is outlined in Fig. 1. This organization is solely functional, with services tailored to the chronic heart failure (CHF) domain.

Procedures (columns). Briefly, this innovative form of decision and informative support will help with procedures related to:

- *diagnosis* of CHF;
- clinical *standard management* and *prognosis* assessment of patients with CHF according to the most recent European Society of Cardiology (ESC) Guidelines;
- *research and development* in the medical and technical areas of knowledge overall pertaining to the CHF domain.

Procedures regarding *management* and *research* overlap: in fact, during the follow-up phase, while supporting the standard CHF management and prognosis assessment, the HFP will assist in collecting biomedical information for research and development purposes.

Environments (rows). The HEARTFAID project aims at developing a tool capable of collecting, integrating, and processing relevant biomedical data and information coming from the main settings actually encountered by patients with CHF. These settings include:

- the *medical environment*, corresponding to HFP level of functioning 1 (i.e. office of the general practitioner), and HFP level 2 (i.e. specialized hospital, with cardiologists involved in outpatient and inpatient care, and with the possibility of running a variety of tests, such as blood tests, EKG, X-Rays, ultrasound imaging studies, etc);
- the *patient environment*, (i.e. patient's home) corresponding to HFP level 3;
- the medical and technological *research environment*, corresponding to HFP level 4.

A future development may be the HFP level 5, where data coming from a number of platforms (levels 1-4) might be integrated at the national or international level (i.e. randomized clinical trials, public health).

The basic levels of functioning of the HFP are articulated in the workflows described below:

- **Workflow 1: medical environment (in Fig. 1: HFP level 1 and 2 and patient n. 1)**

Processes of diagnosis, management, prognosis assessment with patients' data collected and medical recommendations provided both in the office of the family physician and in the specialized cardiology setting.

- **Workflow 2: medical environment and patient's home (in Fig. 1: HFP level 1, 2 and 3 and patient n. 2)**

Processes of diagnosis, management, prognosis assessment, with patients' data collected and medical recommendations provided, as above, both in the office of the family physician and in the specialized cardiology setting.

Of notice, biomedical parameters, relevant symptoms and compliance to prescribed pharmacological and non pharmacological regimens will be monitored by HFP level 3 in patients' homes.

Serial measurements of selected biological parameters will be collected by the patients and by their relatives and will enter HFP level 3.

Furthermore, HFP level 3 will engage with the patients by providing informative material, reminders on medications' schedule, reminders on biomedical measurements.

- **Workflow 3: medical environment (in Fig. 1: HFP level 1 and 2 and patient n. 3) and research environment (either medical or technical) (in Fig. 1: HFP level 4 and patient n. 3)**

Processes of diagnosis, management, prognosis assessment with patients' data collected (and medical recommendations provided) in the office of the family physician, in the specialized cardiology setting, and in the ultraspecialized research setting.

As stated above, in workflow 3, while supporting the standard CHF management and prognosis assessment, the HFP will assist in collecting biomedical information for research and development purposes.

More sophisticated biomedical data entering the HFP at this level may include, for example, continuous non invasive heart rate and beat-by-beat blood pressure measurement. The HFP might in future acquire data regarding innovative heart imaging studies, more thorough heart functional studies (as the cardiopulmonary test with breath-by-breath assessment of O₂ consumption and CO₂ production, etc). This level will collect the largest variety of biomedical data.

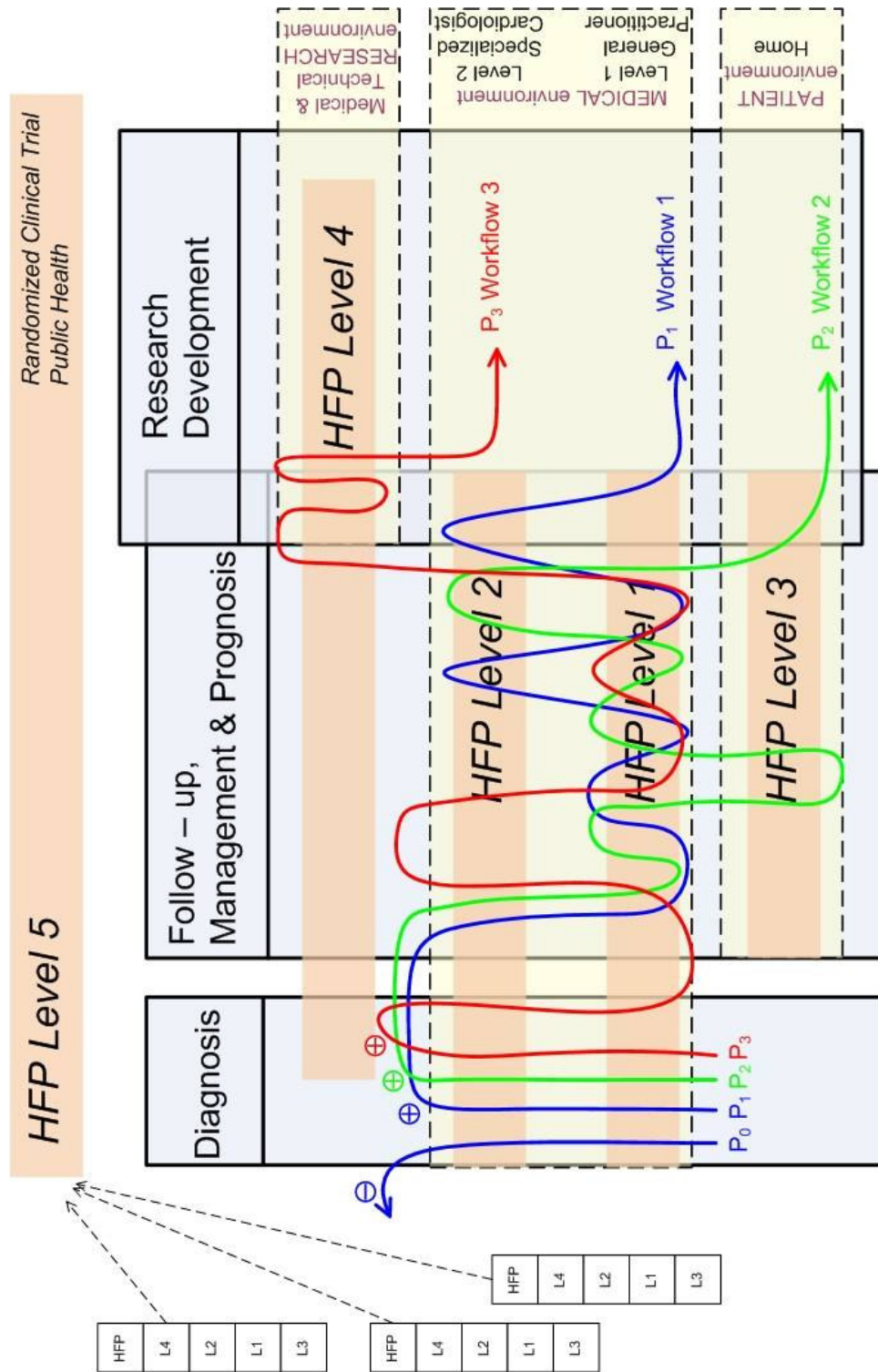


Figure 1: Organization of the HEARTFAID technological platform (HFP).

The three typical workflows identified above will be implemented by the clinical partners (University of "Magna Graecia", University of Milan - Bicocca, Jagellonian University and Istituto Auxologico Italiano) with the cooperation of the technical partners.

In the next chapter we will describe three typical operative scenarios for different HF patients that will enter the three different workflows described above.

Of notice, the distinction among workflows is artificial and has been layed out to exemplify the basic flows of data collection and transmission in the most typical environments encountered by HF patients. Additionally, this distinction has been thought out to facilitate the clinical partners in testing the platform "on site", i.e. in the context of the most typical medical environment.

Of course, given the flexibility of the HFP, the fully functional product will allow to collect and transmit data for each individual patient from all the above environments depending on the always changing needs dictated by the clinical picture. Thus, the HFP will be able to provide decision and informative support regardless of the very unique workflow eventually followed by each patient with HF.

1.3 Sample Workflows

1.3.1 Workflow 1. Heart Failure in the aged population: the life of Maria Kowalska in the Heartfaid age

Mrs. Maria Kowalska is a 75-year-old woman living in the Polish "validation site" region. She has been cared over the past few years by Dr. Tomaszewski, her local GP.

She came one morning in Dr. Tomaszewski's office complaining of recent onset (half an hour) severe shortness of breath associated with palpitations. Her blood pressure was 220/120, pulse 120/min irregular; heart auscultation revealed fast and irregular heart sounds and no murmurs; lung auscultation revealed bilateral basal rales. Dr. Tomaszewski immediately referred her to the emergency department of the nearest hospital.

The emergency doctor on charge, having confirmed the above examination findings suggesting an acute heart decompensation, treated her for a pulmonary oedema in hypertension crisis complicated by (ECG proven) atrial fibrillation. He followed the most recent European Society of Cardiology (ESC) Guidelines in doing so. Her symptoms and vital signs immediately improved and a regular sinus rhythm was pharmacologically restored. As soon as the results of the tests obtained in the emergency room became available (chest X-ray, arterial blood gases, general blood work, cardiac enzymes), and an acute coronary syndrome was ruled out, the doctor on charge admitted her to the Cardiology ward.

In this specialised inpatient environment, shortly thereafter, she underwent an heart ultrasound which essentially revealed the presence of mild left ventricular hypertrophy, a mild decrease in the ejection fraction (i.e. mild systolic dysfunction) with initial signs of diastolic dysfunction. Over the next few days of hospital admission, her cardiac and respiratory symptoms totally resolved and she persisted in regular sinus rhythm (as assessed by continuous ECG monitoring). Her blood pressure was consistently well controlled as well as the remaining of the vital signs. A more thorough collection of her past medical history essentially resulted in longstanding moderately elevated blood pressure values requiring drug treatment which she has always refused to take.

On discharge, the cardiologist Dr. Kaczynski suggested the proper pharmacological regimen to treat her mild heart failure (systolic and diastolic) secondary to longstanding untreated hypertension. Additionally, he suggested her to report to her

GP for some laboratory work to be done in two weeks, and was given a referral for an appointment at the Cardiology outpatient service in four weeks for a clinical check and an ECG. Finally, she was asked to enrol in the HEARTFAID Programme after having received a detailed description of it. She was not entirely convinced about the benefits gained by enrolling in such a programme and refused to do so.

Maria Kowalska, once back home, having started worrying about her medical health, followed carefully the pharmacological and non-pharmacological recommendations she was given on hospital discharge. Additionally, as scheduled, she had a venous blood drawing done to check her kidney function and electrolytes, and reported with the test results to her GP.

Sitting in the waiting room of her GP's office, again she suddenly developed shortness of breath and palpitations. Dr. Tomaszewski immediately examined her: BP was 180/100, pulse 115/min irregular. Heart auscultation revealed fast and irregular heart sounds and no murmurs; lung auscultation revealed no rales.

She was immediately referred again to the emergency room where the physical findings were confirmed and she was found with a recurrence of atrial fibrillation. The cardiologist Dr. Kaczynski treated her arrhythmia pharmacologically and immediately restored a regular sinus rhythm.

She spent a few hours in the emergency room and again was offered by the Cardiologist Dr. Kaczynski to enrol in the HEARTFAID programme and to continue being seen in follow-up both in the specialized cardiology setting and in her GP's office for her cardiovascular problems. In fact, not only her longstanding untreated hypertension had already caused some degree of cardiac dysfunction, but also she was having close recurrences of atrial fibrillation urging her to rush to the hospital for immediate treatment. All together these problems called for a management comprising specialized serial tests/advice and close - out of hospital - update on her condition. Given the need for such a close and frequent interaction between the GP's office and the Cardiology (inpatient and outpatient services) she felt she would have been better cared entering the HEARTFAID programme and eventually accepted to enrol and signed the informed consent form.

In the same occasion, Dr. Kaczynski opened a session on the HFP at his PC and created a newly recruited patient chart with Mrs. Maria Kowalska's demographic data. He filled up and stored the forms with inclusion and exclusion criteria. He entered data on her recent clinical and instrumental evaluations. He also ordered some missing tests to be done in the "validation site" in order to properly complete the baseline evaluation and prognosis assessment and to better plan Mrs. Maria Kowalska's management. He arranged the next visit two weeks later when the examination results would have been ready. Finally, via the HEARTFAID programme he sent Dr. Tomaszewski a note informing him about having started a new patient in the HEARTFAID Programme.

Once Mrs. Kowalska was in the HEARTFAID programme all her results from the diagnostic imaging and non-imaging instrumentation connected to the HFP were acquired as structured data by the HFP and inserted in the HEARTFAID repository. The KDD algorithm processed these new data adjusting the rules on which the Decision Support System was based. Then, the DSS provided a management plan with pharmaceutical and non pharmaceutical treatment for the patient. This information is reviewed and edited by the cardiologist and stored as part of Mrs. Kowalska's HF-EHR.

1.3.2 Workflow 2. Heart Failure in the aged population: the life of Vito Gattuso in the Heartfaid age

Mr. Vito Gattuso is a 68-year-old man living for all his life in the "validation site" region. He has been cared by Dr. Caputo, his local GP for several years. Dr. Caputo

ordered him some tests suspecting a cardiac problem. Vito went to a specialized centre and underwent such tests. From the results there was evidence of heart failure and, after a consultation with his GP, he was suggested to go to the "validation site" where a specialised management of heart failure could be provided.

At the "validation site" a specialist (Dr. Amenta) checked the medical history, symptoms, signs and examinations' results and verified that he met both the inclusion and exclusion criteria (with respect to both the heart failure diagnosis and the HEARTFAID monitoring requisites). Dr. Amenta offered to care for him and to recruit him in the HEARTFAID programme. He explained carefully to Vito and to his wife Maria, which had accompanied Vito there, all of the details of the HEARTFAID programme. Vito accepted to be recruited in the program and signed the informed consent form.

During the same visit, Dr. Amenta opened a session on the HEARTFAID platform at his PC and created a newly recruited patient record with Vito's demographic data. He filled up and stored the forms with inclusion criteria and exclusion criteria. He performed a baseline evaluation which included a detailed medical history collection and a physical examination and entered the chart the corresponding data. Additionally, he entered the results of the tests Vito had previously undergone. He also ordered some missing examinations to be done urgently by Vito in the "validation site" in order to properly complete the baseline evaluation and prognosis assessment and to better plan Vito's management. He arranged the next visit two days later when the examination results would have been ready.

All these information are stored into the specific web-based Electronic Health Record (EHR) of the HEARTFAID system (HF-EHR), which enables both the access and the insertion of cardiovascular and non cardiovascular medical data. The HF-EHR is an innovative integrated service of the platform that other external applications (e.g. other DPR) can exploit to gather, display and use Vito's data (under adequate rights and privacy management protocols).

Finally, Vito is marked as stand-by in the HFP waiting for the completion of the baseline evaluation.

Two days later Vito went back to Dr. Amenta's office with the results of the missing examinations that were included in his HF-EHR record. These results confirmed the diagnosis of Heart Failure. The functionalities offered by the End-User Interaction Services of the HFP, support the identification of a suitable clinical pathway to be followed by Vito and assist the experts planning an adequate pharmacological and non-pharmacological therapy, selecting the vital signs that will be monitored in the domestic environment and during his daily life, and defining a schedule for his following visits if no complication will happen till that date.

This plan was then reviewed by Dr. Amenta, corrected, approved and saved. Vito was then provided with all the necessary devices for the out-of-hospital monitoring with instructions on the clinical protocol to follow for the measurement acquisition. A proper training and a proper test was performed in the office in order to verify that Vito and Maria were able to properly use the devices. In addition, the authorised technical staff will take care to perform the necessary installations in Vito's domestic environment. This will imply configuring and testing all of the devices, the hardware, the software tools and the sensor network that will enable the continuous monitoring of Vito's vital signs. From this moment on, the different component of the HFP will contain specific sections for Vito, thus allowing the expert to visualise and to manage his data, both clinical and not, by accessing the appropriate service.

Vito then went home and continued his daily life following accurately the suggestions provided by Dr. Amenta regarding both the new lifestyle and the medications (which he took regularly as prescribed).

During the monitoring period, some data are acquired automatically by the platform (e.g. environmental data), whilst other measurements should be performed with the help of Vito. A specific service was enabled for Vito that every day at a scheduled time will automatically remind him to acquire, if not yet done, the vital sign measurements according to the specified protocol and with the provided device. The acquired measurements are then transmitted through a specific gateway (fixed or mobile) to the HEARTFAID server and some automatic checks are performed for artefacts detection. If an artefact is detected Vito is requested to repeat the test otherwise the measurements are collected and processed by the HFP.

If the result of the processing suggests some changes in management (different pharmacological or non-pharmacological treatment, different schedule for the measurement acquisition or different schedule for the next visit) or different prognosis, then the specialist is automatically alerted and asked for confirmation (or modification) of the HEARTFAID proposed new plan.

The new plan is stored and sent to Vito for its immediately adoption. Vito can pose questions to his cardiologist in order to eliminate any doubt in the new plan and when he is sure that he has perfectly understood and agreed the new plan he confirms the acceptance and starts the new treatment plan.

Also situations where a nurse visit at home or an immediate admission to hospital is required are supported by the HFP providing the necessary indication to the patient and requiring his agreement and acceptance (patient again can solve his doubt asking information to the specialist in order to have a proper understanding of the actions he has to perform).

Vito is very happy with the system, mainly because he is able to stay at home and to continue his habitual life drastically decreasing the need to go to his GP's office or to the hospital. He feels very well cared about by the HFP. In particular, he appreciates the alerts as they remind him all of the important things he has to do for his health.

During the first year of the HEARTFAID programme, several patients accepted to be recruited into the demonstration trial and a large quantity of data has been collected into the platform database. Using the functionalities offered by the platform, the specialists have been able to perform both statistical and mining analysis on the available data. In particular, they have been able to implement advanced Knowledge Discovery processes that brought to the discovery of novel, non-trivial know-how and rules that are at the moment under evaluation of the medical experts. If the new rules will be validated by the experts, they will be used to enrich the knowledge base of the HFP thus improving the ability of the Support System to assist decision makers in their daily activity.

1.3.3 Workflow 3: Heart Failure in aged population: the life of Massimo Armani in the Heartfaid age.

Mr. Massimo Armani is a 70-year-old retired engineer that recently moved from an isolated rural area of northern Italy to the "validation site" of Milan. After the moving, Mr. Armani has been feeling progressively more fatigued, short of breath than he used to, and has occasionally felt some pain in the anterior area of his chest while carrying boxes up and down the stairs. He thought this was simply due to the unusual load of work he had to face with the moving itself. As soon as he introduced himself to his new GP, Dr. Tronchetti, and summarized his medical history (longstanding well controlled hypertension and hypercholesterolemia), medication list and his recent complaints, Dr. Tronchetti suspected that some new cardiac problem has developed and ordered to him to see a cardiologist.

Mr. Armani went to the nearest specialized cardiology centre affiliated to the University and saw Dr. Paolini. Dr. Paolini, after having listened to and examined Mr.

Armani obtained an ECG and ordered some urgent tests (echocardiogram, exercise stress test, 24-h ECG Holter monitoring).

From the results of such tests there was evidence of mild systolic dysfunction likely secondary to a coronary artery disease and Dr. Paolini decided to admit Mr. Armani to the Cardiology ward for a coronary angiography. This test confirmed the presence of a two-vessel coronary artery disease that was treated with balloon angioplasty and coronary stenting with optimal results.

On discharge, the cardiologist Dr. Paolini suggested the proper pharmacological and non-pharmacological regimen to treat his mild systolic heart failure secondary to a newly diagnosed coronary artery disease. Additionally, he suggested him to report to his GP for some laboratory work and clinical checks to be done regularly, and gave him a referral for an appointment to the Cardiology outpatient service in one month.

Finally, Mr. Armani was asked by Dr. Paolini to enrol in the HEARTFAID Programme after having received a detailed description of it. He was told that in such a particular University network the HEARTFAID Programme had been started both to help the Cardiologist and the GP with standard diagnosis, management and prognosis assessment of heart failure, and to collect data in the context of a research projects.

Mr. Armani accepted with no hesitation. He felt his medical conditions would have been far better followed and cared about by entering the programme. Additionally, he felt he would have contributed, sharing information about his case, to the development of newer and more efficacious diagnostic and management strategies in the field of HF.

1.4 The phases of life of a heart failure patient with respect to HEARTFAID

The life of an HF patient with respect to the HEARTFAID programme can be divided into the following important states/events:

- 1) **Usual life**, before a cardiac dysfunction is suspected. The typical HF patient likely did not follow an healthy lifestyle and had some behaviours or medical conditions that exposed him/her to an increased risk of developing HF. Usually because of some precipitating factor, after an asymptomatic phase (of variable length), HF becomes symptomatic thus urging the patient to seek medical attention.
- 2) **The diagnosis of Heart Failure**, which coincides with the first contact with the Cardiology centre where the necessary specialized diagnostic tests are performed. The diagnostic process coincides also with the first contact with the HFP with the expectation that such support would decrease both falsely negative and the falsely positive diagnosis, and that it would help with the difficult task of diagnosing the presence and determining the prevalence of HF with preserved left ventricular ejection fraction.
- 3) **The follow-up as a patient** affected by a rather complex heart condition calling for a rather complex management.

The Cardiologist, based on the HF aetiology and symptoms' severity will select, according to the most recent European Society of Cardiology (ESC) guidelines, the most appropriate therapeutic approach.

In this context, the HFP will support the specialist in selecting the most appropriate therapeutic regimen resulting from a combination of pharmacological and non pharmacological measures and will provide the patient and his/her relatives with informative material completing the education effort made by the physician. In particular, a detailed description regarding new lifestyle measures is provided by the HFP.

During the follow-up phase, the progress made by the patient will be carefully monitored by the Cardiologist and the GP with the help of the HFP. The patient's symptoms and signs with/without the results of selected tests will be followed by either the medical personnel alone or by such personnel supported by specific functionalities of the HFP. In fact, the HFP will allow to convey serial readings of selected biological parameters measured both by the by the medical personnel and patient himself (or his/her relatives) from nearly every environment, including home. These parameters will be acquired, stored and examined in real-time and without the need for the patient to move from his home environment. This will save time to both the patient and the health professionals and will provide a more detailed control of the patient's health status.

The patient's compliance to the pharmacological and non-pharmacological regimen will also be followed and actively reinforced by the HFP by means of specific functionalities.

During the follow-up phase, thanks to the strict monitoring implemented by the HFP, any time the patient's clinical conditions are about to worsen or have already worsened, the medical personnel will be immediately informed and either the appropriate changes in pharmacological and non pharmacological regiment will be proposed by the HFP and confirmed by the medical personnel, or the patient will be referred to the outpatient or inpatient Cardiology services for testing, consultation or admission. This way, potential precipitating and exacerbating factors of decompensated Chronic Heart Failure will be identified and management will be changed accordingly.

Stable or improving clinical conditions do not imply any change in frequency and quality of monitoring in health parameters. Data demonstrating stable or improving condition may themselves prompt management changes.

The HFP monitoring functionality implies that some of the patients might be provided with a set of devices that they will operate from home. The measurements acquired will be sent automatically to the central system. Such measurements, providing precious indications about the patient's conditions, will enable the HFP to early identify critical situations that needs to be immediately reported to the specialists. In particular, such close monitoring aims at identifying a decompensation of HF before this is clinically manifest. Earlier detection of patient's decompensation permits a better optimization of therapy, a better outcome and a reduction of the health care costs.

It is important to highlight that the HFP will allow acquiring not only the standard clinical parameters, normally acquired also during an hospital visit, but also a wider set of parameters. This functionality represents a significant added value of the HFP with respect to the actual protocols. A simple example is the possibility to equip the patient with accelerometers: this will allow the system to generate an alarm if the patient should suddenly fall or will allow quantifying the daily physical activity performed with the possibility to keep the total and the peak physical activity under control.

Moreover, monitoring continuously some parameters will allow identifying critical states that would otherwise not be detected if such parameters would be measured only during an office visit.

1.5 The phases of functioning of the HEARTFAID platform with respect to the life of an heart failure patient

During the follow-up phase of a patient with an established diagnosis of HF, the platform will assist the medical personnel to follow a number of aspects of the HF

pharmacological and non-pharmacological regimen. In detail, this will take place not only during the scheduled visits but also in the usual patient's environment. and to monitor the patient during his daily life and the scheduled visits. The general activity of the HEARTFAID platform can be synthesized as an iterative cycle with the following steps:

- Measurement
- Analysis
- Decision
- Action

Using a more schematic formalism, we can describe the general workflow of the platform with the block diagram of figure 2.

This cycle will be instantiated and adapted to each of the three typical scenarios addressed in this document:

1. Hospital environment
2. Home Care
3. Patient on the move

For each step of the iterative cycle, it will be important to define the following information:

- Data to be managed (which data, which devices and which clinical acquisition protocol).
- Relations among data (data can be directly measured and obtainable from the devices or can be evaluated after analysis of the raw data acquired by the medical devices). Thus, we will define two kinds of data: directly measured data and calculated data. Calculated data are all measurements that are not directly provided by the medical device itself, but need some additional analysis (with ad hoc developed SW) for their computing. These data should not be confused with the historical data used in the KDD process to discover novel know-how. The DSS analyses new acquired data according to the rules coded in the knowledge base in order to identify relevant situations, while the KDD processes historical data available the entire repository (i.e. belonging to more patients) to identify recurring patterns of interest for the specific cardiovascular domain.
- Flow of information.

For the first step of the cycle, "measurement", we need to specify accurately what will be the data available and that need to be managed, as well as what are the correlations among these data.

The second step, "analysis", can be considered from two points of view:

1. from one side it will be necessary to support the daily activity of the medical experts by automating operations that are currently performed. In other words, the platform should be able to process the available data according to the explicit knowledge of the experts and the know-how available in the specific field addressed in the project;
2. from the other side, the HEARTFAID platform should analyse the available data by means of both standard and advanced mathematical methods in order to extract new information that can be successively used in KDD and statistical process to derive new information, to inference new knowledge or to identify correlations among data.

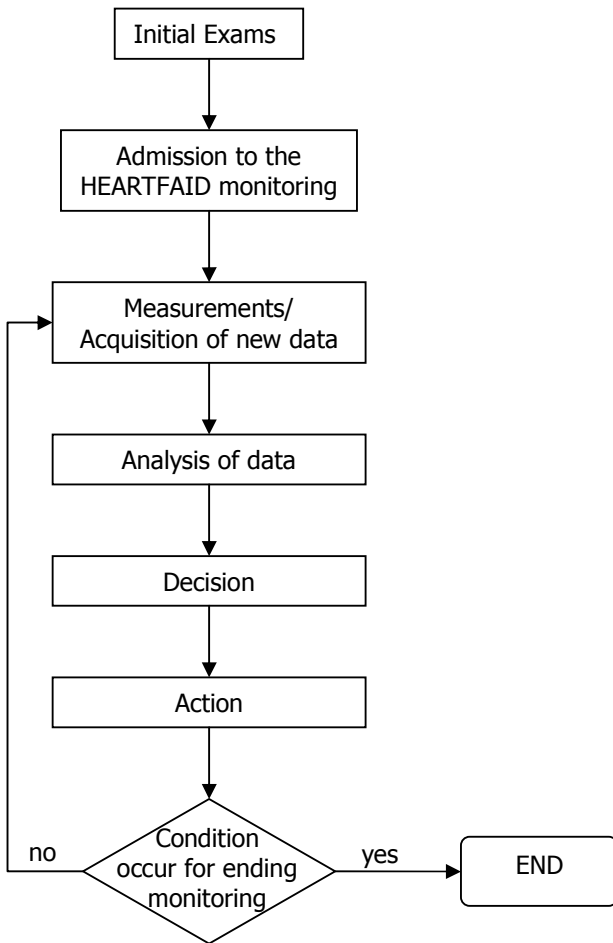


Figure 2. Block diagram of the overall workflow of the platform.

All the data measured and recorded by the platform will be used at a first stage to apply simple inference processes and rules to identify instantaneous critical situations. At a second stage, a Clinical Decision Support System will be implemented to extract relevant information from the data and to perform correlation among different data to identify critical situations not immediately derivable from the instantaneous measurements. This high added value service is based on the definition of adequate knowledge bases that encode the know how of the experts opportunely formalised, as well as any new knowledge that should be discovered by the KDD process implemented on the available data.

In fact, advanced KDD processes are implemented on selected historical data stored in the repository of the HFP with the goal to discover novel, useful and non trivial correlations among data. These correlations are submitted to the domain experts and, if they are validated, they will be coded into well defined rules that enrich the HEARTFAID knowledge base. When new measurements are acquired by the HFP, both from the remote sensors and from specific hospital exams, the DSS checks the new data against the rules coded into the knowledge base and if all the conditions of a critical situation occur, adequate actions are undertaken (e.g. an alarm/alert is issued and sent to Dr. Amenta).

The “decision” step has the goal to support the daily decision activity of the clinicians by exploiting the know-how derived from guidelines, protocols, domain knowledge, inference and reasoning processes, meta-data, ontologies and, of course, the source data. The Clinical Decision Support System of the HEARTFAID platform has the

precise goal to support the process of moving from the "analysis of data" to the "decision making".

The last step, "action", is a direct consequence of "decision making". In fact, according to the measurements acquired from the specific patient, the knowledge derived by the DSS and the decisions taken by the experts, changes will be likely applied to the patient's healthcare program. These changes can be considered of two types:

- changes to the management (pharmacological and non pharmacological) recommended to the patient;
- changes to the HEARTFAID platform in terms of configuration and functionalities offered to the patient.

The HFP will be used not only to acquire information from the final users, but also to provide the patient and his family/relatives important informative and educational services. In fact, the platform will provide an import scheduling support that will improve and facilitate the therapy itself as well as the interaction with both the hospital/clinic and the doctors. In particular the platform will communicate to the final users all the scheduled tasks foreseen in the therapy, such as exercises, exams, assumption of drugs, prescribed dosage, etc., and at the same time the experts will have the possibility to add new tasks or modify the initial therapy according the measurements acquired by the platform. On the other side, the platform will be a valid support to educate both the patient and his relatives about the procedures of the planned therapy, the modalities for operating the acquisition devices, instruction about the use of the platform itself, general information on the disease, as well as more dynamic information such as the effects of the ongoing therapy, the meaning of the measurements acquired with respect to the normal values, what are the expected values for the specific patient, and so on. Of course all the sensible information should be mediated and authorised by the clinical experts.

The future scenarios

The previously described scenarios are especially focused on the follow-up and the management of Heart Failure patients after the diagnosis of their pathology. In this view the HEARTFAID platform will also support the exploration of the aetiology of the patient's Heart Failure.

The adoption of the platform for a validation period will allow the collection of a sufficient amount of data for "making" the platform expert enough to be used also in the diagnosis phase, thanks to the results of statistical and data mining analysis that will be performed on the new available repository.

Therefore, in a future evolution of the platform, the specialists might have an efficient and effective support also for their diagnostic practice.

In a future scenario, the 3 workflows described above will remain valid, with the difference that when the patients have a first contact with the healthcare structure or at the manifestation of early symptoms, the HEARTFAID platform might be used immediately to prevent/forecast a heart failure. In this case the patients will be immediately informed about the HEARTFAID programme explaining them that such programme will help cardiologists in performing a more accurate diagnosis (either it will be positive or negative) and will be asked to join the programme. If patient agrees by signing the informed consent, his data will be immediately inserted in the platform to support the diagnostic phase.

Of course, the diagnosis might be negative and, once confirmed by the cardiologist, the patient will be immediately discharged by the program, but his data will continue to be part of the HEARTFAID repository (negative diagnosis) improving the discriminatory capabilities of the KDD process.

In case of positive diagnosis confirmed by the cardiologists, the patient will enter the follow-up phase as described above.

The HEARTFAID architecture

The HEARTFAID architecture will have to be detailed according to two different points of view:

1. Functionalities and information on which to work;
2. State of the art of the tools for the support of the functionalities of the platform of services.

The architecture of the HEARTFAID platform will have to be represented with a "flow panel". For each activity/event related to the platform, all the involved modules and the generated flows will have to be shown. Furthermore all the activities of the platform for the support of the DSS will have to be saved in a LOG file for a better tuning of the DSS and for allowing confirmation from clinicians (when necessary).

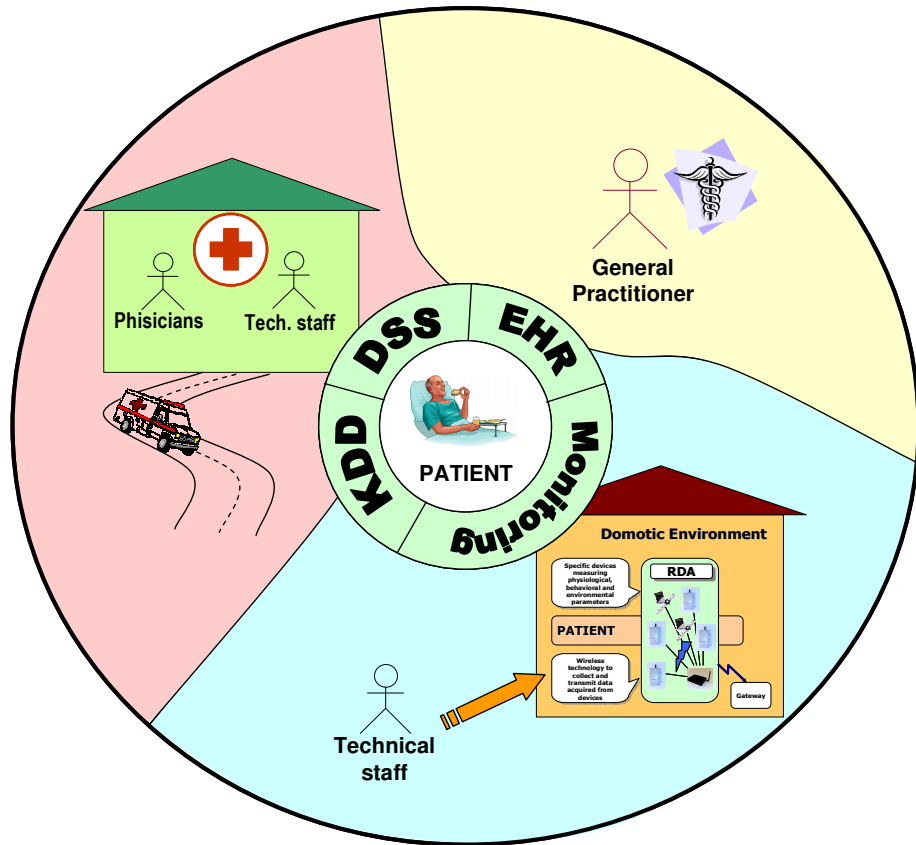


Figure 3. The patient-centric architecture of the HEARTFAID platform of services.