HEARTFAID

D23 – User need analysis and functional specifications of the HEARTFAID platform of services

Submission date: 16/11/2007
Due date of document: 31/07/2007

HEARTFAID

A KNOWLEDGE BASED PLATFORM OF SERVICES FOR SUPPORTING MEDICAL-CLINICAL MANAGEMENT OF THE HEART FAILURE WITHIN THE ELDERLY POPULATION

Project summary	
Project acronym:	HEARTFAID
Project identifier:	IST – 2005 – 027107
Duration of the Project:	01/02/2006 – 31/01/2009
Project Co-ordinator:	UNICAL University of Calabria (Italy)
Thematic Priority:	Information Society Technology
Instrument:	Specific Targeted Research or Innovation Project

Consortium

- UNICAL - Università della Calabria (Italy)
- UNICZ - Università degli studi Magna Graecia di Catanzaro (Italy)
- UNIMIB - Università degli studi di Milano Bicocca (Italy)
- JUMC - Jagiellonian University Medical College (Poland)
- VMWS - Virtual Medical World Solutions Ltd (United Kingdom)
- FORTHNET - Hellenic Telecommunications and Telematic Applications Company S. A. (Greece)
- SYNAP - Synapsis s.r.l. (Italy)
- CNR - Consiglio Nazionale delle Ricerche (Italy)
- FORTH - Foundation for Research and Technology Hellas (Greece)
- RBI - Rudjer Boskovic Institute (Croatia)
- AUXOL - Istituto Auxologico Italiano (Italy)

D23 – User need analysis and functional specifications of the HEARTFAID platform of services.

Document summary	
Document title:	D23 – User need analysis and functional specifications of the HEARTFAID platform of services.
Document classification:	Derivable D23
Dissemination level:	CO
Submission date:	16 November 2007
Due date:	31 July 2007
Authors:	Domenico Conforti – UNICAL Angela Sciacqua – UNICZ Mariaconsuelo Valentini – AUXOL Gianfranco Parati – UNIMIB Katarzyna Styczkiewicz - JUMC Andrzej Kononowicz – JUMC Dragan Gamberger - RBI Sara Colantonio – CNR Massimo Martinelli – CNR Davide Moroni – CNR Ovidio Salvetti – CNR Franco Chiarugi – FORTH George Zacharioudakis – FORTH Sergio Di Bona – SYNAP Davide Guerri – SYNAP Marco Lettere – SYNAP Manolis Stratakis – Forthnet Mariana Dikaiakou - Forthnet Stelios Louloudakis – Forthnet
Work package:	WP6 – End-user application and services
Report version:	1.0

Short description
The main goal of this deliverable is to define and analyze the needs of the End users of the HEARTFAID platform, as well as the functional specifications of the platform of services.

Change record		
Version number	Changes	Release date
0.1	Template	06/07/2007
0.2	Preliminary draft of the document	18/08/2007
0.3	First Draft of the document	01/09/2007
0.6	Advanced Draft of the document	02/10/2007
0.9	Final Draft	06/11/2007
1.0	Final version	13/11/2007

Table of contents

Executive Summary

The purpose of Deliverable 23 is to report and analyze the needs of the users that will interact with the services provided by the HEARTFAID platform, as well as to define the functional specifications of this platform. The outcomes of this deliverable will guide us through the development of the end-user applications and services prototype.
The structure of the document is the following:
At first, an introduction will provide a general overview of the field. Afterwards in the "End-users profiles and needs analysis" section are presented the groups of people affected by the services that HEARTFAID offers, identified and classified into user profiles. This section consists of "The HEARTFAID Stakeholders" subsection, describing the people that have a central role in the project's platform and the "End users' need analysis" subsection which presents the different requirements that have been identified for the user profiles involved in the project.
In the "Main tasks of the HEARTFAID Platform" section the system's architecture is described through the subsections of "Environments", which describes the processes of gathering and organising data, "Workflow Scenarios" presenting possible HEARTFAID scenarios, "The phases of life of a heart failure patient with respect to HEARTFAID", and "The functionalities of the HEARTFAID platform with respect to the life of a heart failure patient", referring to the interaction between HEARTFAID platform and HF patients.
The "HEARTFAID services" section describes the available services through the project's platform. This section consists of "Home monitoring" and "Monitoring on-the-move", regarding the data acquisition at home or on the move and the data transmission to the platform. "Data processing and feature extraction" refers to data collection of the platform during the several diagnostic tests and "The decision support system" subsection presents the intelligent system that takes decisions according to the patients' data.
In the "Functional specifications of the HEARTFAID platform of services" section are described all the utilities that have been developed for the HEARTFAID users. The "General architecture" subsection is referring to the general architecture of the platform. The "Functional specification of HF end-user applications" subsection describes the interfaces and services offered to the users, in order to access the application's utilities. The "Functional specification for data processing and feature extraction" subsection depicts the steps of the data extraction and analysis service and finally in the "Functional specification for the Decision Support Tools" subsection is explaining the set of functionalities specifically designed for aiding the clinicians in managing HF patients.

In the "User Interface" section are described the interfaces implemented to connect the software components. The subsection of the "Organization of access to functionalities" consists of the multitude of services and functionalities that are encapsulated in the HEARTFAID platform. Emphasis in this section has been given to the electronic Care Report Form (eCRF), which depicts the important

enrolment of patients to the HF platform. The subsection named "Interactions with HEARTFAID Image Archive" describes the images transmission and analysis that is performed through the HEARTFAID platform.
In "Security issues" section, security and privacy issues are presented, concerning the project's services. The subsection of "Security Aspects" describes the security needs in medical services. The "Security standards" section consists of the Standards that exist regarding the development of medical applications. The "Security in Medical Devices Interaction ", describes the security that needs to be provided by the platform, during the process of data transmission from medical devices to gateways. The "Front End security" subsection consists of the description of the available security services that exist in the collection and transmission of the sensitive medical data to users, while the "Security of HF services communication" subsection refers to the most important threats the platform has to deal with.
In the "Quality assurance process for the Prototypes" session is defined and presented the overall strategy for undertaking a quality assurance process for the prototypes devised and developed within HEARTFAID project, on the basis of which the quality criteria for measuring suitable performance indexes of the resulting platform are realized. The subsections of "Quality of the Health Care Model ", describes the development and integration of a new health care model and the supporting technologies, which is working to accomplish the final results of improve indices of health-related quality of life and control and reduce the overall economic and social costs of medical care. The "Goals: efficiency and effectiveness improvement" subsection describes how HEARTFAID as an advanced and innovative information technology system enables services to be delivered more efficiently and effectively. The "Quality criteria for the resulting platform" subsection describes the overall quality assurance process of the prototypes developed during the progress of the HEARTFAID project, while the "Validation and evaluation procedures" describe the performance evaluation and validation procedures, which are organized and developed throughout the HEARTFAID project.

1 Glossary of terms

TERM	DEFINITION
3G	Third Generation
ACO	Authenticated Ciphering Offset
ACT	Array Coherence Tomography
ADSL	Asymmetric Digital Subscriber Line
ADT	Admission Discharge Transfer
AECG	Electrocardiographic Ambulatory Holter Monitoring
AmI	Ambient Intelligence
AMR	Automated Medical Record
ANSI	American National Standards Institute
API	Application Program Interface
B2B	Business-to-Business
CDA	Clinical Document Architecture
CDSS	Clinical Decision Support System
CEN	European Committee for Standardization
CHF	Chronic Health Failure
CLI	Call Level Interface
CORBA	Common Object Request Broker Architecture
CPR	Computerised Medical Record
CQ	Continuous Queries
CRF	Clinical Report Form
e-CRF	Electronic Clinical Report Form
DB	Database
DCOM	Distributed Component Object Model
DICOM	Digital Imaging and Communication in Medicine
DM	Data Mining
DMS	Data Management System
DoW	Description of Work
DSS	Decision Support System
DTD	Document Type Definition
ECG	Electrocardiogram
EDF	European Data Format
EDV	End-Diastolic Volume
EEG	Electroencephalogram
EF	Ejection Fracture
EHR	Electronic Health Record
EMR	Enterprise Electronic Medical Record
EN	European Norm
ENV	European Prestandard
EPR	Electronic Patient Record
ER	Electronic Record

ES	Expert System
ESB	Enterprise Service Bus
ESV	End-Systolic Volume
FDA	Food and Drug Administration
GP	General Practitioner
GPRS	General Packet Radio Service
GSM	Global System for Mobile Communications
GW	Gateway
HCI	Human-Computer Interaction
HF	HEARTFAID
HFP	HEARTFAID Platform
HIS	Healthcare Information System
HL7	Health Level 7
HL7 aECG	HL7 Annotated ECG Standard
HTTP	Hypertext Transfer Protocol
ICEHR	Electronic Health Record for Integrated Care
ICT	Information and Communications Technology
ID	Identifier
IEEE	Institute of Electrical and Electronics Engineers
IHE	Integrating the Healthcare Enterprise
IOAI	Information Oriented Application Integration
IP	Internet Protocol
ISHNE	International Society for Holter and Non-invasive Electrocardiology
ISO	International Standards Organization
ISSS	Information Society Standardization System
IT	Information Technology
J2EE	Java 2 Enterprise Edition
J2ME	Java 2 Micro Edition
JAXB	Java API for XML Binding
JAXR	Java API for XML Registry
JDBC	Java Database Connectivity
JMS	Java Messaging Service
JNDI	Java Naming Directory Interface
JSR	Java Specification Request
JTA	Java Transaction API
JTS	Java Transaction Service
JVM	Java Virtual Machine
KDD	Knowledge Discovery in Databases
LM	Link Manager
LV	Left Ventricle
MIME	Multipurpose Internet Mail Extension
MML	Medical Markup Language
MOM	Message-Oriented Middleware
MPI	Master Patient Index

MRI	Magnetic Resonance Imaging
NDA	Non Disclosure Agreement
NYHA	New York Health Association
OBS	Observation
ODBC	Open Database Connectivity
OMF	Observation Message Format
OMG	Object Management Group
ORB	Object Request Broker
OS	Operating System
OSI	Open System Interconnection
PC	Personal Computer
PDA	Personal Device Assistant
PET	Privacy Enhancing Technique
PH	Protocol Handler
PIM	Personal Information Management
PIN	Personal Identification Number
PKI	Public Key Infrastructure
POAI	Portal Oriented Application Integration
QoS	Quality of Service
RDA	Remote Data Acquisition
RID	Retrieve Information for Display
RIM	Reference Information Model
RMS	Resource Management System
RPC	Remote Procedure Call
SCP-ECG	Standard Communication Protocol for Computer Assisted Electrocardiography
SMS	Short Messaging System
SOA	Service Oriented Architecture
SOAI	Service Oriented Application Integration
SOAP	Simple Object Access Protocol
SPECT	Single Photon Emission Computed Tomography
SV	Stroke Volume
TC	Technical Committee
TCP/IP	Transmission Control Protocol – Internet Protocol
TTE	Transthoracic Echocardiography
UDDI	Universal Description Definition and Integration
UI	User Interface
VCG	Vectorcardiogram
WDSL	Web Service Description Language
XDS	Cross-Enterprise Document Sharing
XML	Extended Markup Language
XML-RPC	XML-based Remote Procedure Call
XSD	XML Schema Definition

2 Introduction

HEARTFAID aims at the divising, design, development and deployment of an advanced and innovative technological platform of services and end-user applications that, by collecting, integrating and processing all types of the biomedical data and information that are mentioned in the project proposal, contributes to the optimization of the clinical management of HF and to the reduction of the economic and social costs.

The purpose of this document is to define the user needs of the people that are going to interact with the HEARTFAID platform, as well as to define the functional specifications of the services that will be provided through this platform, in the scope of the HEARTFAID project. In order to achieve these goals, a synergy of programs, components, sub-systems and technologies is required. The functionality implemented by this synergy shall be able to coexist with already existing infrastructures and extend their functionality in order to facilitate the objectives of the HEARTFAID project.

In order to support the medical/clinical management of heart failure within elderly population, the HEARTFAID project has proposed a unified platform of services. The formalization of the pre-existing clinical knowledge and the discovery of new elicited knowledge are important factors for the development of the HEARTFAID platform. The core of the platform is the biomedical and clinical data, acquired mainly by a multi-channel flow: biomedical devices, Electronic Healthcare Records (EHR), Laboratory measurements and so on.

The End-users level is the higher level of the platform, interacting with the external users. This level provides specific services and applications, in order to exploit the functionalities of the developed platform.

Under the broad term “End-user Services” are implied a number of different components, which capacitate access to the application’s utilities. HEARTFAID encompasses many different processing modules, which all require means of effective, bi-directional communication with the users. The challenge, of providing this communication successfully, lies in identifying user needs, determining functional specifications, and finally, designing and implementing a comprehensive and convenient User Interface to address them.

The main volume of work, of the End-User services, will be implemented for the Web-based portal. The main users of this service are the medical personnel, i.e. doctors, nurses, the hospital’s administrative personnel, and research scientists. The portal is in effect the doorway to a multitude of tasks and utilities offered by the middleware platform. The principal objectives of this module are to:

- satisfy all user requirements,
- limit as much as possible the complexity of the interface,
- provide a single access point for communicating with the application
- ensure uniformity of all portal features, such as information display, error-handling, feedback, etc.

Users of the HEARTFAID platform may be roughly classified in two groups, based on their attributes: the medical personnel, and the patients, who have different, but equally important aspirations for the platform. The "Medical Personnel" group is a wide-ranging category that includes all health-care professionals, involved in the research or the treatment of Heart Failure. The users associated with this category are the ones that will mostly interact with the system, and will make extensive use of the system services. The other group of users refers to the "Patients", which includes all people suffering from Heart Failure, who are admitted and monitored by the HEARTFAID platform. Naturally, they are the ones, who will gain the most of the system, although their interaction with the platform is of minimum level.

The core components of the portal are the Electronic Health Record (EHR), the Personnel Management, and the Decision Support System (DSS) Administrator.

The EHR is not a single and complex application but the result of a series of data acquisition and transformation activities. In particular, in the HEARTFAID EHR the data will be gathered from different and heterogeneous sources, such as the electronic Case Report Form (eCRF) and the Remote Data Acquisition sensor networks (RDA) connected to Ambient Intelligence (AmI) platform, used for telemonitoring, as well as other components of the Healthcare Information Systems involved in the HEARTFAID platform.

Since patient's data will be collected also in the research workflow, an important reason for developing the electronic Case Report Form (eCRF) is the fact that not all required data are present in the routine EHR.

The HEARTFAID electronic Case Report Form (eCRF) is one the most significant parts of the web-based portal component of the platform. Its usage is restricted to medical personnel only (nurses, caregivers and doctors) – it is not indented to be accessible for home users. Another reason that explains why the eCRF had to be developed is because not all medical devices can be automatically integrated into the platform.

The eCRF provides the interface for the Patient-Data Management module. The Use Cases that are covered within this front-end module have to provide the user with the appropriate functions, in order to be able to create, retrieve, view, update and delete a patient record, through specified commands.

The same issues apply also for the personnel management records, where the responsible persons for using the Front-End applications are stated. Access to the allocated services of the HEARTFAID platform is granted, according to "Personnel's" attributes.

The Decision Support System is the core of this project, and provides indispensable services to the care takers. The interface to this module is the most demanding aspect of the End-User services, as it may even affect the frequency of use, and the effectiveness of the module, while one of the main objectives of this service is to provide the triggering of advanced alert and notification communication services to HEARTFAID users.

Within this subproject, a number of different information delivery methods have been examined, in order to study and develop an advanced HEARTFAID alert and notification service, dedicated to mobile devices (mainly mobile phones and

PDAs), which is available over GSM network to mobile users (patients and their relatives).
In the framework of this task, the instant communication method of Short Messaging System (SMS) will be used in order to provide HEARTFAID platform with enhanced one and two-way communication services available for mobile users.
The key issues for this service will be the advanced user profiling and the cognitive techniques which should be used in order to dynamically compose and send alert and notification messages to the users, depending on their particular personal profile, based on their attributes (doctors or patients).

3 End-users profiles and needs analysis

Many groups of people will be affected by the services that HEARTFAID offers. These groups have been individually identified and classified into user profiles, to assist in user rights and accessibility management. The requirements of each user profile are studied separately and the facilities to be offered are based on the conclusions drawn from this analysis. The distinct stakeholders and the examination of user needs are presented below.

3.1 The HEARTFAID Stakeholders

Various groups of people are affected by HEARTFAID; therefore many people have a marked interest in the benefits that the project proposes.

3.1.1 Care Givers

This general definition applies to all of the non medical personnel caring for HF patients. This personnel either belongs to the patient's family or social network, (see 3.1.6 Patient's relatives) or to structured social organizations.

The importance of a care giver increases as the patient gets older and less independent. Besides providing general assistance with activities of daily living to the HF patients, the care givers have to face problems specifically related to HF clinical standard management.

The HEARTFAID platform could help selected caregivers authorized by the patient with the following:
- full implementation of the complex pharmacological and non pharmacological recommendations by means of informative material, reminders on medications' and measurements' schedule;
- entering data in the context of home monitoring;
- helping with questionnaire filling;
- facilitate the contact with the medical personnel involved with the HF patient's care.

3.1.2 Specialized nurse

Specialized nurses will mostly access the HEARTFAID platform in the medical environment. Occasionally they can participate in the home care and monitoring of selected HF patients.

Depending on their level of training and specialization, they will be able to assist the medical personnel, the patients and the caregivers in:

1) collecting/entering data concerning:
- history and physical examination
- selected tests (i.e. ECG), both in the home and medical environment.

2) providing the proper education and ensuring compliance to HF treatment recommendations.

3.1.3 General Practitioners

The General Practioners enrolling patients in the HEARTFAID program will collect and enter data by

- referring patients with suspected HF to the specialized Hospital for diagnostic and prognostic assessment and for therapeutic recommendations;
- helping confirmed cases of HF with the clinical standard management by reinforcing education and compliance with both scheduled tests and recommended measures; he may act both in his medical office and at the patient's home;
- referring patients with suspected acute decompensations to the specialized Hospital for proper care.

3.1.4 Specialized Medical Doctors

Specialized medical doctors of the HEARTFAID program, depending on their respective environment (specialized hospital and/or research setting), will collect and enter data regarding history and physical examination and instrumental tests with the aims of:

- confirming the HF diagnosis;
- recommending the standard clinical management;
- assessing prognosis;
- managing acute decompensations;
- by means of research protocols, developing new HF diagnostic and treatment strategies.

The patient will have a central role in the HEARTFAID platform. In fact, the HEARTFAID platform is "patient-centered" and patient is not anymore a passive ring of the chain, but he actively participates in the main phases of his care. Once patient is enrolled in the HEARTFAID program, he will be enrolled as "patient" and, with his HEARTFAID account, he will access all his encounters with a "patient profile". Typically each user registered with "patient profile" will have specific access rights on the "care episodes" of his care quite different from the other existing profiles (i.e. "general practitioner profile", "specialized doctor profile", etc.). The access rights will be defined as a consequence of the "patient needs".

3.1.5 The Patient's Relatives

Some relatives can be crucial in helping with the patient's care. Only the relatives authorized by the patient will be registered at the same moment of the patient enrolment or at a second time upon a patient's request. Such patient's relatives will be the patient's informal caregivers and will participate to the patient's care and assistance outside the primary or secondary care premises. Relatives selected

by the patient will also be informed and updated about the patient's health status. Thus, patient relatives may help the patient in executing the pharmacological and non-pharmacological treatment suggested by the platform, in feeding the platform with the requested information with the frequency requested by the platform, in a correct use of the monitoring devices, and in the correct filling in, and submission of, additional forms or information. But they will also help the patient with the correct understanding of the information provided by the platform. Upon patient's request (at the first visit or at a next visit) a relative can be registered in the platform as "patient relative". He will receive the HEARTFAID account for accessing the platform with the "patient relative profile" for the registered patient. Typically, each user registered with "patient relative profile" will have specific access rights on the "care episodes" of his relative's care quite different from the other existing profiles (i.e. "general practitioner profile", "specialized doctor profile", etc.). The access rights will be defined as a consequence of the "patient relative needs".

3.1.6 The IT Administrators

The system administrators comprise a unique user profile, compared to those listed above, because they are not involved in the health-care related functions of the system. Administrators are responsible for monitoring the system performance and safety and should be assigned full access rights by default. The project consists of various mission-critical components – e.g. the middleware, intelligent decision support, notification services – that are quite demanding in respect to hardware, installation and operation requirements. Furthermore, administrators form the technical support team, which ensures constant availability and unhindered operation of the various applications included in HEARTFAID.
Members of the IT staff will be needed both on the site of the central server (or servers) and on the affiliated hospital and clinics, in case a problem arises that calls for immediate intervention. Expert IT administrators could also make use of remote access to distant installation sites, to resolve especially difficult issues, when their physical presence is not feasible.

3.2 End users' need analysis

Different requirements have been identified for the distinct user profiles involved in HEARTFAID. Each group of users along with the relevant needs is reviewed in the current section.

3.2.1 The medical personnel

The medical personnel expects the HEARTFAID platform to help with crucial procedures overall related to:

- A) diagnosis of CHF;

- B) clinical standard management and prognosis assessment of patients with CHF according to the most recent European Society of Cardiology (ESC) Guidelines;

- C) research and development pertaining to the CHF domain.

- D) medical/patient record keeping.

A) diagnosis of CHF

1. Increasing the number of correct (positive or negative) diagnosis (by decreasing the number of both falsely negative and falsely positive diagnosis) is a priority for medical personnel.
2. The HEARTFAID platform will facilitate the medical personnel in finding the single biomedical parameter or the combination of parameters best identifying subjects with the condition.
3. It is foreseen that the HEARTFAID platform will help in setting new cutoffs and/or new reference values.
4. Medical and non medical health providers practicing in a low resource setting or in a remote facility are often in need of diagnostic support arising from specialized equipments and specialists non readily available at their site.
5. As according to the current guidelines the management of HF depends on NYHA Classification (i.e. class of symptoms' severity), the medical personnel may need support in this complex task.
The HEARTFAID platform will either guide the physician through the established rules of NYHA classification or help in finding other combinations of parameters best defining HF severity.

B) clinical standard management and prognosis assessment

1. As the management of HF is a rather complex combination of pharmacological and non pharmacological measures, a further need is represented by identifying the best array of measures applying to each individual patient.

2. The impact on medical outcomes and health care costs of HF management depends not only on correct recommendations but also on recommendations' full implementation. The HEARTFAID platform will contribute verifying that the prescribed regimen is followed by the patient and by the patient's caregivers.

3. The HEARTFAID platform will allow a more effective and thorough monitoring of patients with HF. In particular, it will assist the medical personnel in classifying patients belonging to different severity classes as stable, improving or worsening by means of selected combinations of biomedical parameters collected in different environments.

In particular, home telemonitoring of relevant symptoms and parameters is expected to improve classification of HF symptoms' severity, perform closer monitoring and earlier appropriate management changes, identify earlier potential precipitating and exacerbating factors of decompensated CHF.

4. Prognostic determination in HF patients is achieved by integrating a number of clinical and instrumental data. The HEARTFAID platform will assist the medical personnel in this difficult task by integrating data coming from the medical settings and the home environment. Furthermore, on large patient samples, it will allow also to determine the prognostic weight of newly suggested variables among demographic, historical, clinical, electrophysiologic, functional, and echocardiographic ones collected in different environments.

5. On the public health level, there is a growing need to verify if guidelines' implementations improve the quality of clinical practice and the utilization of health resources.

6. Compliance with treatment largely affects the results of treatment itself. The HEARTFAID platform is expected to increase compliance by providing the HF patient and his caregivers with informative material, reminders on medications' and measurements' schedule.

C) research and development pertaining to the CHF domain.

New diagnostic and prognostic strategies are constantly being evaluated seeking improvements in HF patients' outcome. The HEARTFAID platform, while assisting with standard HF care, will fulfil the need of such developments.

D) medical/patient record keeping.

A standardized organization and easy consultation of medical data contributes to the effectiveness of any form of care and has captured a growing attention in the medical world. Data organization, services and functionalities are developed in the HEARTFAID platform pursuing an improvement of the effectiveness of standard management of HF.

3.2.2 The patients and their relatives

The patient, at the first visit, will give an informed consent for his registration as "patient" in the HEARTFAID platform. He has to be able to check his demographic information (read-only) where the date and time of his "informed consent" is shown. He will have the possibility of revoking his informed consent and from that date/time no other encounter related to the patient will be added to his record.
He can view (read-only) the list of registered "patient relatives", "specialized nurses", "general practitioners" and "specialized doctors" involved in his care. Furthermore, an IT administrator will be available for any technical problem.
A medical report of his first visit (date/time) will be available to him (read-only).
In case of a positive diagnosis, the treatment and the required monitoring will be available to him (read-only) with the necessary instructions for a correct use of the devices (in case of home monitoring). Informative material completing the

education effort made by the physician (detailed description regarding new lifestyle measures) will be available to the patient and to his relatives.
Patient will have to perform the monitoring (with automatic connected devices) with the requested frequency (daily, twice a day, etc.) and he can check the measurements acquired in his record. In case a measurement is out-of-range he can receive a warning (repeat the measurement) or an alarm telling him that treatment/therapy could change.
Patient will have also to fill in some forms (for the manual connected devices) and a questionnaire with a specific frequency. All this information can be checked by the patient as well as any retrofit sent by the platform as a result of the information sent by the patient.
In case a change in the therapy/treatment is suggested, patient is requested to confirm his acceptance and after the acceptance is sent only the new plan will be shown to the patient (only the current treatment is available to patient).
Furthermore, patient can access a report for each visit he had in hospital or primary health care centers. He should also be able to access any hospital discharge letter for any period of stay in the in-patient departments.
Patient does not have any interaction with the DSS but he will simply view (read-only) the results of the DSS once confirmed by the doctors.
Patient relatives (informal caregivers) substantially will need the same functionalities of the patient, but they will not have the input functionalities (forms, questionnaire, etc.). These inputs will be available only with the patient account.
Furthermore, patient relatives might be informal carers of more than one patient. In such case (only when they have more than one patient), after their log-in an initial selection page for the patient selection have to be presented.

3.2.3 The IT administrators

To access the applications of the HF Platform we have chosen the web portal approach to identify and manage different user's profiles, to determine the general scenarios in which they could be involved, to assign the right capabilities to access the applications of the platform and to address their strategic objectives.

For the first prototype of the web portal we will take into account the case studies of the enrolment of a new patient, the activation of the monitoring system on connected devices, and the activation of the CDSS on the acquired data.
In this case we identified the following main steps:

- Authentication of the user
- Acquisition of the minimum set of data related to the enrolment of the patient (demographic data, inclusion and exclusion criteria);
- Visualisation of the patient's data;
- Activation of the monitoring system;
- Activation of the Alarm service using the CDSS.

Each class of services (i.e. enrolment, AmI services, Clinical Data Visualization/Insertion/Management, CDSS, Image Analysis) will be accessible

through a dedicated Portlet within the Portal. After the used has been Authenticated and *profiled*, and a specific patient has been selected thus enabling a *patient context* (for more details see Deliverable D20), the access to the available services will be enabled by using the opportune Portlet shown by the web interface.

In this context, we can distinguish between two views of the services exposed by Portal: a Vertical view and a Horizontal view. The vertical view is related to the set of services that allows a *direct access* to the functionalities of the different modules of the HF platform such as, for example, the configuration of the AmI framework, the management of the CDSS, the access to the images of a selected study. In other words, this view comprises all the services that are directly related with single functionalities of the modules of the platform. On the contrary, the Horizontal view involves all the services that integrate different functionalities exposed by the modules of the platform such as, for example, the enrolment of a patient that involves functionalities exposed by the Electronic Patient Record, by the Master Patient Index and by the central repository. Moreover, the Horizontal view includes the services related to the configuration of workflows that involve more that one module, e.g. activation of an alarm service that involve the CDSS, the Alarm system, the Data Manager and so on, as well as all the services related to user management (creation, deletion and modification of the users allowed to access the platform) and profiling (assigning, modification and removal of access rights).

In order to manage the access to the available services, the system takes into account set of profiles each of which will be associated with a set of access rights (or capabilities). When a user is authenticated, a specific profile is assigned and, therefore, a set of access rights for that user is identified. The access rights, which can be opportunely configured, define the capabilities of the user to access each single Portlet of the Portal, and therefore the authorization to access the available services.

In the first platform prototype we will take into account three different profiles:

- The Administrator
- The Restricted User
- The Portal Administrator

A Supervisor user has a global vision of the system. He can perform low level and high level configuration of the system, and has the capabilities to access all the available services of the platform. Typical actors that can be associated to this profile are the specialists, the family doctor, the cardiologist who is enrolling the patient, the
system administrator.
A restricted user can access only to a subset of the available services on the platform, for example it will not be allowed to configure alarms, to configure the ambient intelligent monitoring on acquisition devices and cannot activate the

CDSS on acquired data. Typical actors that can be associated to this profile are nurses that need to access the patient data but are not allowed to change the information of the patient or to activate a decision support on monitored data.
A special user profile of the web portal is the Portal administrator. An administrator can define new profiles, define new application areas (i.e. Portlets), associate new applications to an application area. The portal administrator is then in charge of registering new users, assigning them a profile and other personalized capabilities.

These are example profiles that will be used to demonstrate the configurability of the Portal and, hence, of the Platform. Of course, it will be possible to configure any number of profiles, each of which can be associated with different access rights for each Portlet of the Portal.

4 Main tasks of the HEARTFAID Platform

In order to guarantee the interoperability among the services offered by the HF platform, we will rely on the so called Service-Oriented Architectures (SOA). SOA is a set of components which can be invoked, and whose interface descriptions can be published and discovered (W3C).

A service-oriented architecture is essentially a collection of services. These services communicate with each other. The communication can involve either simple data passing or it could involve two or more services coordinating some activity. Some means of connecting services to each other is needed.

Service-oriented architectures are not a new thing. The first service-oriented architecture for many people in the past was with the use of DCOM or Object Request Brokers (ORBs) based on the CORBA specification.

If a service-oriented architecture is to be effective, we need a clear understanding of the term service. A service is a function that is well-defined, self-contained, and does not depend on the context or state of other services.

The technology of Web services is the most likely connection technology of service-oriented architectures. Web services essentially use XML to create a robust connection.

Figure 4.1 illustrates a simple model of service-oriented architecture. It shows a service consumer at the right sending a service request message to a service provider at the left. The service provider returns a response message to the service consumer. The request and subsequent response connections are defined in some way that is understandable to both the service consumer and service provider. How those connections are defined is explained in the Web Services Architecture. A service provider can also be a service consumer.

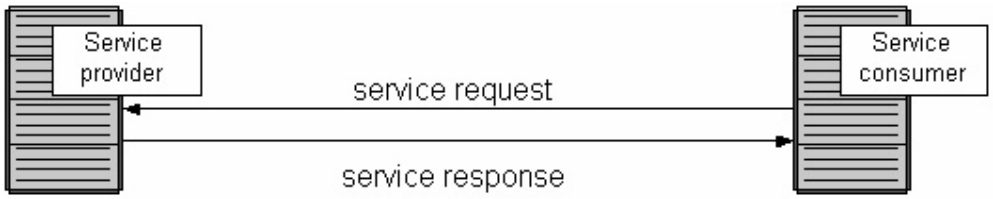


Figure 4.1: Service-Oriented Architecture

SOA is an evolution of distributed computing based on the request/reply design paradigm for synchronous and asynchronous applications. The individual functions of an application in the HF platform will be modularized and presented as services. What's key to these services is their loosely coupled nature; i.e., the service interface is independent of the implementation. The applications of the platform can be built by composing one or more services without knowing the services' underlying implementations. For example, a service that is provided by the HEARTFAID platform can be implemented either in .Net or J2EE, and the application consuming the service can be on a different platform or language.

Service-oriented architectures have the following key characteristics:

- Services are loosely coupled: minimizes dependencies between services.

- Contractual: adhere to agreement on service descriptions.
- Autonomous: control the business logic they encapsulate.
- Abstract: hide the business logic from the service consumers
- Reusable: divide business logic into reusable services.
- Composable: facilitate the assembly of composite services.
- Stateless: minimize retained information specific to an activity.
- Discoverable: self-described so that they can be found and assessed.
- Services are discoverable and dynamically bound.
- Services are self-contained and modular.
- Services stress interoperability.
- Services have a network-addressable interface.
- Services have coarse-grained interfaces.
- Services are location-transparent.
- Services are composable.
- Service-oriented architecture supports self-healing.

Each SOA service has a quality of service (QoS) associated with it. Some of the key QoS elements are security requirements, such as authentication and authorization, reliable messaging, and policies regarding who can invoke services. In this way, we can define various access levels, according to user's attributes (e.g. doctors and patients).

4.1 Environments

Gathering and organizing data is a major problem for many, especially complex applications like the clinical / medical applications.
The HEARTFAID platform should combine collection, integration and process of relevant biomedical data coming from the main settings encountered by patients with Chronic Heart Failure (CHF).
The reference study cases that have been recognised according to the different healthcare pathways of patients with confirmed heart failure are divided into three main categories (see Figure 4.2).

- The *medical environment*: includes the processes that are performed on data collected both in the office of the family physician and in the specialized cardiology department (diagnosis, management, prognosis assessment and medical recommendations). Cardiologists are involved in outpatient and inpatient care, with the possibility of running a variety of tests, such as blood tests, ECG, X-Rays, ultrasound imaging studies, etc.
- The *patient environment*: refers to patients' data that are collected both in the office of the family physician and in the specialized cardiology setting, however, biomedical parameters, relevant symptoms and compliance to prescribed pharmacological and non pharmacological regimens will be monitored at patients' home. Selected biological parameters will be measured and collected by the patients themselves and/or by relatives, caregivers and specialized nurses.

- The medical and technological *research environment*: concerning patients' data that are collected, in the office of the family physician, in the specialized cardiology setting, but also in the ultra specialized research setting. While supporting the standard CHF management and prognosis assessment, the HFP will assist in collecting biomedical information for research and development purposes.

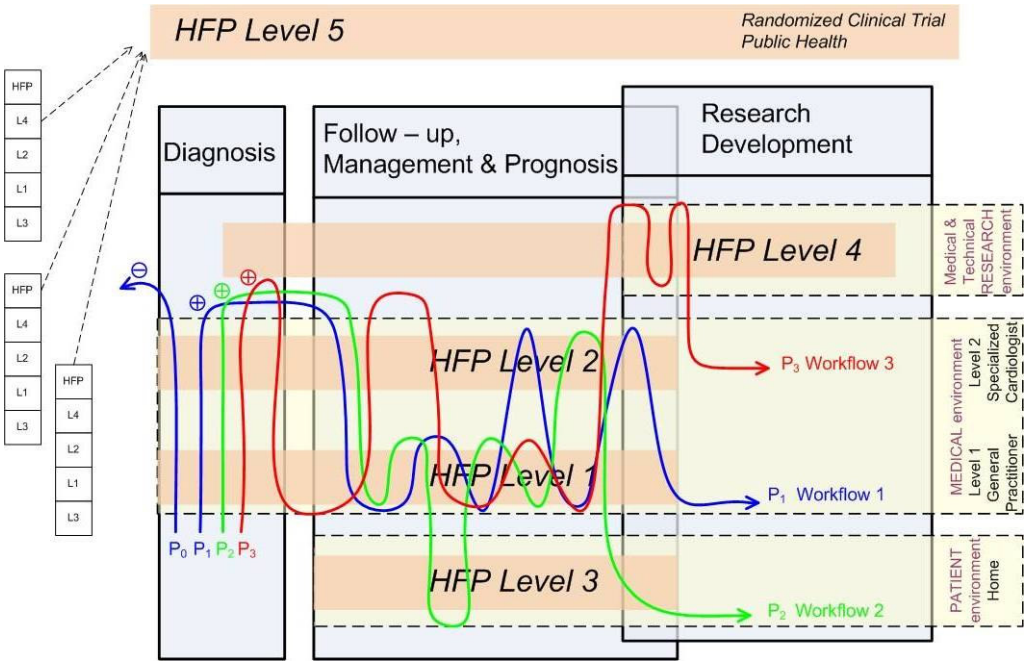


Figure 4.2: Organization of the HEARTFAID technological platform (HFP). The basic levels of functioning of the HF platform are articulated in various workflows.

4.1.1 Workflow 1: medical environment

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.

4.1.2 Workflow 2: medical environment and patient's home

Trajectory of patient of type 2 depicts a care delivery process in which the diagnosis, management and prognosis assessment are provided with patients' data collected and medical recommendations provided both in the office of the family physician, in the specialized cardiology setting and in patients' home. 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 and research environment

While all the other functionalities will be the same as the routine workflow, a main peculiarity of the research workflow is its capability of collecting more information typically not available in the routine workflows.

While the patient receives the standard care, the extra information collected by HFP level 4, provides evidence in favour of potentially more effective diagnostic and treatment strategies. The DSS plays in this context a crucial role. Once such newly developed strategies will be acknowledged by the European Society of Cardiology HF guidelines the DSS algorithms will be updated for routine care (HFP levels 1,2,3).

Additional work is mainly focused in the collection of other information/medical examinations in order to improve the performances of the DSS (its algorithms can be modified for this workflow).

Going more into the details, several additional medical devices (not used in the routine workflows) may be added for this workflow in automatic or manual way. Medical devices can be used in primary/secondary care premises or at home/on-the-move.

For each medical device (automatically integrated) used in primary or secondary care premises the acquisition of the medical examination has to be performed with a software accessible from the user interface of the medical personnel and finally raw data will be available in the repository.

For each medical device (manually integrated) used in primary or secondary care premises the acquisition of the medical examination has to be performed using a CRF from the user interface of the medical personnel and finally only the relevant information without raw data will be available in the repository.

For each medical device (automatically integrated) used at home/on-the-move the acquisition of the medical examination has to be performed with a software accessible from the user interface of the patient and finally raw data will be available in the repository.

For each medical device (manually integrated) used at home/on-the-move the acquisition of the medical examination has to be performed using a CRF from the user interface of the patient and finally only the relevant information without raw data will be available in the repository.

Signal/image processing can be applied to all the automatically integrated medical devices in order to extract relevant features from the acquired examinations. These relevant features together with the relevant information acquired using the CRF for the manually integrated medical devices can be used as further input for the decision support system in the attempt of improving its statistics indexes (i.e. sensitivity and specificity).

4.2 Workflow Scenarios

4.2.1 Scenario 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 enzimes), 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.

4.2.2 Scenario 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.

4.2.3 Scenario 3. Heart Failure in the 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 develoment of newer and more efficacious diagnostic and management strategies in the field of HF.

4.2.4 Scenario 4. Heart Failure in the aged population: the life of Pietro Guarneri in the HEARTFAID age

We consider Mr. Pietro Guarneri, a 65 years old patient, former smoker, suffering from hypertension from several years. Five years before he had an Acute Myocardial Infarction and he underwent to aorto-coronary bypass. The patient had a post ischaemic dilated cardiomyopathy, with a systolic dysfunction. The patient was enrolled in the platform six months ago and during this period he has

been telemonitored. He referred slight limitation of physical activity, comfortable at rest but ordinary activity resulted in fatigue and dyspnoea and he belongs to NYHA class II.
The TTE (*transthoracic echocardiography*) examination showed an LV EF (*left ventricle* ejection fraction) of 40%, ESV (end-systolic volume) of 114 ml, EDV (end-diastolic volume) of 190 ml, and SV (Stroke Volume) of 76 ml, the LV end-diastolic diameter 6.0 cm.
The patient was treated with ACE-inhibitor, beta-blockers, spironolactone, aspirin and statin. Neither pulmonary nor systemic congestion signs were present. Blood examinations of renal function and electrolytes were normal. As mentioned previously, during these six months, the patient has been telemonitored. In particular, the pharmacological therapy has been followed with care and no relevant changes have been identified by the platform.

Present situation

Suddenly, the patient observes a worsening of its symptoms, with a marked limitation of physical activity. After he completes a periodic questionnaire suggested by the platform (based, for example, on Minnesota questionnaire) the change in the symptoms is automatically detected and found relevant. Minnesota Questionnaire score is 52. A medical visit is proposed and performed immediately.
At the visit the NYHA class changed from II to III. No changes in the signs is observed by the physician, apart from a slight worsening of blood pressure (150/90 mmHg) and a heart rate increased of 10 beats. After an ECG is performed that confirms the increase of 10 beats in the heart rate. The physician, supported by the CDSS, decides however to evaluate other parameters by echocardiography. TTE is performed during the visit and a list of parameters are evaluated and images are analyzed by the sonographer.
After the examination is performed, the images and the parameters manually computed by the sonographer are uploaded in the platform.
Left ventricle volume and ejection fractions are computed again by automatic methods, exploiting the available image sequences. They are compared with the historical data of the patient.
EDV increases to 210 ml, ESV increases to 145ml, SV is 65 ml, EF decreased from 40% to 30%. Mild tricuspidal insufficiency is Doppler-detected by its regurgitation. By tricuspidal regurgitation entity, the pressure gradient (mmHg) between right ventricle and right atrium is measured. Pulmonary pressure was then estimated. With this aim the subcostal view is taken into account; so as to determine Inferior Vena Cava (IVC) diameter and its collapsibility index. Collapsibility index refers to the inspiratory response of the IVC diameter and is defined as the decrease in percentage of the diameter.
The pulmonary pressure is estimated to be 40 mmHg by using a lookup table with entries consisting in the tricuspidal gradient, IVC diameter and collapsibility index. Since this value indicates a sligth pulmonary congestion, the CDSS suggests to the physician to integrate the pharmacological therapy with diuretics, for example loop diuretics or thiazides.

Since in the last month there are no up-to-date information about the renal function and electrolytes, the CDSS suggests a safe low dosage and to perform blood examinations, which are scheduled for few days later. The therapy consists in loop diuretics, for quicker beneficial effects.
The patient returned to his home and continues to be monitored in the subsequent days. In particular control of weight, urine output, blood pressure, symptoms are scheduled daily and after the first week of treatment, blood examinations are requested to the patient.
The blood examinations, after the first week, are uploaded to the platform. An up-titration program for the diuretics is compiled by the CDSS, considering in particular symptoms and electrolytes balance, creatinine clearance, blood pressure, weight slope and urine output. Control of weight and urine output is daily scheduled and blood examinations every week.
After review and approval by a physician, the up-titration program is sent to the patient. A visit is scheduled in one month, to appreciate the response to the therapy.
During the first week of this month the patient is monitored, he has persistence of symptoms, thus he follows the up-tritation program of diuretics and for the other part of the month symptoms get better until the visit. During that visit, the patient feels better and the symptoms are relieved, so NYHA class is moved back to II. However, the CDSS suggests to the physician to explore the possible origins of the change in the symptoms reported in the previous visit (the probable cause of heart failure decompensation). In particular with the aim of controlling the ischaemic disease, a stress test is scheduled.

4.3 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 coicides 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 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.

4.4 The functionalities 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 4.3.

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. on the one hand, 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. on the other hand, 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.

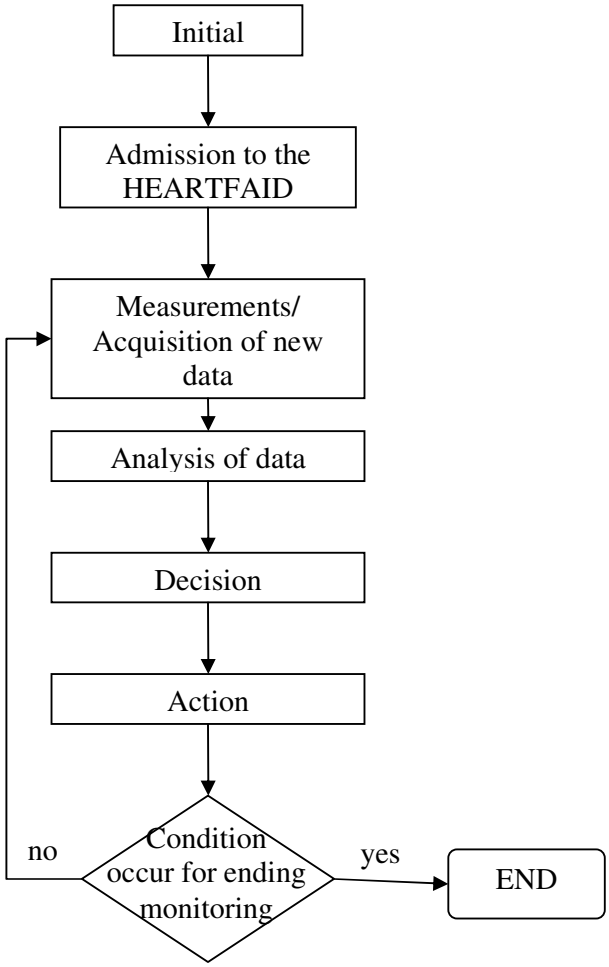


Figure 4.3: Block diagram of the overall workflow of the platform.

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.

5 The HEARTFAID services

5.1 Home monitoring

For the home monitoring, a specific set of information will be collected with a frequency established by the specialized doctor. Patient is made aware of the required frequency and clinical protocol for the acquisition of the necessary data. Training about the proper use of the medical devices has been made to the patient and to his registered relatives.
If the information is not collected within a few hours from the expected time an alert is sent to the patient and his registered relatives in order to remind them to perform the data acquisition.
The following medical devices are used:

- ***Nonin 4100* – Pulse Oximeter**
- ***A&D UA-767PBT* – Ambulatory Blood Pressure Monitor**
- ***A&D UC-321PBT* – Electronic Scale**
- ***MagIC* – Multiparametric Monitoring Vest**

All these devices are connected (via Bluetooth) automatically to the platform using a specific software installed at the home client station that acts also as an acquisition gateway. Patient has to login the home client software to go to the acquisition page and to start the acquisition from the desired device.
For the first 4 devices one (or a few) numbers are sent to the data repository and associated to the registered patient, while for the vest a stream of data (raw data) is sent to the data repository.
The measured parameters will be:

- ***Nonin 4100* – Pulse Oximeter**
  - ✓ ***HR (heart rate), SpO2 (oxygen saturation)***
- ***A&D UA-767PBT* – Ambulatory Blood Pressure Monitor**
  - ✓ ***SBP (systolic blood pressure), DBP (diastolic blood pressure), HR (heart rate)***
- ***A&D UC-321PBT* – Electronic Scale**
  - ✓ ***WG (weight)***
- ***MagIC* – Multiparametric Monitoring Vest**
  - ✓ ***CM (chest movements, correlated to the respiratory rate), ECG (one-lead ECG), AX, AY, AZ (3-axes accelerometers)***

Another device will be used in the home monitoring but it will not be automatically connected:

- ***BF-906* – Body Impedance Analyzer**

This device will be integrated using an eCRF form that will be accessible from the "patient profile" interface. The patient or his relatives will fill in the acquired data in the eCRF form and submit it to the data repository.

The measured parameters will be:

- Body fat (%)
- Body fat weight

- Target fat (%) (min/max)
- BMI (body mass index)
- Body impedance
- Basal metabolic rate (BMR) (Kcal)
- Target weight (min/max)
- Lean weight
- Lean (%)
- ***Water liters***
- ***Water (%)***
- Target water (min/max)

Only the Water liters and the Water (%) are useful for early detection of heart failure decompensation and only these values will be filled in a form by the patient or his relatives.

The DSS makes a first check about the data integrity (for all the devices except the vest). If values are highly out of the normal range for the patient then a request for a new immediate acquisition is sent to the patient and his relatives.
Furthermore the Minnesota questionnaire has to be filled in by the patient and submit to the data repository. The Minnesota questionnaire (see below) will be a form available in the "patient profile" interface of the home client software.

The following questions ask how much your heart failure (heart condition) affected your life during the past month (4 weeks). After each question, circle the 0, 1, 2, 3, 4 or 5 to show how much your life was affected. If a question does not apply to you, circle the 0 after that question.

Did your heart failure prevent you from living as you wanted during the past month (4 weeks) by -	No				Very Little					Very Much
1. causing swelling in your ankles or legs?	0				1	2	3	4	5	
2. making you sit or lie down to rest during the day?	0				1	2	3	4	5	
3. making your walking about or climbing stairs difficult?	0				1	2	3	4	5	
4. making your working around the house or yard difficult?	0				1	2	3	4	5	
5. making your going places away from home difficult?	0				1	2	3	4	5	
6. making your sleeping well at night difficult?	0				1	2	3	4	5	
7. making your relating to or doing things with your friends or family difficult?	0				1	2	3	4	5	
8. making your working to earn a living difficult?	0				1	2	3	4	5	
9. making your recreational pastimes, sports										

or hobbies difficult?	0	1	2	3	4	5
10. making your sexual activities difficult?	0	1	2	3	4	5
11. making you eat less of the foods you like?	0	1	2	3	4	5
12. making you short of breath?	0	1	2	3	4	5
13. making you tired, fatigued, or low on energy?	0	1	2	3	4	5
14. making you stay in a hospital?	0	1	2	3	4	5
15. costing you money for medical care?	0	1	2	3	4	5
16. giving you side effects from treatments?	0	1	2	3	4	5
17. making you feel you are a burden to your family or friends?	0	1	2	3	4	5
18. making you feel a loss of self-control in your life?	0	1	2	3	4	5
19. making you worry?	0	1	2	3	4	5
20. making it difficult for you to concentrate or remember things?	0	1	2	3	4	5
21. making you feel depressed?	0	1	2	3	4	5

If the information is not collected within a few hours from the expected time an alert is sent to the patient and his relatives in order to perform the required examinations (sending them to the data repository) or to fill-in the required questionnaire or CRFs.
As a result of the information sent to the data repository (after the data integrity check or artefact rejection), the DSS can decide some actions (change of the therapeutic plan, change in the acquisition schedule, change in the time of the next planned visit, etc.) that once validated will be sent to the patient and his relatives for its acceptance and start-up.

5.2 Monitoring on-the-move

The purpose of this type of services is to enable the on-the-move biomedical data acquisition and the transmission of these data to the HEARTFAID platform. In order to achieve this goal the portability and wireless connectivity of medical devices/sensors has to be combined with the increasing connectivity capabilities of mobile devices (e.g. smart phones, PDAs etc) carried by the patient.
For the monitoring on-the-move the information that will be collected is the same as that of the home monitoring, with the exception of the *BF-906* – Body Impedance Analyzer that is not suitable for an on-the-move setting. The gateway will be represented by a mobile phone (with Bluetooth interface) or by a PDA (with Bluetooth and GPS/GPRS functionalities). The Mobile Client will have to implement the same acquisition interface like the Home Client taking into account, of course, the limitations of the display and user interface of a mobile phone or PDA.

In order to build this type of services the following elements have to be implemented:

a) Data acquisition modules

These modules will enable the communication between the mobile device and the medical device/sensor in order to transfer the biomedical data from the medical device to the mobile device. Considering that in the scope of HEARTFAID the medical devices/sensors support Bluetooth wireless connectivity, a wireless Bluetooth channel has to be established (with the mobile device acting as client or server depending on the communication protocol supported by the medical device). In order to implement the software modules for data acquisition, the communication protocol has to be disclosed by the vendor of the medical device.

The software modules enabling the biomedical data acquisition were developed in J2ME (Java2 Micro Edition) and executed in devices supporting the JSR-82 API, which enables the development and execution of Java Bluetooth applications in mobile devices.

The connectable devices for the on-the-move environment can be seen in the following table.

Device Model	Device Type
Nonin 4100	Pulse Oximeter
FRWD Sports computer	Heart Rate
MagIC	Multiparametric Monitoring Vest

More details on the above devices and their features can be found in D19-Prototype of the Data Acquisition and Transmission Infrastructure.

b) Data transmission

The transmission of the acquired biomedical data takes place over IP utilising the supported connectivity for mobile devices over GPRS/3G networks. Regarding the on-the-move monitoring, although the creation of XML messages could be performed at the mobile phone's side, the transmission of XML messages usually involves transmission of larger volumes of data. For this reason, for the case of the on-the-move monitoring, the data is sent to an intermediate gateway, which is responsible to create the XML messages from these data and transmit them to the HEARTFAID platform. The service logic is implemented using ASP.NET service components and the XML messages are created using the standard API provided by the Microsoft.NET framework.

5.3 Data processing and feature extraction

The HF platform will enable collection of large amount of different patient data. Besides data describing patients at the first visit (patient enrolment), the platform will collect also patient data during follow up visits, including the findings of several diagnostic tests (e.g. echocardiography, ECG, Holter…) and, whenever

possible, the associated raw data (e.g., respectively, ultrasound images, chunks of ECG recordings, RR intervals…).
Especially relevant is the fact that HFP will enable collection of relevant continuous monitoring data like heart rate, weight, body temperature, respiratory rate, and water content.
In respect to such data set the platform will be a unique source of valuable information about HF patients. The results of the analysis of the collected data will be used for the constant improvement of the platform's knowledge base that is used by the decision support system. But the results could be relevant also in the broader sense for better understanding of the disease in general and as a starting point related to different research activities.
In this setting, signal and image processing represents a fundamental tool for the automatic or semiautomatic data analysis and for the extraction of features relevant to knowledge discovery purposes.
Further, of course, signal and image processing may provide methods for the computation of parameters which are often manually computed and whose interpretation can then be readily performed by a physician. Thus, signals and image processing is useful to speed up diagnostic procedures, while, at the same time, reducing intra- and inter-observer variability through the use of automatic or semi-automatic methods.

In summary, data processing and feature extraction services in HEARTFAID have a twofold goal: from one side they focus on data extraction and analysis for knowledge discovery purposes (as described in Section 5.3.1 below), while for the other side, they should provide tools for feature extraction from raw data by signal and image processing methods, as described in Section 5.3.2.

5.3.1 Data extraction and analysis services

The most relevant task of the data extraction and analysis service is to enable user directed access to the collected data and to data in the form appropriate for the subsequent analysis. Data extraction is based both on the subset of attributes (i.e. laboratory assessment, medication, changes in CHF status) that have to be analysed and on the subset of examples (i.e. patients older than 75 years that are in NYHA class 3 and have ejection fraction less than 40) that are set of examples for which the analysis if performed. Optional conditions for data extraction may be the location and time of data collection.

In the data extraction service the special attention must be devoted to the preparation and transformation of temporary related data. It can be noted that not only continuous monitoring data are temporary related. Actually the majority of the data collected by the platform are time related sequences of the data because most of the patient information is recollected at each visit (therapy, physical examination, laboratory assessment, chest X-ray and so on). The data analysis process must enable analysis of the changes in the data sequences (significant increases and/or decreases of constantly monitored data, patient worsening status,

changes in therapy) but also this properties must be allowed to determine selection of the patient subpopulation that is analysed (patients that during follow up changed from NYHA 2 to NYHA 3, patients that stopped taking some medication).

In general there are significant differences between sequences of continuously monitored data and sequences collected at visits to specialized institutions. The former are long numerical sequences with more or less constant time difference among samples. There is small or no significance of a single measurement. In contrast to that the later are short (with 1-8 samples), with variable distances among samples and high importance of each sample. Analysis of long sequences must be based on statistical properties where the major problem is the selection of the time interval in which analysis will be performed. Short sequences should be analysed primary on the bases of the differences in detected or measured values in subsequent visits.

Special, but very important subtype of data extraction is when we want to analyse causes or consequences of some important events. For example, events can be decompensation, changes in NYHA class value, or changes in therapy. In this case we are interested especially in the time interval before the event (i.e. in case of worsening) or after the event (i.e. in case of medication). Such analysis requires very complicated data transformation process and complicated user interface. It is a relevant research task to determine if there is a possibility to include also such data extraction options into HF platform web-based interface.

It is assumed that in principle the data analysis process itself will be performed outside the platform with tools most appropriate for the goals that the user has to achieve. But there is a possibility that the platform itself enables some data analysis. At the basic level it is statistical analysis of patient characteristics for the selected subpopulation. Significantly more complicated is implementation of data mining tools for the knowledge extraction purposes. The HF platform will have the possibility that the data prepared and extracted by this service directly enter the knowledge discovery process under the web-based control. Moreover, the presentation of the results obtained by such analysis will be also web-based.

5.3.2 Signal and Image processing services

Signal and Image Processing (SIP) services aim at extracting in an automatic or semi-automatic fashion parameters useful in other components of HEARTFAID platform, e.g.:

- Parameters to be inserted directly into the platform as a finding of some examination (for example left ventricle ejection fraction from US images or heart rate variability from RR intervals in a Holter recording)
- Parameters needed to activate some type of reasoning/inference in the CDSS (for example, if inference on the knowledge base shows that the

computation of parameter *X* may break ties during a diagnostic task, then SIP services are invoked to compute parameter *X*)

- Optionally, parameters to be computed off-line for knowledge discovery purposes

Since SIP services have many connections with other HFP components, their integration requires special care. In particular, since some image processing algorithms will be only semi-automated, easy-to-use interfaces should be implemented to allow for user interaction and feedback.
The situation is best explained through the following example, taken form echocardiography workflow and regarding the computation of left ventricle ejection fraction.

An over-reading sonographer would like to compute the left ventricle ejection fraction. The first point to be addressed is access and selection of the data on which some kind of processing should be performed. In this case, the sonographer will have very likely to choose an image sequence taken from an apical two or four chambers view.
Therefore, among the bunch of images and images sequences (about 20/30 instances in our validation sites) contained in an echo examination, he needs to choose quickly the right one for his purposes. Since image quality is not important for this preliminary selection, low resolution images are enough so as to prevent tedious long data transfers (the full examination may require 100Mb).
Supposing that the examination is already stored in an archive in a structured format, the selection task could be accomplished through a web interface (see Section 7.2.4 for topics concerning interaction with the image archive through the web).
Then, the sonographer will need to run a segmentation algorithm on the selected image sequence and appreciate its results. For this purposes, he needs higher resolution images that should be transferred to his client station. Further, very likely, such algorithm wouldn't be able to run within the browser sandbox. Thus, an external application is required. Somehow, the unique identification number of the image sequence selected in the web-browser is passed to the external application.
Only at this point, real image processing starts. Before starting image analysis, anyway, the sonographer may want to perform for example pan and zoom and contrast enhancement by tools provided in the GUI. A set of algorithms is provided in the GUI among which there is, for example, computation of left ventricle ejection fraction. Clicking on this algorithm, the user is prompted to click on a point in the image belonging to the left ventricle cavity. After that, a segmentation algorithm is triggered. Default parameters and the coordinates of the point selected by the user are passed to the algorithm. When the algorithm stops, the result of segmentation are shown to the sonographer. The sonographer is prompted to state if the result is satisfactory. If the answer is positive, ejection fraction is computed according to Simpson's rule. Otherwise, the user may choose to run the algorithm with manually tuned parameters or, even, decide to manually trace the contour, a last chance to be used in presence of extremely poor acoustic

windows or implanted artificial valves. When a satisfactory result is eventually reached, the sonographer should be able to store the segmented image sequence in the image archive for further reference and to insert the computed value of ejection fraction in the eCRF.

This short example sheds light on several features of SIP services: the need of quick data selection tools within a web interface perhaps, the exchange of information between the web interface and an external application in which algorithms eventually run and the interaction with HEARTFAID repositories, namely the eCRF and an image archive.

5.4 The decision support system

Within HFP, an informative and decision support set of services, the HEARTFAID Clinical Decision Support System (CDSS), will be devised for intelligently aiding clinical operators in the daily management of HF patients. Actually, HF routine practice presents several aspects in which an automatic, computer-based support could have a favourable impact. Precisely, four problems have been identified that would highly benefit of HEARTFAID CDSS point-of-care intervention; they can be referred as *macro domain problems* and listed up as: (i) HF diagnosis, (ii) prognosis, (iii) therapy planning, and (iv) follow-up.
Further detailed decision problems have been identified for specifying these macro domains, focusing as much as possible on the medical users' needs; explicative examples are:

- Diagnosis, assessment and severity evaluation of heart failure
- Identification of suitable pathways
- Planning of adequate, patient's specific therapy
- Analysis of diagnostic exams
- Suggestion of changes in management and treatment
- Early detection of patient's decompensation

In order to design and develop an effective and reliable CDSS able of facing such decisional problems, innovative results on computational modelling, knowledge discovery methodologies, visualization and imaging techniques, and the medical knowledge of the relevant domain have to be opportunely integrated. In deed, the core components of HEARTFAID CDSS are

- formalized clinical knowledge, consisting of pre-existing guidelines, experts' know-how procedures, and new elicited knowledge discovered by KDD processes;
- robust and reliable reasoning approaches, based on computational models of *Machine Learning* (ML) and *inference* methodologies on declarative and procedural domain knowledge;
- innovative methods for biomedical signal and image processing.

The decision support services mainly rely on *inferential reasoning* on the available domain knowledge, which has been formalized according to a *symbolic* representation formalism based on *ontologies* and *inferential rules*. However,

computational approaches appear also beneficial in most of the problems to be addressed and are currently under development. Actually, mathematical models and ML methods allow for facing those decisional problems whose solution cannot be formalized in *symbolic* representations, owing either to the lack of assessed knowledge or to the characteristics of the problem (i.e. high levels of complexity and variability). In some cases, making a decision requires an investigation on the hidden, complex, often non-linear correlations among data, together with high-level analytical processing functions. In such cases, the knowledge needed for the solution should be acquired directly from data (*inductive knowledge*) and stored in the developed model (e.g. *Artificial Neural Networks* – ANN, *Support Vectors Machines* – SVM), which induce sub-symbolic knowledge from a data-driven processing.
Moreover, the analysis of biomedical signals and images relevant to HF (e.g. ECG, Echocardiography,…) is a peculiar functionality due to the need for providing well-established and defined parameters extracted from the data as part of the inputs to the CDSS. In addition, within a long-term research environment, signals and images processing may provide *novel representation features,* i.e. non-standard parameters that can add more insight in heart failure domain, for example giving new methods for early diagnosis and prognostic stratification.

A better insight into the decision support services can be obtained by analyzing the decision-making problems addressed and the main functionalities of the HEARTFAID CDSS, as summarized in the following sections.

5.4.1 Decision-making problems

Improving the effectiveness and efficiency of HF clinical practice requires the HEARTFAID CDSS to face the main decisional problems as detailed below.

Diagnosis
The CDSS will aid physicians in improving their diagnostic performance: even though diagnostic procedures are very well codified in HF Guidelines, diagnostic errors are still present in clinical practice. The CDSS will be able to process patient's status and assess the accordance of patient's symptoms and signs with the diagnostic criteria. More in general, the response of the CDSS diagnostic functionality will regard:

- diagnosis of HF;
- assessment of HF severity;
- evaluation of patient's current clinical conditions.

The knowledge required consists in the evaluation criteria, specified in the guidelines and in procedural rules elicited from the clinicians. Confidence values will be evaluated and associated to the different passages of the diagnosis, so that more possibilities can be presented to the clinicians, supporting differential diagnosis. Moreover, the CDSS can suggest further diagnostic examinations to be performed, if necessary for reaching a more reliable diagnosis.

Prognosis

Prognostic evaluation is among the hardest decisional tasks in HF management due to the absence of generally agreed operative information. In addition, for each of the possible conditions (i.e. *stable, improving, rapidly worsening,* or *slowly worsening*) both the predictive value and the prognostic evaluation objectives may change. Prognostic stratification during an acute unstable phase, for instance, should guide immediate decisions, while, in a stable phase, it could have a long term aim and should predict destabilization and death in mid and long term.

In this context, HEARTFAID CDSS will formulate patient's prognosis, taking into account the implications of different patient's status. Additionally, it should also help in verifying if the clinical classification of acutely decompensated HF adds prognostic value to the NYHA classification.

Computational decision models for predictive analysis can be required to accomplish this task. Innovative techniques for survival analysis using ML and statistical methodologies should be then provided. Moreover, if new cut-offs and/or reference values for individual, or combinations of parameters will be discovered by KDD processes, they should be suitably encoded into the HEARTFAID CDSS knowledge bases, thus allowing to a further increase of the efficacy.

Therapy planning

HEARTFAID CDSS will suggest, based on guidelines recommendations, the pharmacological and non pharmacological measures that best apply to each individual patient. The number of possible actions and the complexity of the whole context suggest the usefulness of an automatic tool able to remind the available therapeutics options.

In particular, HEARTFAID CDSS should provide assistance in planning the therapy by carefully considering HF aetiology, gravity, physiopathological conditions, and by evaluating interactions with other coexistent diseases and/or drugs taken by the patient. Altogether, the response of the CDSS will regard:

- pharmacological treatment suggestions
- life style modification alerts
- uptritation support
- compliance to guidelines recommendations.

Follow-up

The CDSS is responsible of assuring the adequate follow-up of HF patients by interpreting telemonitored data so as to prevent adverse events and early detect patients' worsening. Telemonitoring will play a key role in such situations by assuring the collection of relevant information inherent symptoms and biomedical parameters (e.g., blood pressure, heart rate, respiratory frequency).

The available domain knowledge will be formalized to allow the CDSS interpreting the acquired data and early detecting patients' decompensation, suggesting changes to the therapy, advising new diagnostic examinations. Among these tasks, the automatic recognition of decompensation events is an absolutely innovative functionality, which will likely benefit from the definition of reliable

computational decision models able to process a set of telemonitored symptoms and signs.
The follow-up can be conceived as the overall functioning of the HFP and, hence, represents the most complex problem, which can entail facing all the other problems, i.e. making a diagnosis for assessing the patient's status, planning a new therapy, formulating a prognosis and scheduling new examinations/next visits.

5.4.2 Decision support functionalities

The CDSS supports HF management, i.e. diagnosis, prognosis, therapy and follow-up, by using patients' heterogeneous information (i.e. actual status, anamnesis, clinical history, diagnostic parameters, clinicians' evaluation) and applying two type of reasoning: *inferential* and *computational*.
Inferential reasoning consists in *inductive* and *deductive* reasoning on the available domain knowledge, and it is strictly correlated to the knowledge representation formalism. The fundamental aim is developing a formal description of the domain (i.e. relevant concepts, their properties and interrelations) and carefully formalizing the declarative and procedural knowledge, derived from the guidelines and the experts' know-how. Ontologies combined with rules have been chosen since the more suitable and up-to-date methodology for solving both tasks. Actually, rules-based approach appears the more appropriate, since easily understandable by a non-specialised audience, e.g. clinicians. In this way, they can be more tempted in contributing to the knowledge elicitation and representation processes. An inference engine can then be devised for the corresponding reasoning processes.
Computational reasoning is involved in those difficult HF decision problems whose solution is still debated in the medical community, due to the lack of validated and assessed evidences. It consists of *inductive reasoning* and relies on applying computational decision models, which can be developed according to different methodologies (e.g. ML including *Soft Computing* and *Statistical Pattern Recognition*, or *Linear* or *Constraint Programming*).
Defining ML decision models requires the identification of a set of input parameters for modelling the problem to be faced; a set of *exemplars* of the problem, and a *training* process for data-driven knowledge extraction. This process relies, in practice, in tuning the *model free parameters*, iteratively until the desired decision accuracy is reached.
Processes involved in the CDSS functioning can be, then, grouped into the following categories:

- *Signal and images processing*, developed for assessing patients' status and acquiring diagnostic parameters. Processes belonging to this category consist of calls to algorithmic procedures, are activated on demand, and might require the user's interaction, e.g. procedure for estimating the ejection fraction in echocardiographic images;

- *Inference,* involved in inferential reasoning, for assessing patients' status, formulating diagnosis and prognosis, assisting therapy planning, and patients' monitoring. Generally speaking, they consist in querying the knowledge base for inferring new facts or new actions to perform, are activated on demand and can involve the users' in interactive dialogues;
- *Computational decision,* concerned with computational reasoning for patients' HF severity and prognosis assessment, and for patients' monitoring. They mainly correspond to on-demand applications of the decision models developed.

The HEARTFAID CDSS architecture has been designed according to a multilevel conceptualization for distinguishing among

- the *knowledge level*, corresponding to all the information needed by the system for performing tasks, e.g. data, domain knowledge, computational decision models;
- the *processing level*, consisting of the system components that are responsible of tasks accomplishment by using the knowledge level;
- the *end-user application level*, including the system components whose functionalities are specifically defined for interacting with the user.

More in detail, the CDSS architecture consists of the following components (Fig. 5.1):

- *Domain Knowledge Base*, consisting of the domain knowledge, formalized from the guidelines and of the clinicians' know-how;
- *Model Base*, containing the computational decision models, signals and images processing methods and pattern searching procedures;
- *Meta Knowledge Base,* composed by the strategy knowledge, i.e. about the organization of the CDSS tasks.
- *Brain*, the system component endowed with the reasoning capability, which is divided into the meta and object level;
- *Explanation Facility*, providing a means to explain conclusions taken.

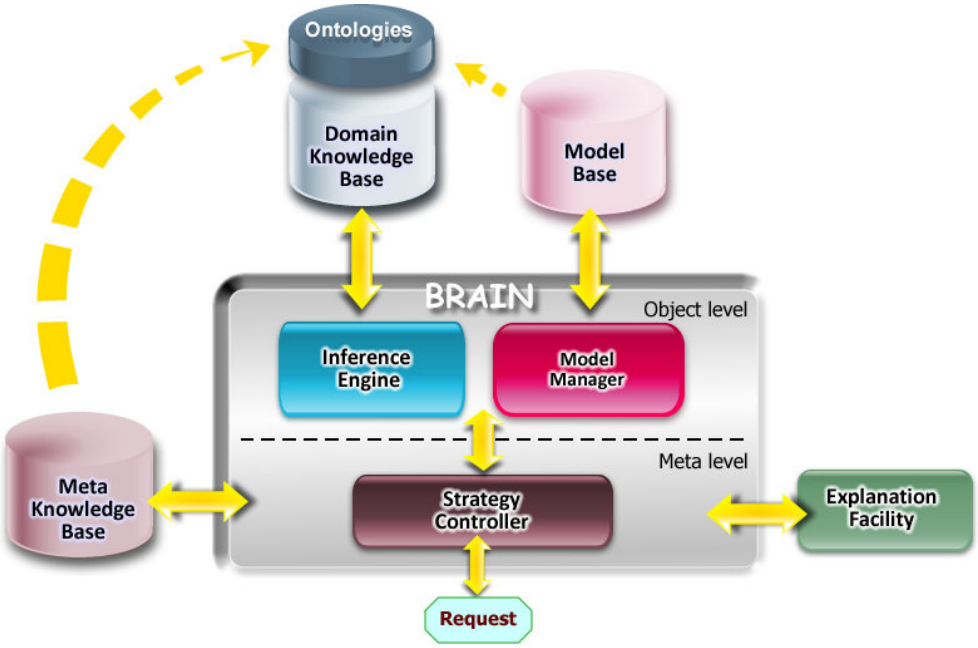


Figure 5.1. *The general view of the HEARTFAID CDSS architecture – dashed arrows correspond to reference to the ontologies, while the others denote a direct communication*

6 Functional specifications of the HEARTFAID platform of services

The HEARTFAID platform of services encompasses all utilities that have been developed for the users of HEARTFAID. This entails the middleware application, the eCRF and web-based tools in general, the telemonitoring tools and the mechanism developed for the Alarm and Alert system. The functional specifications give an accurate picture of the final product that will be developed to address each of these areas. Any decisions that are made in the basis of functional or technical considerations are explained and any alternative courses of action are outlined.

6.1 General architecture

In a large modern enterprise, it is almost inevitable that different parts of the organization will use different systems to produce, store, and search their critical data. Yet, it is only by combining the information from these various systems that the enterprise can realize the full value of the data they contain[1].

In a scenario where the data sources are several, distributed, pre-existing and heterogeneous it is not possible to think of a solution that creates a new data source by physically merging the others. This is the case of the HEARTFAID context (see Figure 6.1): the HEARTFAID platform includes, in fact, different data sources for storing patient related clinical data that is produced and edited from a traditional web-based application, observational data that is produced by sensors, imaging tools, analysis algorithms, alarm systems, reporting results kept in a document oriented repository. Moreover, in most cases the different systems of the platform, such as the web application, the AmI platform, the sensor network, the image analysis tools and so on (these module will be shown in more details in Deliverable D20), are possibly not aware of being part of a bigger picture.

1 Data integration through database federation by L. M. Haas, E. T. Lin and M. A. Roth

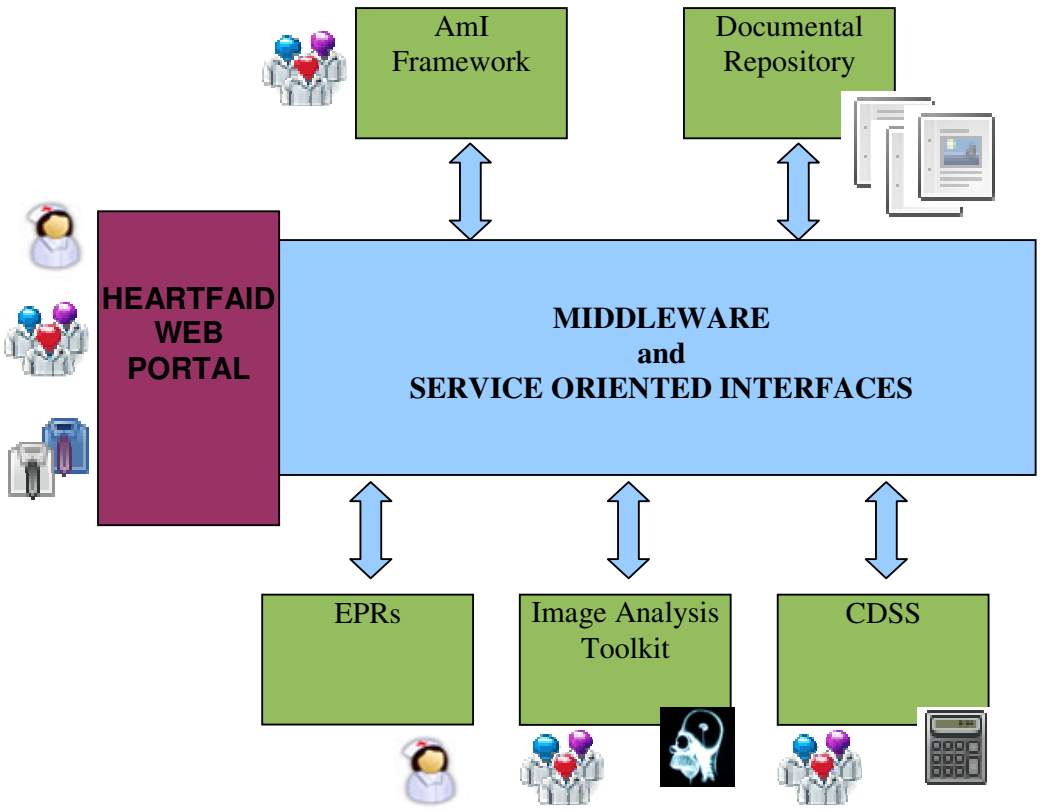


Figure 6.1. *The HEARTFAID context.*

What needs to be done is agreeing upon the **integration interface.** Each system must somehow clarify the data it wants to share, the functionalities it wants to promote to the overall infrastructure for being a component functionality of a higher level service, the user, role and access rights it wants to be granted.
All these systems (data bases and functionalities) have to be put together by an **integration middleware**. Parts or combinations of these services/functionalities will be shown to the final users as front-end functionalities that can be exploited for obtaining specific supports. It is obvious that the different end-user services are typically as complex as the functionalities provided by the single systems of the platform, or even more complex since they are in charge to combine the functionalities of the platform. Therefore, the front-end functionalities must be integrated, homogenised and, finally, interlaced through a higher level middleware that is the interoperability middleware.
The most evident part of this layer will be the HEARTFAID PLATFORM PORTAL, which will be accessible from the network and will integrate the access procedure to exploit all the services of the platform.
Concerning the END-USER SERVICES and APPLICATIONS that will be exposed by the HF platform, we have to distinguish between the native interfaces (if they are needed) and the specific portal interfaces.
The partners that are in charge of developing native interfaces (for example Electronic Patient Records, AmI framework, KDD application), can choose the

more indicated approach (web, rich client, client server etc) to realize them. Moreover, these native interfaces can be pre-existing tools.
In addition to the native interface, the portal will expose a set of services that will interact/combine the *internal* services of the HF platform by adopting a SOA approach.
The Interoperability middleware will provide the portal with the required information and will schedule required procedures using the different components of the platform.
We propose to implement the HEARTFAID Portal using a Portlet approach. Each portal will support a different functionality of the HF platform. According to the functionality, ***the Portlet acts as a front-end that parametrizes and activates the flow of actions*** which implement a specific service. This flow of actions is stored inside the middleware encoded with ***a proper coordination language***.

6.2 Functional specification of HF end-user applications

The "End-user applications" consist of the interfaces and services offered to the users, in order to access the application's utilities. As illustrated by the project's architecture, HEARTFAID encompasses many different processing modules, which all require means of effective, bi-directional communication with the users. The challenge of providing this communication successfully lies in identifying user needs, determining functional specifications, and finally designing and implementing a comprehensive and convenient User Interface to address them. This section attempts to provide an accurate description of the End-User service components and to outline the functional specifications for each one. It is divided into three main sections, which correspond to the three main subsets of End-User services: patient telemonitoring, web-based portal, alert and alarm service.

6.2.1 Patient Telemonitoring

Heart Failure patients should be frequently and consistently monitored by expert physicians. Remote monitoring can help health providers to develop a home monitoring program for such patients, with a great saving of resource and a better service for the patients. The telemonitoring service is a very important tool for observation and assessment of the patient's condition. The telemonitoring software is based on client/server architecture, with emphasis on robustness and security. The functional specifications of the client and server modules are presented below.

6.2.1.1 Client-side Component

Each patient that participates in HEARTFAID will be provided with the equipment and training to record and send to the system accurate readings of vital signs, biometrics, and optionally the patient's own remarks/complaints relevant to his/her medical condition. To achieve this task, a user needs:

i. Sensor device(s), to make the readings,
ii. A PC or PDA, that will retrieve the data from the sensor, and

iii. Access to the Internet, to send the collected data to the HEARTFAID system.

The best way to illustrate the client-side component's functionality is by picturing Mr.Armani, the 70-year-old heart failure patient that is described in 4.3.3. Following his diagnosis, Mr.Armani decided to enrol to the HEARTFAID platform, and take advantage of the telemonitoring service. He may use a PC or a PDA, whichever he finds more convenient; in either case, he will follow the same simple steps to complete the process. The User Interface is designed to be straightforward and to require a minimal amount of user input, since by limiting the user input, the possibility of error is also limited. A detailed description of the remote monitoring software is provided in Deliverable 19, but an overview of the control flow is included below:

- Mr.Armani initiates the software, which detects the sensor device(s). If the detection is successful, a message appears to inform him that he can start collecting sensor readings whenever he wants.
- After the software is properly initialised, Mr.Armani can use his sensors and record medical readings, as required. He has a specific time interval to complete all readings – the interval is configurable. After the timeout is reached, the data acquisition process proceeds, even if Mr.Armani has not finished with his readings – although this would be rather improbable, since he is given ample time.
    a. Alternative Route 1: Mr.Armani may choose to stop the process, while it is still running.
    b. Alternative Route 2: Mr.Armani may choose to omit part of the data acquisition, so he interrupts the process and instructs the software to send the partially accumulated data.
- Once the readings are complete, the module bundles them together and generates an XML file that adheres to a format agreed upon by Synapsis, VMWS and Forthnet.
- The XML file is sent to the HEARTFAID middleware server through the Internet.
- The module uses a synchronous communication protocol when accessing the middleware server, and awaits an acknowledgment of successful delivery. If such an acknowledgment is received, the module displays a confirmation message. The module makes a total of three efforts to connect to the server; if all three fail, Mr.Armani is notified with an appropriate message.

6.2.1.2 Server-side Component

The middleware server is the other integral component of the telemonitoring module, which should be available "24*7" to listen for requests from the remote clients. Unlike its client counterpart, the server needs no specialized equipment. The server hardware, a broadband connection, and a port open to the Internet suffice. The server architecture is detailed in previous deliverables, but the control flow of the telemonitoring component is presented below:

- As mentioned above, the server is listening for client requests continuously. When a request is received, some limited processing takes place, to ensure the XML file is well-formed, complete and not corrupt. If these simple requirements are fulfilled, the server sends an acknowledgment of successful delivery to the client. If not, the server sends a negative acknowledgment, to indicate the need to retry.
- Once the data is correctly received, the server saves the data to the permanent storage and starts validation and processing, as discussed in section 5.

6.2.2 Web-based Portal

The web-based portal constitutes a feature-rich electronic tool that allows HEARTFAID users to enter, manage and process medical data. This tool is designed for use in the hospital and research environments and it is not intended for home users. The functional specifications of the portal were given in detail in D11, but the core components are mentioned here for consistency:

a. The eCRF, which is the on-line tool for Case Report Form submission. This interface has been generated with use of the printed CRFs, supplied by the consortium's medical experts. It allows for recording of the Heart Failure specific observations and examination results.
b. The DSS management, which includes the interface to configure and execute data processing algorithms on selected subsets of the data.
c. The Knowledge Base management, which comprises of the interfaces used to organize and control intelligent data processing algorithms.

The initial intention of including Personnel Management to the web-based portal was later dismissed, since this functionality is already included in every EHR system and need not be duplicated by the HEARTFAID portal. As mentioned repeatedly, the efforts of the project are not towards building an EHR system, but rather an extension of the EHR system, specifically for patients of heart failure.

6.2.3 Alert and Alarm service

HEARTFAID platform should be able to provide advanced alert and notification communication services through an interface dedicated to mobile devices (mainly mobile phones and PDAs) for both patients and medical staff.

The instant communication method of Short Messaging System (SMS), often called text messaging, will be used in order to provide HEARTFAID platform with enhanced one and two-way communication services available over GSM network for mobile users. SMS messaging service is the most reliable and secure notification system for reaching HEARTFAID users and it is also addressing the patient's confidentiality matters as it is delivered to personal mobile phones.

Personalised access technologies to the HEARTFAID platform will also be used to ensure that access to medical data from the professionals and the patients will be easy and secure.

The main issues for the alert and alarm service will be the existence of an advanced user profiling and cognitive techniques which should be used in order to dynamically compose and send alert and notification messages to HEARTFAID

users according to their attributes and depending on their particular personal profile.

SMS messages that will be sent through the HEARTFAID platform are generally divided into four categories:

- **Reminders:** Predefined SMSs are transmitted from the HFP to the patients on specific time intervals, in order to remind them about the medications they have to receive. The time intervals are prescheduled according to the patient's profile, which is stored in the platform.
  Delayed medical data entries from the sensors to the central database of the system will be detected with a scheduler running at preset intervals. The patients will be notified that the required readings from the sensors have not yet been received. This function will also be based on patient profiles, where the scheduler will be periodically checking whether a required sensor reading has been received on the desired time interval, specified by the superintendent doctor.
- **Alerts:** Warning SMSs are transmitted in order to alert both the doctors and the patients, in the case where the readings received by the medical sensors used by a patient, show a recrudescence of their vital signs, or, in general, in the case that a serious health risk is detected by the system. If the data received from the sensors is below or above the desired levels the messages will be automatically triggered by the platform. The examination of the data is performed in the central database of the HFP and the messages are dynamically generated and individually set for each patient giving the superintendent doctors the opportunity of writing specific SMS messages to their patients, including specific medical instructions.
- **Notifications:** In the case of input "error" readings from the sensors inaccurate data are sent to the main database and the messaging function will also be triggered. For example, if a heartbeat reading exceeds the maximum possible level of heartbeats (e.g. 540 heartbeats, which is impossible for a human), then a predefined text message is transmitted, in order to provoke the patient to retransmit medical data from the sensors to the central database of the platform.
- **Confirmations:** Confirmation SMSs are sent to the patient in the case that all the requested readings from the sensors have been properly received, stored and examined by the HEARTFAID system, These SMS messages are also predefined and their purpose is to reassure the patient that all the readings have been properly received.

6.3 Functional specification for data processing and feature extraction

The data extraction and analysis service consists of following steps:

1) selection of the data source (retrospective or collected by the platform)

2) presentation of all available attributes
3) interactive selection of attributes
4) selection of relevant time windows for continuous monitored data
5) interactive selection of a patient subset
6) selection of special events (optional)
7) statistical analysis of selected attributes
8) iterative statistical analysis with differently defined patient subsets
9) preparation for knowledge discovery process
10) selection and starting the knowledge discovery process
11) presentation of the results of the knowledge discovery process

Selection of the data source
It is assumed that the service will normally work with the data collected by the platform but there exists the possibility to analyse retrospective data as well. A good example is the data set collected by Italian Association of Cardiology (ANMCO). It is a big dataset representing *prognosis evaluation* for more than 18000 HF patients collected in Italian hospitals in the period of 1995.-2005.

Presentation of all available attributes
At this step all data available descriptors (attributes) that are present in the selected data set are listed. If the number of attributes is large then attributes can be presented in groups, optionally so that the user can select directly all attributes in the group or select only some members of the group. There is a possibility that some basic statistics for attributes is presented already at this step (i.e. mean value and range for numerical attributes and a short list of most frequent categories for categorical attributes).

Interactive selection of attributes
By selecting attributes the user determines the range of data analysis. The process is interactive because it can be realized through many pages, depending on grouping the attributes in one or more levels. Once finished, the selection is fixed for the whole remaining process.

Selection of relevant time windows for continuous monitored data
If continuous monitored data are selected then the user should select the preferred time window in the range of one day to one year. The choice will influence all remaining steps. Optionally, there is a possibility to allow for two different time windows in the same process or that the time window is different for different continuous monitored data. In any case, the limitation is not significant because there is always a possibility to repeat the analysis with differently selected windows. The time windows are fixed and the user can select only from the fixed set.

Interactive selection of a patient subset
This is similar to attribute selection but more complex because besides attributes that will be used for selection, the user must specify the range that will be

included in the analysis. Also, by doing more restrictions the patient data sets may be significantly reduced so that the user must be on-line informed about consequences of selecting some conditions.

The first step in the process is selection of attributes that will be used for specification of the subset. For each selected attribute the user should be informed about the *type of the attribute* (numerical, nominal) and *its domain* (range for numerical and list of categories for categorical). The second step is selection of the range which is followed by the report on the current total number of examples that satisfy the condition. The process can be repeated iteratively for more than one attribute allowing relative complex subset descriptions.

This type of data extraction and transformation is complex because there are many possible solutions and none of them covers all potentially relevant situations. In the web based interface the practical realization should find a good compromise between very general solution and the one that will be acceptable and practically useful for typical users.

For knowledge discovery tasks the procedure may be repeated twice with intention to select the target class subset and the non-target (control) class subset.

Selection of special events
There is special interest to analyse some consequences and causes of special events. The data transformation process for such analysis is complicated as well as definition of the events. Therefore this step is optional as a research task in platform development. A possible solution is a set of predefined events with fixed data transformation templates that can be only selected and not changed by web based interface.

Statistical analysis of selected attributes
Statistical analysis is performed unconditionally for each attribute separately irrespective of the values for other attributes. For numerical data the computed values are: *mean, median, minimum, maximum, range, and interquartile range*. For categorical data computed values are: *mode* (the most frequent value) and *relative frequency of mode*.
It must be noted that most of attributes in platform data set are time sequences that at first have to be transformed in a potentially large set of numerical and categorical attributes in the following way:

a) long numerical sequences

From one long numerical sequence for analysis are interesting: the complete sequence, the window at the beginning of the sequence, and the window at the end of the sequence. In the case when the selected window width is longer than the sequence itself, all three sequences can be identical. For each of these sequences following characteristic parameters are computed: mean, median, minimum, maximum, range, and slope. Important are also differences of corresponding

parameters. For example difference between the maximum value in the whole sequence and the maximum in the first window, the difference between the maximum value in the whole sequence and the maximum in the last window, and difference between the windows. In this way we can compute 36 different parameters per one long sequence and per patient. Finally all of them are treated as numerical attributes and for each of them we make a summary over all patients by computing before mentioned values: mean, median, minimum, maximum, range, and interquartile range.

b) short numerical sequences

For short sequences numerical values collected in additional visits we compute: number of points, mean, median, minimum, maximum, range, and slope. Added are real values at the beginning of the sequence and the final value in the sequence. All these nine numerical values are treated as separate numerical attributes and for them values: mean, median, minimum, maximum, range, and interquartile range are computed over the selected patient population.

c) short categorical sequences

For short sequences of categorical values collected in additional visits we compute: number of points, mode, relative frequency of mode, and the number of points in which values change. Added are values at the beginning of the sequence (during patient enrolment) and the value at the end (final visit or the last available additional visit). In total we have 3 numerical values (number of points, relative frequency of mode, and number of points in which values change), and 3 categorical values (mode, value at the beginning, value at the end). The last three values can be identical if the sequence has only one point. Finally, for these six values summary is reported over all selected patient subset: mean, median, minimum, maximum, range, and interquartile range for numerical attributes and mode and relative frequency of mode for categorical attributes.

Because for some attribute sequence the obtained results can be very complex the results will not be presented on a single page but they will be references by web links and displayed only when explicitly asked.

Iterative statistical analysis with differently defined patient subsets

Statistical analysis is always done for each attribute separately. Relations among attributes are obtained by repeating the analysis for different subsets of patients. For example, if we want to know about differences in distributional properties of heart rate for different NYHA classes we will at first select NYHA class 1 as our subpopulation and compute its statistical properties for attribute heart rate, memorize the result, select NYHA class 2 subpopulation and compute its statistical properties. Finally, the comparison of the results will potentially report on statistical relevant differences between the two subpopulations suggesting relevant relations between attributes describing NYHA class and heart rate. For this functionality it is necessary to be able to *memorize results* of statistical

evaluation in previous iterations and to perform *statistical tests of significance* between so saved results.

Preparation for knowledge discovery process
Preparation for knowledge discovery assumes two steps: definition of the target and the non-target (control) class and selection of the data format.
The first task can be done in two ways: by repeating the subpopulation subtask twice, once for the target and once for the non-target class, or by defining the complete knowledge discovery domain by the first subpopulation and selecting its target part by the second subpopulation. The later has the advantage that target and non-target classes are always disjoint but the former approach is more general.
The WEKA standard 'arrf' format is the default format also for HF platform. Export to a simple text file with different delimiter types is an option for off-line knowledge discovery.

Selection and starting the knowledge discovery process
At this phase it is assumed that there will be two tools for knowledge discovery process: *random forest* and *subgroup discovery*. The user will be able to select between these tools and afterwards to select some parameters that are tool specific like number of generated trees or generality of rules. The number of parameters will be as small as possible in order to ensure simplicity of the user interface. It will be allowed that two or more users access knowledge discovery tools at the same time.

Presentation of the results of the knowledge discovery process
Presentation of the results obtained by the knowledge discovery process will be in the form of dynamically generated web page. There will be no downloadable files.

6.3.1 Signal and Image Processing services

The signal and image processing services will cover the following topics:

1) Complete web-based diagnostic viewing

Physicians may need to have quick access to raw data (US images, ECG recordings…) stored in HFP repositories for reviewing and for selection of particular instances that should be treated in post-processing workflows.

Therefore services for browsing data like image sequences, ECG recordings, RR intervals acquired for one patient or a user-defined group of patients should be provided. The quality of the retrieved data is not a primary concern here and, thus, for example, compressed versions of the images stored in the archive would suffice.

For what regards images, some of these characteristics are implemented in standard DICOM servers, although with some limitations (see Section 7.2.2.2), whereas in electrocardiography the lack of an accepted standard could lead to

some complications.

2) Additional integrated application for signal and image processing in post-processing workflows

A part from the previous web based data browsing, it is likely that signal and, especially, image processing will need an additional external application. This application, installed to a workstation, should be able to cover all the issues in post-processing workflow, ranging from data retrieval to actual processing and secure storing of the results. More in detail, the following items should be taken into account:

i. Query/Retrieve of images and signals

It should be possible to query and download images and signals from HFP repositories, with the aim of processing them. In particular, methods for secure data transfer and suitable interfaces should be developed. In the realm of medical images, some standard methods to achieve these results are included in DICOM network services (see Section 7.2.2.1), while for signals (e.g. chunks of ECG recordings) this will be depend tightly on the actual implementation of the repository.

Further, it would be nice to allow for data exchange with the web based interface described in 1). More in detail, particular instances of signals and images selected browsing the data in the web interface should be easy to download in the external application, e.g. without retyping their unique identifiers. This issue may be solved, for example, by including a worklist in the web interface where the user can put the data he wants to review or process. Then, the external application may retrieve this personal worklist for the authenticated user and proceed with data retrieving from the repository.

ii. Consistent display of images and signals

The retrieved signals and images should be consistently displayed to be meaningful for diagnostic purposes. In particular, the size of an image, its aspect ratio, orientation and color-map should be exactly the same as seen on the imaging device screen and, thus, these features must be maintained across different monitors.

iii. Tools for performing common measurements

Apart from standard visualization tools (e.g. pan & zoom, contrast correction, selection of rectangular sub-region), the external application should provide methods to perform common measurements, such as linear, angular or area measurements on the image domain or on the area of display of a signal, involving some mouse interaction. Whenever possible, the results of these measurements should be converted into physical units; for example, the value of a linear measurement on an image should be converted from pixels to *mm.*

Further, it should be possible to label somehow the computed values, perhaps choosing from a predefined list of tags (for example choosing EDD from a list of tags for LV measurements to denote End Diastolic Diameter of the Left Ventricle).

iv. Invocation of signal and image analysis algorithms implemented in the platform

The signals and image processing algorithms implemented in the platform (for example QRS detection from ECG recordings and left ventricle ejection fraction from US sequences as described in HEARTFAID Deliverable 15) should be integrated into the external application. Running this kind of algorithms may require some other user interaction, such as 1) clicking on a particular point in the image domain, 2) stating clearly which data type is being processed (e.g. an apical 4 chambers view *or* an apical 2 chambers view), 3) defining the range of elaboration (e.g. the starting and end frame in an image sequence) and, finally, 4) setting some internal parameters of the algorithm.
Of course a basic interface should also be provided in which an algorithm runs with the default parameters associated to the data type.

v. Data visualization facilities

Some visualization facilities should be provided both for signal and image processing. For example the result of a segmentation algorithm should be displayed as a superimposed layer to the original image to evaluate (visually) the performance of the algorithm. This also applies to QRS detection and classification algorithms.
Besides it would be interesting to produce also some synoptic tables with the evolution of the patient's data if the Holter ECG device is able to export the raw data. This could be useful for example in continuous monitoring of RR intervals and the computation of Heart Rate Variability (HRV). The trend of HRV, indeed, is of strong prognostic value. Such synoptic tables are currently implemented in many telemonitoring systems, e.g. in Medtronic CardioSight.

vi. Numeric signal & image report

After having completed the processing task (for example after having performed some area measurement), it is important to provide a tool for unambiguous semantic documentation of the diagnosis. Besides information about the scheduled procedure, the observer ID, and links to previous reports, the report should include 1) links text with images, signal waveforms that are used as *evidence* in the report and 2) numeric measurements. The tags of numeric measurements should be intelligible by other components of the platform, such as the eCRF and the CDSS. To achieve this, some kind of universal identifiers, for example those provided by UMLS could be employed.

vii. Secure storing of annotated reports

Finally, such annotated report should be securely stored in a repository. Only at this point, the data, contained in a structured and clinically meaningful report, will become available to the other platform components.

viii. Secure storing of the results of processing in the form of annotated images and signals

At the same time, the images and signals waveform, linked to the report as evidence document, should be uploaded to a repository. This, apart from enhancing the clinical validity of the report, will allow for data reviewing and follow-up. For example a segmented image sequence should be saved as a DICOM object (carrying thus information about the patient, date of creation, modality, pixel physical units among others) with its own UID and sent to a DICOM server for secure storing.

6.4 Functional specification for the Decision Support Tools

The HEARTFAID CDSS supplies a set of functionalities specifically designed for aiding the clinicians in managing HF patients. Summarizing, such functionalities will allow the users to:

- formulate a diagnosis and exploit the CDSS to confirm it;
- query the system for obtaining diagnostic or prognostic evaluation;
- exploit the system for the prescription of the most appropriate therapy (in deed, the system is able to process all the clinical information about patients, available pharmacological treatments and their contraindication and inadvisability);
- obtain suggestions on patients status and actions to be done for their management.

The user interface is responsible for all the interactions and communications with the users and makes an important contribution to the CDSS value in terms of user productivity and effectiveness. Given this level of responsibility, the interface must deal with factors related to human interaction, accessibility, erase of use, user skill level, error capture and reporting, and issues related to documentation.
In particular, fitting the *routine workflow* of medical professionals is, among others, an important requirement for the acceptance of the CDSS in practice. The user interface should then presents all the HFP functionalities, including the CDSS ones, in a proper and integrated fashion that will require the users neither too much learning nor relevant changes to their routine activities, while meeting their needs as much as possible. This means, for instance, that users should be able to access the CDSS functionalities in an easy and natural way while managing the clinical information of a patient. A strong cooperation with the medical operators may be profitable for understanding their expectations on how the CDSS will support their activities.
From another point of view, the CDSS can be exploited by the clinicians for testing and research purposes, e.g., for exploring the consequences of therapy

changes or for analyzing diagnostic examinations to assess new parameters. This implies an explicit intent of the clinicians to query the CDSS that goes beyond the routine practice. We can then foresee two different usages of the CDSS: *routine* and *research workflows*.
From the platform design point of view, the HEARTFAID CDSS component is a resource able to offer a number of functionalities and to interact with the other resources for performing its tasks.
Each decision-making problem, as introduced in the previous chapter, can be translated into a *request* or a *class of requests* committed to the CDSS, which is then activated *on-demand*. The system handles every request according to a specific encoded policy, interacting, when necessary, with the other platform components.
The interactions with the user interface can consist of exchanging messages, which can be made of strings, files, XML encoded files and so forth. After launching a specific command from the user interface, a specifically correspondent request message is sent to the CDSS which starts its processing for supplying a response. In particular, the response can consist of a composite answer that contains:

- a *conclusion*, which pertains diagnosis, prognosis, patient's state assessment and so forth;
- a *list of possible actions* to be undertaken by clinicians which can involve another functionality of the platform, e.g., scheduling of a new visit or new examinations, changes of therapy, repository update and so forth.

In this perspective, the user interface should assure an adequate visualization of the list of possible actions, suggested by the CDSS, and the management of the one selected by the user. To avoid burdening the interface and to increase the ease of requests handling, a specific component of the platform, more precisely of the middleware, should be in charge of activating the CDSS and opportunely handling its responses by transferring the request that corresponds to the action selected by the user to the pertinent platform component, e.g. the *agenda*, the repository management system and so forth.
Three scenarios of possible interactions can be identified:

- *Single request-response*: a request is issued by the interface and the CDSS directly supplies a single final response;
- *Interactive request-response series*: for responding a request, the CDSS requires to establish a dialogue with the user;
- *Execution of interactive algorithms* (*models*): during the elaboration of a request, the CDSS requires the execution of an algorithm, contained in the model base, which involves an interaction with the user.

In the first case, the CDSS does not need any further information to be supplied via the user interface; hence, the communication between the two components is a single step procedure, which ends with the opportune display of the response.
It can alternatively happen that the CDSS requires the user to supply additional information. In such situation, the interface should include a "section" for

visualizing the requests form the CDSS and the answers from the user, e.g., a form of possible entries.
In the third situation, the *locus of action* should be passed to an application, contained in the Model Base, which implements a signal or image processing method. Such an application should be equipped with a dedicated, tiny user interface which allows the user to interact by setting some parameters or by graphically working on images (e.g., tracing a line or a rectangle).

For better illustrating the description above, we can consider the management of Pietro Guarneri, as described in the 4th scenario (Section 4.3.4 "the life Pietro Guarneri in the HEARTFAID age") and point out the various operations involved. The situation falls within the clinicians' routine workflow, so CDSS interventions have to be managed by the platform.

The patient answers a questionnaire through his browser and sends the information to the interface handler that checks eventual missing values. Then the component in charge of managing the platform events (which can be referred to as event controller – EC) stores this information into the repository, gets historical data and opportunely invokes the specific CDSS service in charge of handling the correspondent request.
The CDSS analyzes data and answers supplying the current patient's status, i.e. worsening of symptoms, and a set of suggested actions the clinician should undertake, i.e. schedule a new visit, change the NYHA class, and change the therapy and so forth. Then EC stores CDSS results into the repository.
When the physician-in-charge logs on into the HEARTFAID platform, the list of patients is displayed ordered by their severity status and the timestamp of the last related event. Then he chooses to analyze the situation of Pietro Guarneri and the change in patient's status is shown along with the list of suggested actions, for instance as a list of operations that can be selected. He then approves the schedule of the visit and the EC forwards the request to the *agenda* component that opportunely records it and informs the patient.
During the visit, the physician inserts his observations into the patient's record and decides to approve the change of the NYHA class: he selects the corresponding action within the list and the EC takes care of registering the change in the patient's record. He performs an ECG for further investigations. Once he submits the information obtained by the ECG, a request for its interpretation is sent by the EC to the CDSS, which suggests performing an echocardiography as displayed in the suggested actions list.

Within the research workflow, a specific area of the user interface can be dedicated to the interactions, it can be a separated window that the user can explore when needed. A list of possible query is displayed along with a set of parameters that the user can select to submit together with the query. The CDSS response can be displayed in the same area/window as conclusion and list of suggested actions.

7 User Interface

Implementing clean interfaces to connect software components is a quite important task in a project that presents modularity, scalability, extensibility and generality as its main features. Moreover, in many cases the project encompasses distributed computing resources, be it software like processes and data or hardware resources like embedded micro or nanodevices, gateways, servers or storage devices. In these scenarios the design complexity for component interfaces grows rapidly involving mechanism for interprocess communication, design of information exchange protocols, remote service requests and remote service discovery, synchronization, handling of heterogeneity.
There is a great number of possible comparison arguments for studying component interfacing software. Possible choices are:

- **Data Representation**: What kind of data is moved and how it is wrapped to preserve typing information among possibly heterogeneous components.
- **Transport Protocol**: How data is moved across the connection that binds the (possibly distributed) components.
- **Service Description** and **Service Location**: How services available on servers are described and if such a description exists for a specific implementation. What kind of formalism can be used for discovery of service availability?
- **Language Binding** and **Language Paradigm**: In which programming language the formalism can be embedded and what kind of paradigm does it conform to (object oriented, functional, streaming)?
- **Remote Reference**: What is the representation of a reference to a remote service supplier component?
- **Synchronisation**: Whether the communication underlying the component interaction is implemented in a synchronous or asynchronous way.

A very important note is that many bridge middleware tools exist that enable components using different architectures for their interfaces to transparently communicate with each other.
As a final remark, it should be noted that often the only way to interconnect components that are distributed on an open network such as the Internet, is to encapsulate all information into HTTP packets. This technique is called tunnelling and it is useful to bypass security firewalls that often enable only HTTP communications to access the target server machine.

7.1 Organization of access to functionalities

The multitude of services and functionalities that are encapsulated in the HEARTFAID platform have been carefully organized depending on the exposed functions and prospective users. Important features of the software system are the

tools designed and developed for data entry, such as the electronic Case Report Form and the patient enrolment system, which will be discussed in this section.

7.1.1 The eCRF prototype

An important part of the portal is the electronic Case Report Form (eCRF), a sophisticated remote data entry system. One of the main concerns while designing the eCRF was simplify access to the form for the medical personnel, therefore system requirements for client computers have been minimized. To access the eCRF it is sufficient to have a common web browser with enabled JavaScript (e.g. Internet Explorer or Firefox).
Access to the HEARTFAID eCRF is granted only to registered users. After providing the username and password (Figure 7.1) the user is authenticated, authorized and redirected to the application's main page. HEARTFAID's users are in respect of the eCRF divided into two main categories: normal users and administrators. Normal user are physicians, caregivers or nurses who need access to patient's from their medical centre only, whereas administrators are computer specialists who manages the data, hence have access to all stored forms.

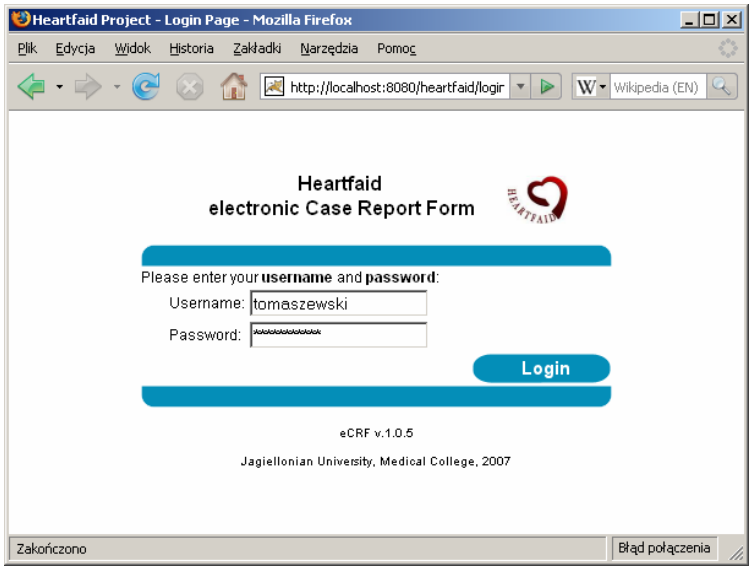


Figure 7.1 Login Screen

The table in the main page (Figure 7.2), which is visible after successful login, presents a list of all HEARTFAID patients registered in the eCRF system. Rows contain data of individual patients. The first column of the table contains the patients' ID numbers. Following columns show information about the eCRF subforms. The link *Add* means that a new form of a type indicated by the column can be created. Selecting the *Edit* link allows changing of an already existing form. Only one instance of the Baseline Evaluation and Final Evaluation form can be created for a single patient. The number of Additional Visit Forms for a single patient is unlimited.

New patients can be added by pressing on the "Add Patient" button. Patients' records and forms can be removed by administrators only.

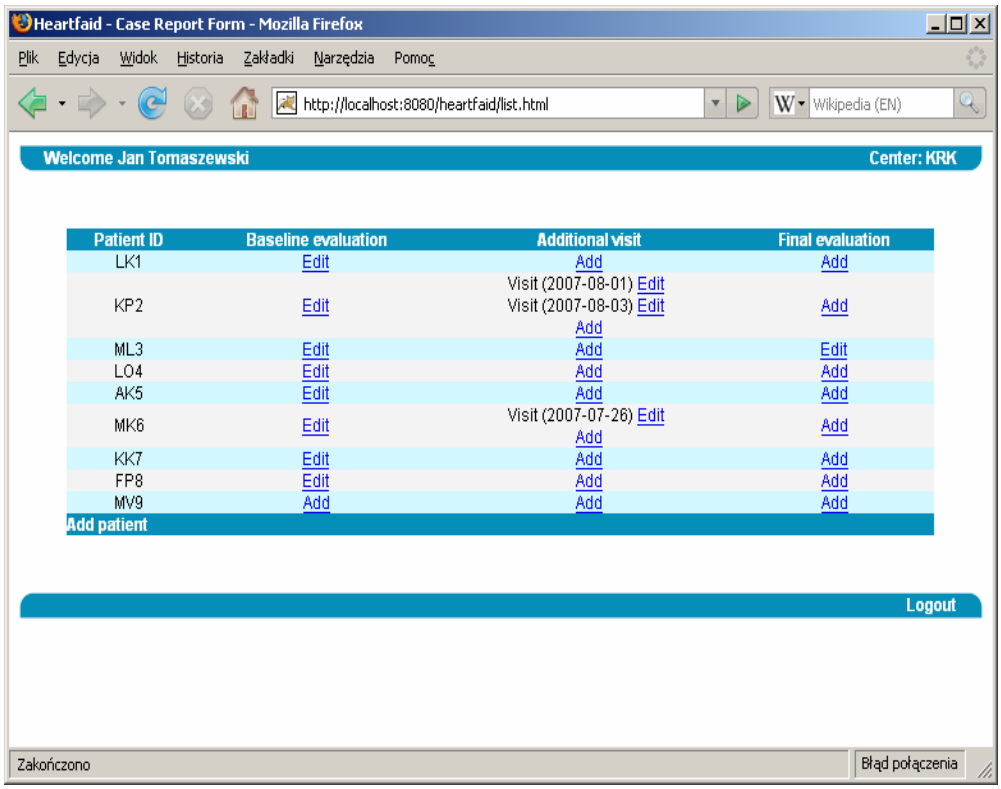


Figure 7.2 Adding/ Selecting eCRF forms

After a form is opened, either by creating a new form (clicking on the *Add* link in the appropriate cell) or modifying an existing one (clicking on the *Edit* link), the first page of the selected form is presented. The user may navigate through the form either by clicking on the forward and backward arrow buttons in the bottom of the page (Figure 7.3, Navigation Bar) or by selecting a desired page in the right side bar (Figure 7.3, Table of content). But before a page can be changed on the server it undergoes a validation procedure If the page contains errors, a list of invalid fields is displayed and the user has to make appropriate corrections (Figure 7.4). A page is automatically saved if the user moves to another page. Pressing the *Submit* button in the *Navigation Bar* stores the form on the server and returns the user to the main page.

As it has been already described above, the questions in eCRF may be put into groups, which can be placed into further groups (group nesting). Groups are denoted by rectangular shapes enclosing all elements from the group (Figure 7.3, Question groups). Some groups are activated (i.e. values may be entered into the group's fields) only if a given value is entered in one of the preceding fields. As a simple example of validation a group presented in Figure 7.3 may be taken. This

group contains a single question “max.” and is activated only if the user answers the question “ST depression” with “Yes”.

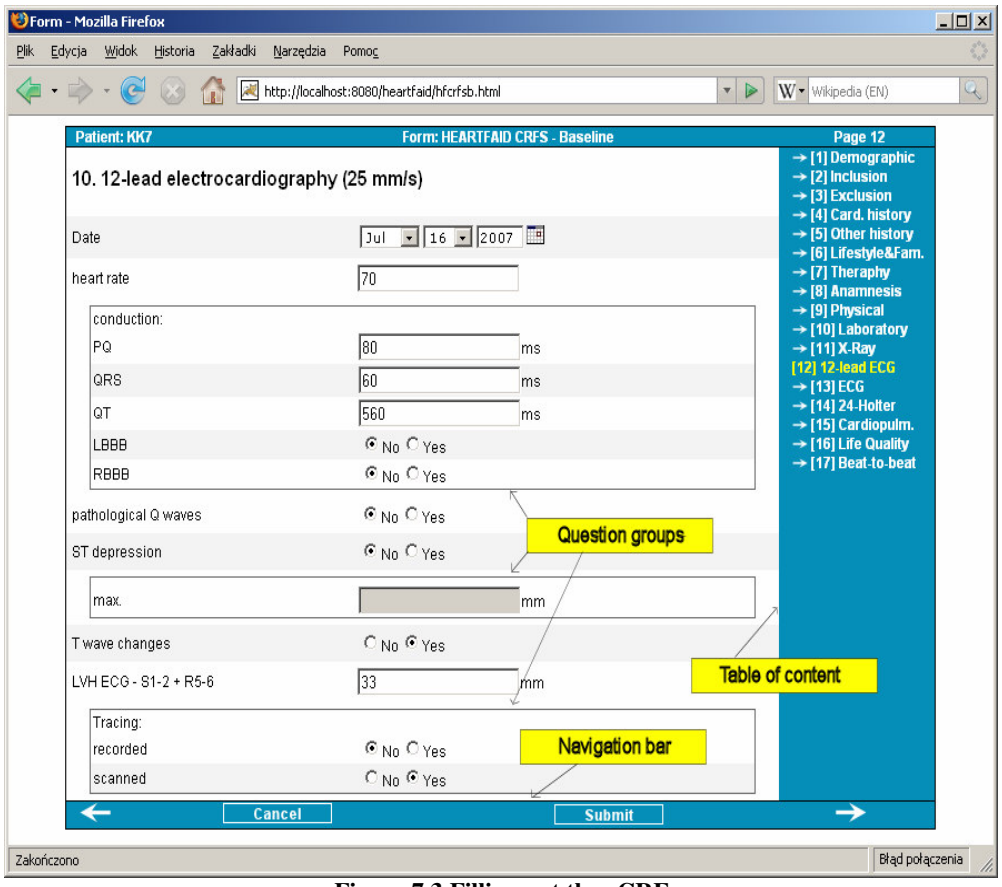


Figure 7.3 Filling out the eCRF

Questions in the eCRF require answers of diverse types what results in the need of adequate input field. The standard set of controls like radio buttons for boolean fields, text fields or text areas for textual and numerical values has been extended by more complex widgets e.g. for inserting date values or the specification of drug therapy.
The component for selecting drug therapy (**Figure 7.5**) allows the selection of a drug from a predefined medication list. The content of the list may be different for individual medical centres and may be changed easily. If a drug is not present in the list the user may insert it manually. Besides the drug brand name also the drug international name, its class name and information about the dosage are entered.

The user closes the eCRF application by pressing on the logout button located at the main page.

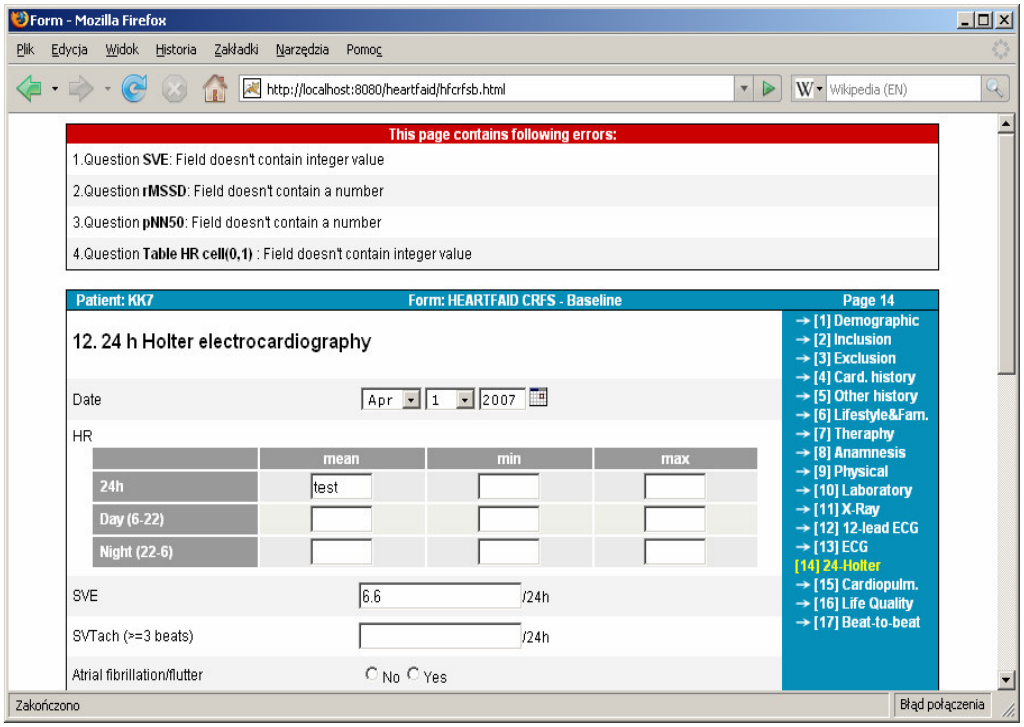


Figure 7.4 Validation

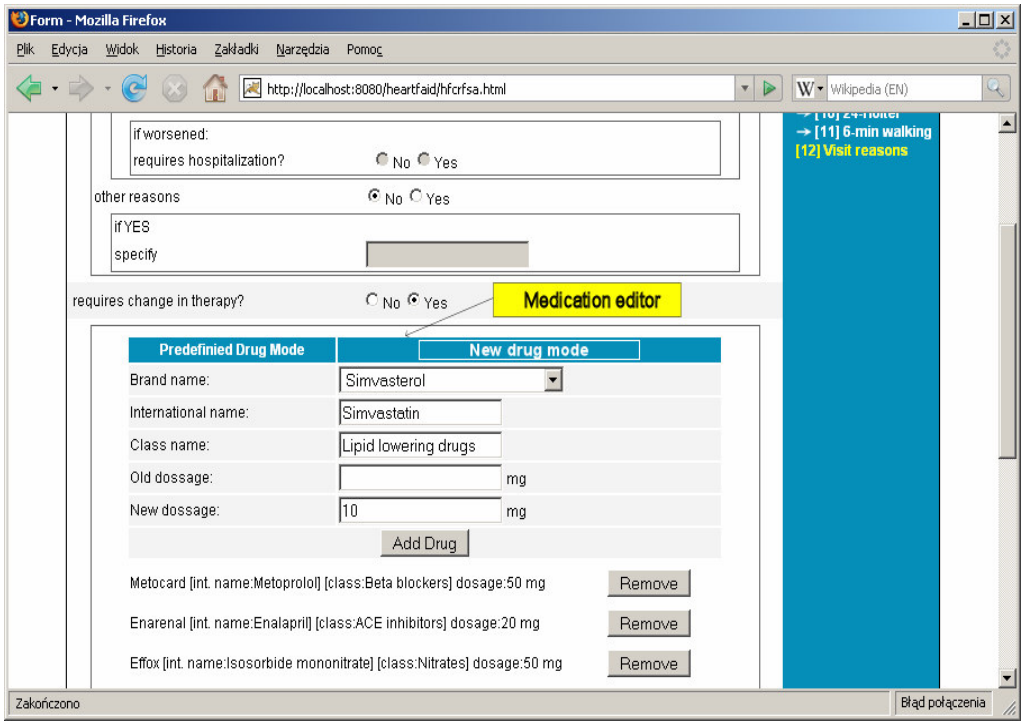


Figure 7.5 Medication Editor

7.1.2 Patient Enrollment

This functionality is presented through a scenario of use:
Patients Sutherland refers to the OFFICE of the Cardiologist Gheorgiu that is responsible for testing the HEARTFAID PLATFORM DEMO (HFP_D).
Patient Sutherland already carries the diagnosis of HF and accepts to be enrolled among the patients that will help in testing and validating the HFP_D.

One may assubme that at the end of the enrolment visit patient Sutherland is assigned to Workflow 2 (medical environment -specialized cardiology office- and patient environment).

The Cardiologist Gheorgiu launches the HFP_D on his PC, where she encounters the User Interface displayed in Table 1.

Users …… …… …….	
NEW PATIENT PATIENTS' ARCHIVE MONITORED PATIENTS	
DSS KDD SUMMARY DATA	

Table 1: Suggested Front-End

Double clicking NEW PATIENT → opens a page with both demographic and medical info (Table 2).

DEMOGRAPHIC INFORMATION Date of enrolment …. *(→ important to apply prognostic rules later on !!)* Name …… Address …… Tel … Gender …. SSN …. Etc ….

Etc …. Etc … *(→ cannot proceed in entering the following medical information if certain fields of the demographic info have not been completed to ensure that every patient is linked to only one possible record. Make it as safe as possible to avoid mistakenly updating the wrong medical record while seeing a patient.*
MEDICAL INFORMATION

Table 2: Demographic Information entry

Double clicking on MEDICAL INFORMATION brings up a table that is subdivided as in Table 3.

HISTORY AND PHYSICAL EXAMINATION
Reason for visit Family History Medical problems Lifestyle information Pharmacological treatment Non Pharmacological treatment Symptoms Signs (Physical examination)
TESTS
Laboratory tests Chest X-Ray 12-lead ECG Echocardiography 24-H Holter ECG Monitoring Exercise test Cardiopulmonary exercise test 6-minute walking test Ambulatory BP monitoring Bioelectrical Impedance Quality of life questionnaire Autonomic parameters Other tests to be added …..
REMOTE MONITORING
Body weight

Body temperature Blood Pressure Heart rate Respiratory rate Oxygen Saturation Total and % body water ICF (intracellular fluid) ECF (extracellular fluid)
SUMMARY OF VISIT

Table 3: Medical Information entry

REASON FOR VISIT
Routine (scheduled appointment) Y / N Specific complaint or reason ……..…… Triggered by HF platform Y / N (Y only in follow-up)
FAMILY HISTORY *(first degree relatives)*
- hypertension Y/N - coronary artery disease Y/N - diabetes mellitus Y/N - hypercholesterolemia Y/N - hypertrigliceridemia Y/N - obesity Y/N - cerebrovascular disease Y/N - primary cardiomyopathy Y/N
MEDICAL PROBLEMS *(Instructions:* *- the first part covers the medical history relevant to heart failure;* *-in the second part of this section, past and ongoing medical problems will be entered in the HEARTFAID platform as a list with the date of onset and the date of resolution.* *Diagnosis with no date of resolution are intended as ongoing.* *Next to each diagnosis some free text can be entered by the physician.* *The HEARTFAID platform will subsequently code the listed diagnosis according to a coding system example ICD-9.* *Next to each diagnosis, some text can provide detailed information about it).*
- Heart failure Y/N date diagnosis: dd/mm/yyyy …… text

Systolic Y/N
Diastolic Y/N

- Hypertension Y/N date diagnosis: dd/mm/yyyy …… text

- Coronary artery disease Y/N date diagnosis: dd/mm/yyyy …… text

- Valvular heart disease Y/N date diagnosis: dd/mm/yyyy …… text

Mitral Y/N stenosis Y/N regurgitation Y/N
…… text
Aortic Y/N stenosis Y/N regurgitation Y/N
…… text
Tricuspid Y/N stenosis Y/N regurgitation Y/N
…… text
Pulmonary Y/N stenosis Y/N regurgitation Y/N
…… text

- Peripheral vascular disease date diagnosis: dd/mm/yyyy
…… text

- Cerebrovascular disease date diagnosis: dd/mm/yyyy
…… text

- Diabetes Mellitus type I II date diagnosis: dd/mm/yyyy
…… text

- Dyslipidemia Y/N high LDL cholesterol
Low HDL cholesterol
High triglicerides

- Overweight/ obesity date diagnosis: dd/mm/yyyy …… text

- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy
text ……

- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy
text ……

- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy
text ……

- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy
text ……

- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy text ……
- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy text ……
- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy text ……
- ……. date diagnosis: dd/mm/yyyy date resolution dd/mm/yyyy text ……
LIFESTYLE HABITS
- smoking N Y cigarettes/day beginning date …. mm/yyyy P (past) quitting date …...mm/yyyy …… text - physical activity sedentary light intermediate, aerobic heavy very heavy …… Number session/week …… text - alcohol intake ……. Number Units/week (one unit = 1 glass wine, 1 can of beer, 1 aperitif, 1 shot of digestive/liqueur) …… text - dietary habits g of salt /day …… N of servings fruit + vegetables /day ……. N of fish meals / week ……. N of red meat meals /week…… N of fat cheese meals/ week …… N of deserts/week …… text

Table 4: Details of Encounter

PHARMACOLOGICAL TREATMENT *(Instructions: enter in the first column the GENERIC name; there are databases that automatically search the correspondent BRAND names and CLASS that should appear in the second column; the physician should be able to select the brand name that applies). The reason for this is that TREATMENT RULES ARE BASED ON DRUG CLASSES !!*							
Generic name	brand name	Dose	Units	Time(s)	Route	Beginning date dd/mm/yyyy	
				…. …… …...			

Table 5: Pharmacological Treatment

NON PHARMACOLOGICAL TREATMENT			
		Beginning date dd/mm/yyyy	
Example pace maker	…. Text		
Example ICD	…. Text		

Table 6: Non-Pharmacological Treatment

SYMPTOMS *(i.e. what is complained by the patient)*

Fatigue Y/N

Dyspnoea (= brethlessness) Y/N

NYHA Class I □ *(def → No limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea, or palpitations).*

NYHA Class II □ *(def → Slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations or dyspnoea).*

NYHA Class III □ *(def → Marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms)*

NYHA Class IV □ *(def → Unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with*

any physical activity).

Orthopnea Y/N
Nocturnal dyspnoea Y/N
Peripheral oedema Y/N
Irregular heart rhythm Y/N
Tachycardia (fast heart beat) Y/N
Bradycardia (slow heart beat) Y/N
Other …… text
Other …… text
Other …… text

SIGNS *(i.e. what is detected by the physician by means of the physical examination).*

Weight ……. (Numeric, kg, pounds)
Height ……..
Temperature ……
Arterial oxygen saturation …… (numeric, %)
Respiratory rate …… (numeric, respirations/min)
BSA (body surface area) …….. Numeric, m^2 (calculated by the platform)
BMI (body mass index) ..... *Numeric (calculated as weight/height^2)kg/ m^2*

Sitting blood pressure and heart rate (see e-CRF)

	SBP / DBP	HR
1st	……/ ……	……
2nd	……/ ……	……

Standing blood pressure and heart rate (see e-CRF)

	SBP / DBP	HR
1st	……/ ……	……
2nd	……/ ……	……

Jugular veins congestion Y/N if Y ….. cm above the jugular notch ….

Carotids bruit right Y/N
left Y/N

Heart:

Rhythm	Regular Y/N	
S1	Normal	Abnormal: Increased Decreased
S2	Normal	Abnormal: Increased Decreased
S3 present	Y/N	

S4 present	Y/N		
Systolic murmur	Y/N	Intensity… (from 1 to 6/6)	site …. base apex other…….. (text)
Diastolic murmur	Y/N	Intensity… (from 1 to 6/6)	site …. base apex other…. (text)
Other: …. text			
Lungs			
	Breath sounds: Normal	Abnormal	site …. text
Crepitations	Y/N	site … (text)	
Effusion	Y/N	site … (text)	
Other	…. (text)		
Abdomen			
Liver	Pain	Y/N	
	Enlargement	Y/N	if Y ……(number) cm
Other	…..		
Lower Extremities			
Right Oedema	Y/N	if Y …. +,++,+++,++++	
Left Oedema	Y/N	if Y …. +,++,+++,++++	
Peripheral arterial/venous circulation		normal abnormal	….. text
Other	….. text		

Table 7: Detailed HF Symptoms

TESTS
LABORATORY TESTS
Complete blood count Date (see e-JUMC CRF)

Biochemistry (see e-CRF)	Date		
other ……..	Date		
other ……..	Date		
other ……..	Date		
BNP			
Pro BNP			
(see e-CRF)			
Urine Date	dd/mm/yyyy		
Normal	Y/N		
glucose	numeric	mg/dl	
proteins	numeric	mg/dl	
blood	zero, +,++,+++		
ketons	…. Numeric	mg/dl	

CHEST X-RAY

Date:	dd/mm/yyyy	
Normal	Y/N	
Cardiothoracic ratio	…….. (numeric)	
Pulmonary circulation congestion	Y/N	text ……
Pulmonary oedema	Y/N	text ……
Effusion	Y/N	text ……
Radiologist's comment	….. text	

12-lead ECG (25 mm/s)

Date	dd/mm/yyyy	
Rinus rhythm	Y/N	
Atrial flutter	Y/N	
Atrial fibrillation	Y/N	
Other	..... text	
Heart rate	…. beats/min	
PR interval	…. ms	
QRS duration	…. ms	
QT interval	…. ms	
Presence of abnormalities	Y/N	
AV conduction abnormalities	Y/N	grade I A-V block

Y/N		grade II A-V block type I
Y/N		grade II A-V block type II
Y/N		grade III A-V block
Y/N		
IV conduction abnormalities	Y/N	Left bundle branch block
Y/N		Right bundle branch block
		Y/N
ECG signs of ischemia	Y/N	describe (text): i.e. ST depression 3 mm in leads V3 – V6. i.e. q wave in inferior leads
LVH *(left ventricular hypertrophy)* Lyon S1-S2 + R5-6).	Y/N	(criteria: Sokolow-

ECHOCARDIOGRAPHY

Date: *dd/mm/yyyy*
Quality
Examination recorded *Y/N*

Left ventricle

end-diastolic diameter	….. (numeric) mm
end-systolic diameter	….. (numeric) mm
interventricular septum diastolic thickness	….. (numeric) mm
posterior wall diastolic thickness	….. (numeric) mm
end-diastolic volume	….. (numeric) ml
end-systolic volume	….. (numeric) ml
ejection fraction	….. (numeric) %

Method : Simpson's 2D
4D

Right ventricle

end-diastolic diameter			….. (numeric) mm
TAPSE			….. (numeric) mm
Left atrium			
Anteroposterior diameter			….. (numeric) mm
Aorta			
Root diameter	….. (numeric) mm		
Ascending aorta diameter	….. (numeric) mm		
Aortic Valve			
Aortic regurgitation	Y/N	grade: +,++,+++,++++	
Aortic stenosis	Y/N	gradient mean ….. (numeric) mmHg	gradient peak ….. (numeric) mmHg
Mitral valve			
E max	….. (numeric) m/s		
A max	….. (numeric) m/s		
E/A ratio	….. (numeric)		
Deceleration time	….. (numeric) m/s		
Mitral regurgitation	Y/N	grade: +,++,+++,++++	
Mitral stenosis	Y/N	gradient mean ….. (numeric) mmHg	gradient peak ….. (numeric) mmHg
Diastolic dysfunction	Y/N		
(EROA, Doppler shift)	……		
Tricuspid valve			
Tricuspid regurgitation	Y/N	grade: +,++,+++,++++	

Pulmonary artery pressure ….. (numeric) mmHg

Regional contractility

ASE Segments from 1 to 16 enter the following code:

1. Normal
2. Hypokinetic
3. Akinetic
3. Dyskinetic
4. Scar/thinning
5. Not seen

Other …. *text*

24-H HOLTER ECG

Date: *dd/mm/yyyy*

Rinus rhythm Y/N
Atrial flutter Y/N
Atrial fibrillation Y/N
Other ..... text

HR	mean	min	max
24 h	……..	……	……
Daytime (8-22) ……		……	……
Night-time (22-8) ……		……	……

Maximum R-R interval ……. Sec

N of R-R intervals > 3 sec …….

	isolated	couples	>= 3 beats
SVE/24 h	……	……	……
VE/24 h	……	……	……

VF/24 h ……

AV conduction abnormalities	Y/N	grade I A-V block	Y/N
		grade II A-V block type I	Y/N
		grade II A-V block type II	Y/N
		grade III A-V block	Y/N
IV conduction abnormalities	Y/N	Left bundle branch block	Y/N
		Right bundle branch block	Y/N
ECG signs of ischemia	Y/N	describe (text): …….	
Heart rate variability:	SDNN	ms	
	SDANN	ms	
	rMSSD	ms	
	pNN50	%	
	Total power	….	
	HF	….	
	LF	….	
	VLF	….	

EXERCISE TEST

Date: *dd/mm/yyyy*
Protocol …….

	Basal	*Peak*
BP(SBP/DBP)	…/….	…/…
HR	…/….	…/…
% of predicted HR by age		……..
Load METS		……
Load Watts		……
Tot Min Exercise		……
Criteria for test interruption		…….. *text*

Test was positive for ECG criteria of ischemia *Y/N*

Other			……..…… *text*

CARDIOPULMONARY EXERCISE TESTING

Date: *dd/mm/yyyy*
Protocol ……..

	Basal	*AT*	*Peak*
BP(SBP/DBP)	…/….		…/…
HR	…/….		…/…
% of predicted HR by age			……..
O2 sat	……		……
O2 pulse	……		……
Load METS			……
Load Watts			……
Tot Min Exercise			……
VO2 (ml/Kg/min)	……	……..	……
VCO2 (ml/Kg/min)	……	……..	……
RQ	……	……..	……

VE/VCO2 slope ……..

Criteria for test interruption …….. *text*

Test was positive for ECG criteria of ischemia *Y/N*

Other ……..…… *text*

6-MINUTE WALKING TEST

Date: *dd/mm/yyyy*

	Baseline	End
BP (mmHg)	……	……..
HR (bpm)	……	……..
SpO_2 (%)	……	……..
walking distance (m) ……		

BIOLECTRICAL IMPEDANCE

Total body Water Intracellular body water Extracellular body water Na/K exchange Free Fatty Mass (Muscle Mass)
QUALITY OF LIFE QUESTIONNAIRES
(see e-CRF)
REMOTE MONITORING ***(check the parameters that will be remotely monitored for this patient among the possible ones).***
Body weight Body temperature Blood Pressure Heart rate Respiratory rate Oxygen Saturation Total and % body water ICF (intracellular fluid) ECF (extracellular fluid)
SUMMARY OF VISIT ***(instructions: by clicking on it, all of the information entered as MEDICAL INFORMATION should appear on a page for the physician review. It will include the data entered and the text next to it).*** ***At the end, the SUMMARY OF VISIT, will have a text section for clinical impression and new recommendations.*** ***This summary is supposed to be printed out, signed by the physician (whose name, title etc should appear at the end of the summary), and given to the patient at the end of the consultation.***
Date Patient XX Reason for visit *data entered ….* Family History *data entered ….* Medical problems *data entered ….* Lifestyle information *data entered ….*

Pharmacological treatment *data entered ….* Non Pharmacological treatment *data entered ….* Symptoms *data entered ….* Signs (Physical examination) *data entered ….* Tests *(data entered)* **Impression and recommendations.** *…. The clinical impression will be free text……* *….. You may put here the table of the PHARMACOLOGICAL THERAPY for the physician to be updated, if needed, at the end of the consultation.* *….. You may put here that the patient has been recommended HOME MONITORING and specify the selected parameters.* *….. You may preview the possibility of downloading INSTRUCTIONS FOR THE PATIENTS on how to monitor the selected parameters at home.* *….. You may put the date for a scheduled follow-up visit and the name of this subject in the calendar for the physician use reminding him of due follow-up visits.* Best Regards, Dr XY

Table 8: Test Results and Medical Findings

7.2 Interactions with HEARTFAID Image Archive

7.2.1 Image archive for echocardiography workflows

Nowadays echocardiography is a digital modality, offering the opportunity to coordinate its workflow in an IT framework. When considering echo workflow, we are mainly interested in transthoracic echo (TTE), for its versatility and portability and for its fundamental importance in the management of heart failure patients.

An echo study generally consists of digital images (single- and multi-frame), measurements and an interpretive report.

Images are obtained by a sonographer who may make preliminary measurements and preliminary observations. According to IHE [1], the over-reading echocardiographer must have access to all of this data in discrete, structured format to synthesize a final report.

In an echo lab reached by HEARTFAID, it would be optimal to upload the original images, the annotated ones and the final report to the integrated HFP of services. However, the treatment of digital images, both original and annotated, poses several problems, due to the discrepancy between the ideal hospital (just

from an IT point of view, of course) and the situation usually encountered in a real one.

7.2.1.1 Ideal echocardiography workflow

In the ideal situation, the hospital is equipped with a HIS and a PACS dedicated to cardiology and, finally, echocardiography devices are persistently connected to the hospital network. For a patient, pre-admitted and registered in the Hospital Information System before undergoing an echocardiographic examination, a visit is scheduled and demographics and procedure information (for example why the visit is required, which parameters should be estimated during examinations,...) are transmitted accurately to the echo device. After the examination, images are securely stored to the PACS and can be displayed at any imaging workstation. Echo measurements, performed anywhere, are correctly associated and securely stored with the study as discrete, structured data which can be interpreted by another workstation and finally incorporated into a report.

In particular, interoperability is guaranteed among HIS, PACS, Echo devices and various radiology workstations.

7.2.1.2 The actual workflow

In a real-world example, instead, echo devices are not connected to any network. Sometimes, a workstation provided by the echo device vendor and running proprietary software, is associated. This workstation has one (or several) storage units to setup a local picture archive for the echo lab. Although potentially connectable to the hospital or global network, the local archive often can export images only to physical devices (e.g. by CD-rom burning). In most cases, luckily, images are exported according to DICOM standard and, thus, there exists no format problem.

For what regards echo measurements and findings (usually printed to paper and inserted into a patient's folder) cardiologists typically have to retype the information into a separate reporting system, since cross document sharing (XDS) seems not to be feasible (via HL7 export, for instance). Further, review of already annotated images is not possible, since annotation is made through the proprietary software of the echo device.

7.2.1.3 Discussion

Given such a discrepancy between ideal and real world, the HEARTFAID image archive should try to cope with the nowadays IT structures of its validation sites, with a view towards the future that -as far as we can see- will resemble more and more the ideal situation described above. In particular, it is essential for the success and diffusion of the platform to offer:

- State of the art interoperability. In this way, HFP could easily be connected to an ideal hospital IT infrastructure, allowing for the exchange of images, measures, reports, demographics and procedural information directly from the HIS/PACS to HFP and *vice versa*. Notice indeed that whereas original images have of course as source only the echo lab, procedural information and reports will be mediated by the CDSS. For example, CDSS may suggest which kind of parameters is more useful to be evaluated for a given

patient during a TTE session. This list could be directly sent to the echo device. In such a way the sonographer has directly on his screen, besides patient demographics (reducing the risk of misspelling in his name), the purpose of the examination. Further some of the measures and annotated images will be produced through image analysis tools provided by the platform; this data may be of interest also for the HIS/PACS.

In such a situation only (though by no means trivial) security/privacy/non-repudiation concerns are left.

- Customizable modules to solve IT infrastructure lacks. In particular, for what regards the image archive, this means to develop methods and interfaces for uploading echo images to HFP and query/retrieve images from the archive.

The rather obvious answer to these two items, at least for echocardiography workflow, is to adhere to standards (namely DICOM) and integration profiles (provided by IHE). The methods offered by the standards, suitably inserted in an interface, allow for image uploading, query/retrieve and review of reports from any workstation also in case of IT infrastructure lacks.

7.2.2 DICOM Servers

Since the 1970s, the emerging idea of a digital image archive (PACS) and electronic image distribution in a hospital created the need to exchange digital images between medical devices of different manufacturers. The American College of Radiology (ACR) and the National Electrical Manufacturers Association (NEMA) formed a working group in order to develop an image exchange standard. After some first failure, DICOM [2] was released in 1993 to offer an open vendor independent platform for the communication of medical images and related data, supporting PACS networks and guaranteeing interoperability. DICOM standard, which is composed of several parts, is continuously being extended and updated. The last part "WADO" was released in 2003.

It is important to point out that DICOM is not just an exchange format for medical image data. Actually DICOM goes far beyond, defining among several others:

- Data structures (formats) for medical images and related data
- Network oriented services, e.g.:
  - Image transmission
  - Query of an image archive (PACS)
  - Web-access to images
  - Print (hardcopy)
  - RIS - PACS - modality integration

  Formats for storage media exchange Requirements for conforming devices and programs.

For these reasons, any implementation of a DICOM server can't be merely a database of images in DICOM format, since storing, querying, retrieving, web-access are prescribed by the standard.

7.2.2.1 Network Services

DICOM network services are based on the client/server concept. In case two DICOM applications want to exchange information, they must establish a connection and agree on the following parameters:

- Who is client and who is server
- Which DICOM services are to be used
- In which format data is transmitted (e.g. JPEG compressed or uncompressed)

Only if both applications agree on a common set of parameters, the connection can and will be established. In addition to the most basic DICOM service image transmission (the so-called *Storage Service Class* such as C-STORE), several advanced services are available. The following two, for example, may reveal useful in HFP:

- The DICOM image archive service ("Query/ Retrieve Service Class") allows to search images in a PACS archive according to user-defined certain criteria (patient, time of creation of the images, modality etc.) and to selectively download images from this archive
- The DICOM modality worklist service allows to automatically downloading up-to-date worklists including a patient's demographic data from an information system (HIS/RIS) to the modality.

7.2.2.2 Web Services

Users of medical information systems may benefit from rapid and reliable access to reports and images. For example it would be important during an examination to retrieve on the fly reports or even images of the previous examination. Within HFP it is likely that such access will be based on web technologies also for image retrieval and visualization. The access to relevant DICOM *persistent objects* (i.e. images and reports, not logs of workflows) should be either in native DICOM format for advanced use or rendered into a generic format (e.g. JPEG, PDF) that can be presented with off-the-shelf applications. DICOM standard offers the so-called "WADO" (Web Access to DICOM persistent Objects) to answer these needs. It is a web-based service for accessing and presenting DICOM persistent objects, consisting in a simple mechanism for accessing a DICOM persistent object from HTML pages or XML documents, through HTTP/HTTPs protocol, using the DICOM UIDs (study, series, and instances). We refer to [3] for a discussion of WADO and the presentation of several scenarios.

Security Concerns and Current limitations of WADO

Clearly the information contained within DICOM objects may be considered as Protected Healthcare Information (PHI). Thus the protocol used, that is HTTP, can be replaced by HTTPs for that purpose. Further, DICOM standard defines two optional parameters, *anonymize* and *annotation*, which control respectively the

absence of patient identification in a retrieved DICOM object and the presence of patient identification burned into the pixel data of images. It is likely, however, that for patient enrolled into HFP personal information will be erased and replaced with an ID (the same used in eCRF) before storing images in the HEARTFAID image archive.

When dealing with echocardiography, one usually deals with multiframe images (i.e. image sequences). It would be interesting to be able to retrieve and visualize multiframe images via a web-based service. However, considering the size of such kind of images, some sort of *streaming* is necessary. Currently, up to the best of our knowledge, no kind of streaming is suggested or prescribed by DICOM standard. In particular, WADO consents the access only to the first frame of a multiframe image.

7.2.3 Beyond DICOM

As we saw, DICOM defines a complex standard to guarantee interoperability among different DICOM compliant devices ranging from DICOM server to radiology workstation, from imaging devices (US, CT, X-ray...) to HIS. Any DICOM compliant device comes with a DICOM conformance statement in which the portion of implemented DICOM features is described. In practice, however, conformance statements are only comprehensible by experts and they are frequently inadequate since often only a minimum set of features is documented. In some cases interoperability problems tend to occur because some inconspicuous details do not go together.

Further, DICOM standard alone is not able to cope with the complex echocardiography workflows described in Section 7.2.1.

To answer these needs, IHE (an initiative by healthcare professionals and industry) [4] tries to improve the sharing of healthcare information by promoting the coordinated use of established standards such as DICOM and HL7 to address specific clinical needs in support of optimal patient care.

IHE Technical Framework defines specific implementations of the afore-mentioned established standards to achieve seamless transmission of information among physicians, medical specialists, nurses, administrators and other stakeholders.

In particular IHE provided a Cardiology Technical Framework [5, 6] (written by the American College of Cardiology (ACC), the Radiology Society of North America (RSNA) and Healthcare Information and Management Systems Society (HIMSS)). Echocardiography workflow is included [1] with the aim of:

- Providing echo measurements interoperability
- Ensuring images and measurements are securely stored
- Uploading echo reports to a repository
- Reconciling patient demographics

In IHE terminology, this is obtained implementing several *actors* (ADT/HIS, Scheduler, Acquisition modality, Image Manager, Evidence Creator). Since there is an obvious relationship between IHE actors and various modules in the HFP

related to the image archive, it is at least reasonable to explore IHE Cardiology Technical Framework in the close future. For the moment, it is timely to use a DICOM server implementation which integrates IHE actors, that is, according to IHE terminology, *Image Manager/Archive* and optionally *Report Manager* and *Report Repository*.

7.2.4 Interfacing the Image Archive

7.2.4.1 Current Implementation

From the previous discussion, the good features expected from HEARTFAID Image Archive may be summarized as follows:

- DICOM network services
- Web access to DICOM objects
- Easy development of web interfaces for Image Archive Management
- Easy development of web interfaces for image uploading
- Implementation of IHE actors
- Extendibility to meet HFP needs (interaction with CDSS and Image Analysis Tools)
- Multi-platform or platform independent

Among different open-source implementation (CONQUEST [7], DCMTK [8], DCM4CHE [9]), DCM4CHE, a Java implementation of DICOM, has been chosen according to the previous requirements list. For sake of completeness, an overview of DCM4CHE components is presented in Figure 4.1.

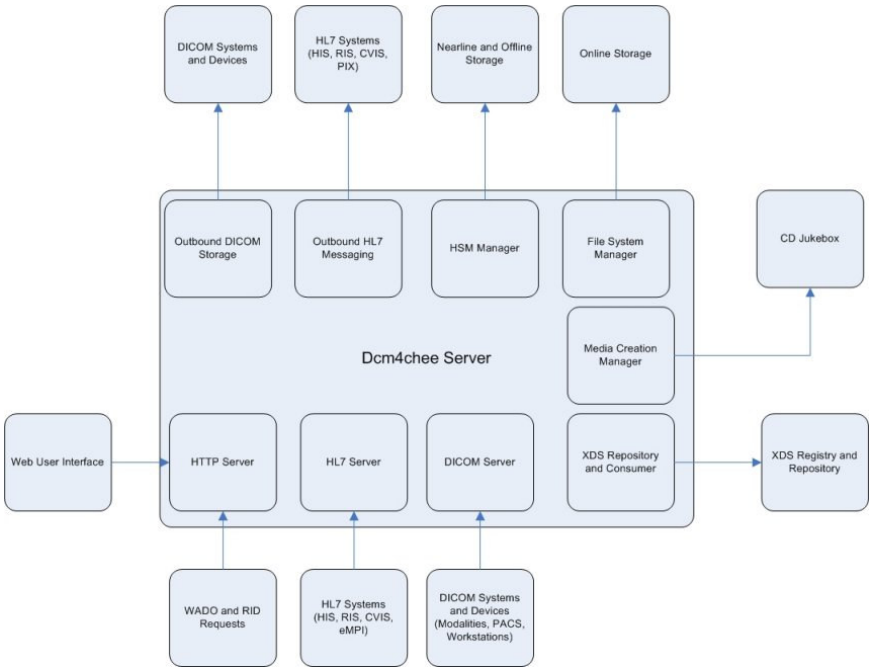


Figure 7.6: Overview of DCM4CHE components

Besides being an image archive, DCM4CHE provides a toolkit of standalone applications and methods to make network communication and interface development easier. Unfortunately, the documentation of DCM4CHE is not completed yet, so it is somewhat difficult to grasp its architecture.

In the current installation, DCM4CHE has an underlying MySQL DB, though other choices (e.g. PostgreSQL) are conceivable. Both the Dicom and MySQL servers accept network connection. Thus it is possible to query directly the DB for low level platform management purposes (e.g. user name, group, password harmonization).

7.2.4.2 Interface for Image Archive Management

DCM4CHE comes equipped with two web-interfaces for Image Archive Management. The first interface allows among others for

- Making queries about patient studies in the DB
- Editing Patient information e.g. for anonymization purposes
- Visualization of images by WADO
- User administration for the management of user name, group, password
- Management of recognized DICOM entities (that is for example name and IP address of DICOM clients that are allowed to retrieve information)
- Audit Record, to monitor the jobs required to the Dicom server

This first interface should be easily modified and integrated into HFP. Harmonization of Patients demographics and user data may be, for example, directly obtained through queries to the DB.

The second interface is a standard jmx-console *Mbean view*, that allows for invoking Mbean operation for internal server configuration and WADO services plus archive management procedures. As such, it is not necessary to integrate it into the platform, since it mainly addresses archive administrators.

7.2.4.3 Interface for Data Transmission

Clinical partners should be able to upload image to the image archive. If the echo lab is equipped with a PACS connected to the network, connection may be directly established with HEARTFAID Image Archive. However, since this seems not to be feasible in the validation sites, an interface dedicated to image upload should be provided.

The current implementation has been tested with K-pacs and Conquest (both acting as client) to upload images to the Image Archive.

Since K-pacs is free, it could be eventually used for this purposes, setting up a workstation running it in every validation site. Optionally, it is conceivable to develop a web interface calling the standard DICOM C-STORE method (implemented for example in DCM4CHE Toolkit) to upload DICOM images (or more general DICOM media) to the platform from anywhere.

7.2.4.4 Interface for Image Display

Image display interface should answer to the following needs of HFP:

- Reviewing of images by the referent physicians
- Reviewing of images for second opinion
- Quick access to image data (for example access to data of the previous examination in the same room where the new examination is carried out to appreciate changes in the clinical situation)
- Quick selection of images for post-processing workflow. For example, a physician may want to compute again a) left ventricle ejection fraction or b) end diastolic LV diameter. In case a) very likely he will select an image sequence taken from an apical view, while in case b) he will select a particular M-mode image. In any case, he needs to select quickly and easily a suitable image from the bunch of images in the patient's study.

WADO services, implemented in DCM4CHE, are of course useful, but are not sufficient to deal with image sequences, since no kind of streaming is implemented.

It would be useful to add some features to WADO services, so as to include video streaming in some format or at least frame navigation (that is buttons to move forward and backward in the image sequence). Of course the images displayed in this way, besides being suitable for quick identification, are not suitable for diagnostic purposes, since the compression rate could be too high.

7.2.4.5 Final remarks

As a final remark, it is worthwhile to point out that DCM4CHE community is pursuing a new child project, called Xero, that provides a new web interface for clinical access to patients and studies (as opposed to the Web-based user interface described above which was mainly intended for administrators). This component is intended for users such as nurses, doctors and perhaps patient's relatives who can't easily install a full radiology client station. This web-interface should in principle give an answer, among others, to the interface problems described in the previous subsections, i.e. user administration, data query/retrieve, data transmission, consistent display of images, display of multiframe images (at least through frame navigation), numeric image reports and final reports. See [10] for further information.

References to Section 7.2

[1] IHE Echocardiography Workflow and Evidence Documents Integration Profiles, http://www.ihe.net/Cardiology/committees/upload/IHE\%20Cardiology\%20Echo\%20white\%20paper\%20March\%202006\%20v.5.pdf, 2006

[2] DICOM: http://medical.nema.org/

[3] E. Cordonnier (ETIAM, France) *WADO presentation*: medical.nema.org/dicom/workshop-03/pres/cordonnier.ppt, 2003

[4] IHE: http://www.ihe.net/

[5] IHE Cardiology Technical Framework Vol.1, http://www.ihe.net/Technical_Framework/upload/ihe_CARD_tf_vol1_2.pdf, 2006

[6] IHE Cardiology Technical Framework Vol.2, http://www.ihe.net/Technical_Framework/upload/ihe_CARD_tf_vol2_2.pdf, 2006

[7] conQuest: http://www.xs4all.nl/~ingenium/dicom.html

[8] DCMTK: http://dicom.offis.de/dcmtk.php.en

[9] DCM4CHE: http://www.dcm4che.org/

[10] Xero project: http://www.dcm4che.org/confluence/display/ee2/Xero

8 Security issues

In recent years, advances in computing and telecommunication technologies have greatly expanded user requirements, applications, functions and tools available to all users of data processing systems, in almost every field of application. Because of the different components, operations, resources and users, computer networks, and especially Internet, are becoming a very convenient target for attacks and illegal operations, a non secure domain. From a general perspective, security refers to a complex of measures, which may be broadly classified as procedural, logical, and physical, and which are aimed at the prevention, detection, indication, and correction of certain kinds of system misuse, both accidental and deliberate [9].

In the context of computer-based systems **safety** is defined as the freedom from unacceptable risk of harm. In this definition, the terms harm and risk have particular interpretations, and these are:

- harm is the physical injury, or the damage to health or property, that may be caused by the system;
- risk is the probable rate of occurrence of a hazard (a hazard is understood to be a situation in which there is a potential for human injury) causing harm and the degree of severity of the harm.

Thus, the concept of risk has two elements:

- the frequency with which a hazard occurs;
- the consequences of the hazardous event.

Security is the protection of information systems against unauthorized access to or modification of information, whether in storage, processing, or transit, and against the denial of service to authorized users or the provision of service to unauthorized users, including those measures necessary to detect, document, and counter such threats.

A basic element of the security in healthcare is the health information which is defined as any information, whether oral or reported in any form or medium, that is created or received by a health care provider, public health authority, life insurer and relates to:

- the past, present, or future physical or mental health or condition of an individual;
- the provision of health care to an individual;
- the past, present, or future payment for the provision of healthcare to an individual.
-

Privacy, on the other hand, includes the right of individuals and organizations to determine for themselves when, how and to what extent information about them is communicated to others.

Individually identifiable health information is any health information that:

- identifies the individual, or
- there is a reasonable basis to believe that the information can be used to identify the individual.

At one end of the spectrum of identifiability, data are completely anonymous and not linked to any identifiers. This is the least sensitive type of information. However, depending on how the anonymization process is carried out, some risk may remain for the anonymized data to be re-identified (e.g. through processes such as data matching).

8.1 Security Aspects

Computerised information systems allow us to store and handle vast amount of data. The scenery of these systems is rapidly changing because of the massive use of data communications. As a consequence, the number of users that have access to data networks is increasing rapidly. This development has its parallel in the medical sector, where systems are used to store various kinds of patient information and where advanced imaging equipment can directly be coupled to databases that store the images in digitised form. [10]

Confidentiality. Patient confidentiality is breached whenever anyone other than the patient, the patient's physician or other healthcare professional directly responsible for the patient's care learns any private patient information. An IT application must preserve the confidentiality of the patient medical data by the development and the deployment of advanced security mechanisms.
Integrity. Data integrity is defined as the property that data has not been altered or destroyed in an unauthorized manner.
In order for patients to be treated appropriately for their medical condition, physicians and other clinical staff must have accurate and complete information on the patient. Healthcare professional rely upon and trust the information stored in the Electronic Healthcare Record systems or transfer through telemedicine applications.
There are also other applications where integrity will need to be assured, such as when transmitting an email message, examination orders and results, healthcare record segments, etc. between two parties.
Availability. IT applications and their stored data must be always available and useable upon demand by an authorized user or system.
Accountability. IT applications for healthcare and their users, i.e. the healthcare professional, must be accountable for their actions concerning the treatment of a patient. This means that someone has to be always able to trace the actions of the healthcare professionals that are related to the usage of the IT application (i.e. maintaining audit logs). This is important not only for the data insertion or modification to the Electronic Healthcare Record systems, but also for the data that are shared during a telemedicine session including the opinions that are exchanged.
Accountability and confidentiality are closely related to authorization that refers to the process of identifying a user and granting privileges to the use and his processes. Once a user is identified (reliably), the privileges, rights, property, and permissible actions of the user are determined by authorization.

8.2 Security standards

A standard is an expert consensus document that provides a benchmark for a product or service. [1]

Health is an area that is dependent on information both for accurate patient care and for the management of health services. As Kokolakis, Gritzalis and Katsikas [2] point out, when dealing with the healthcare environment we need to consider trust and quality assurance when employing interoperable services.

Medical practices must be accountable to their patients in order to maintain the basic relationship of trust between doctor and patient. Therefore there is a need to reassure patients that their privacy is not eroded in the electronic environment. [3]

Standards are therefore critical to the consistency of information sharing and its effectiveness. In order to provide any discourse on the use and effectiveness of standards, it is constructive to understand the position of law and standards.

From a standards perspective, we refer to ISO 17799, which was developed in 2000 to assist in the development of security plans. It is a code of practice focused on high-level security management. It was revised in 2005 to cover current technology and ebusiness practice. "ISO/IEC 17799:2005 is intended as a common basis and practical guideline for developing organizational security standards and effective security management practices" [4].

As a code of practice it cannot be used for certification, so a standard has recently been developed (ISO/IEC 27001 *Information security management system requirements*) which will be certifiable. This new standard specifies the requirements for security implementation which is customizable for individual organizations [5].

In Australia, the AS/NZS 17799 is the Australian Standards version of the ISO17799. A complementary standard to the original ISO17799 guidelines called AS/NZS 4444 was superseded by AS/NZS 7799.2:2003 *Information security management - Specification for information security management systems* in 2003. However, it was acknowledged that there was a need for more specificity in the area of health than for other business entities. Subsequently the HB174-2003 *Information security management – implementation guide for the health sector* was developed specifically to assist health organizations interpret the original standard [6]. In addition, other AS/NZS standards specifically addressing health identification of both the patient and health providers have been developed, as have guidelines for the security and use of electronic medical records [7].

It should also be mentioned that other standards exist for specific aspects of health information, particularly for use in e-health information exchange. HL7 is one such standard, which has been developed as a principal standard for clinical information exchange [8]. HL7 has been based predominantly on the HIPAA guidelines. In addition, significant effort is being put into development of healthcare information systems security in Europe by the European Committee for Standardization (CEN).

8.3 Security in Medical Devices Interaction

Once the information are arrived from the medical device to the gateway (host), all the security aspects have to be treated according to the existing normative for the health informatics products. In "Building the Foundation for Medical Device Plug-and-Play Interoperability" Richard Schrenker and Todd Cooper state "Once device data are routed beyond the immediate host connection (for example, via a LAN to a remote application), security must be maintained to ensure privacy and source authentication. This is especially true given the requirements mandated by the Health Insurance Portability and Accountability Act of 1996 (HIPAA)". CEN TC251 WGIII (security) and ISO TC 215 WGIV (security) have always strongly considered HIPAA in their work and all the existing European and International standards related to security take into account HIPAA. Thus the storage of the information, the data retrieval and the access from terminals are covered by the existing European normative for **Confidentiality**, **Integrity**, **Availability** and **Accountability** in health IT applications.
Security in medical device interaction is however related to the information transmitted between the medical device and the gateway.

8.3.1 Transmission from medical devices to gateways

When sensitive data (and health measurements are typically sensitive) are transmitted from a medical device to an immediate host (gateway) either wireless or wired, the overall system should minimize the risks that these data can be intercepted and associated to a specific patient.
Individually identifiable health information is any health information that:

- identifies the individual, or
- there is a reasonable basis to believe that the information can be used to identify the individual.

At one end of the spectrum of identifiability, data are completely anonymous and not linked to any identifiers. This is the least sensitive type of information. However, depending on how the anonymization process is carried out, some risk may remain for the anonymized data to be re-identified (e.g. through processes such as data matching).

8.3.1.1 HEARTFAID devices and general security principles

Devices could be divided into three categories depending on their capabilities:

1. Devices in this category can only prove their identity to the gateway by claiming to have a specific identity. Either because they have an identifier or because they are wired to a specific port on the gateway. This does not provide any protection against spoofing. Also these devices can't store information such as access control lists, so they will accept any request they receive.
2. Devices in this category support symmetric cryptography for proving their identity towards the gateway and securing the communication channel. This is a local identification, since only one other device is able

to trust this device, namely the device (usually the gateway) that knows the secret key as well. These devices might be able to store some additional data such access control lists, but it is not a requirement.

3. These devices support public key cryptography. This gives them a global identity since they are able to prove their identity to other devices. They are also able to send confidential data to the server even if the gateway is compromised and they can roam between gateways. They can also store their own access control list, so they are able to refuse a message sent to them if it is against the domain policy.

All devices have a unique identifier and are stored in the server. Associated with each device should be information about which category the device belongs to. This can be used to make policies such as "only accept blood pressure measurements from devices that can prove that the data has not been altered since it left the device".

When the server needs to communicate with category 1 and 2 devices, the gateway will act on their behalf. This provides adequate security for most cases assuming that the gateway is not compromised.

For handling key and lifecycle management of devices, we can use a scheme based on the resurrecting duckling policy that consists of the following principles:

1. **Two state principle**

The device is always in one of two states: imprintable or imprinted. In the imprintable state the device is not associated with the platform and can be taken over by anyone. When the device is imprinted it will only allow communicate compliant with the domain policy. This could mean that only a specific user is allowed to read data from it, or that it will only communicate with one specific gateway.

2. **Imprinting principle**

The transition from imprintable to imprinted happens when a device receives an imprinting key from a gateway. This can happen in different ways depending on the capabilities of the device and the security level needed. Examples include: Physical contact between the gateway and the device, side-channel imprinting by having a user type the same PIN code on both the gateway and the device, key transmitted over a short range wireless protocol such as IrDA or some other key exchange protocol.

3. **Death principle**

Death is the transition of a device from imprinted to imprintable, and may only occur under certain circumstances (note that death is not the same as broken). Examples of circumstances that might lead to the death of a device are:

a. Death by order of a specific user
b. Death by old age after a predefined time
c. Death on completion of a specific transaction

Upon the death of a device, all data should be erased from the device, its certificates revoked and the device should be deleted from the database. This device is no longer a part of HEARTFAID.

8.3.1.2 Patient identification and biometrics

An important issue is the association of the incoming measurements to a specific patient. Patient/medical device association might be automatically guaranteed with the use of biometric sensors. A biometric sensor, fingerprint sensor to be specific, also known as the fingerprint reader, is a fingerprint image capture device, the very front end of the biometric fingerprint identification/verification module. The fingerprint sensor captures the fingerprint images, matches the uniqueness of each print read by the sensor and compares it to the one stored in its module or local system database. Currently main vendors are Fujitsu, AuthenTec, Biometric Access Corp (BAC), Digital Persona U.are.U, Identix and SecuGen FDA01. All the types of the fingerprint sensors are generally known as optical, semiconductor, and ultrasound sensors. Among all the sensors, semiconductor sensors are considered to be low cost, optical sensors are considered to have a high degree of stability and reliability, while ultrasound sensors are very precise and fraud-free though expensive to implement. False Rejection Rate and False Acceptance Rate are two of the most important fingerprint security benchmarks and can vary according to different applications and configurations.
In the current technology, biometric sensors are distinct devices not integrated in vital sign measuring medical devices. The use of such biometric sensors in the HEARTFAID platform will imply the implementation of a specific driver for such sensors and however being each driver independent from the other, still we will not have any guarantee (in terms of strong authentication) of the patient holding/wearing the vital sign measuring medical devices. Nevertheless, it is expected in the next years to have an integration of these biometrics sensors inside the vital sign measuring medical devices, if reliable technology will be realized at affordable prices. In such case the future generation of vital sign measuring medical devices will be able to strongly authenticate the patient who holds/wears the device, eliminating any doubt on the belonging of the acquired measurements.

8.3.1.3 HEARTFAID medical devices

For the time being we are at the mercy of existing technology and medical devices do not have any biometrics sensor integrated into them. Thus, strong patient identification cannot be guaranteed and security needs to be approached identifying threats and providing reasonable answers for each threat.
All medical devices currently integrated in the HEARTFAID platform do not transmit any patient first/last name together with the vital sign measurements and the association measurements-device is made in the gateway and then, in the server, the device-patient association is used to assign the measurements to the patient. In case of other medical devices have to be integrated in the platform, privacy and security issues have to be considered. Of course the use of off-the-shelf devices implies that the communication protocol is the one implemented by the manufacturer in the medical devices. If the implemented protocol only allows the transmission vital sign measurements together with patient data, then methods for secure de-identification of the patient have to be applied at the medical devices (i.e. transmission of a patient code instead of first and last name). The availability from a manufacturer of a medical device with only unsecured protocols or where

any reliable way to de-identify the patient cannot be applied will lead to consider that device as unsecured and unsuitable to be integrated in the HEARTFAID platform.
A second security issue that needs to be considered is the intrusion of unauthorized medical devices in the HEARTFAID platform. In this case a medical device starts its transmission and sends data to a gateway without being authorized. This situation is not possible in the HEARTFAID platform because each device has to be registered with its unique ID before starting its operation (it has to become imprinted) and this will be possible only for devices previously authorized by administrators to operate in the platform.

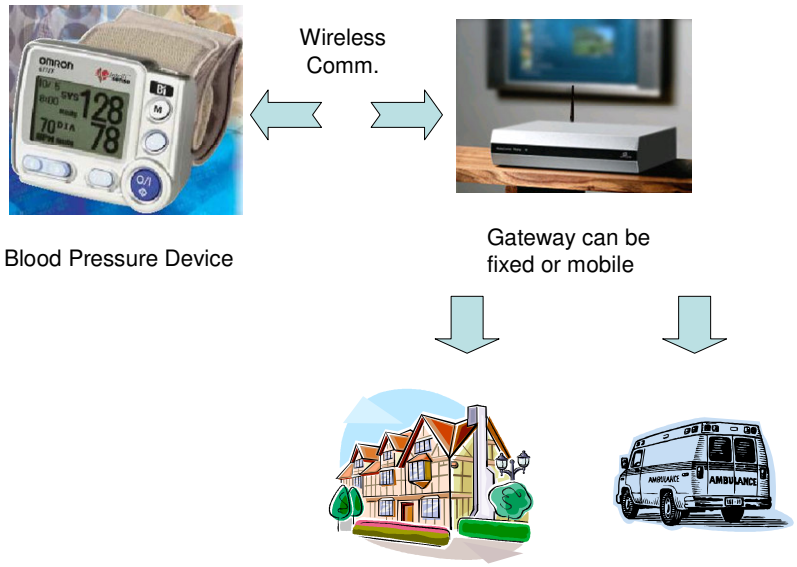


Figure 8.1: Communication between a medical device and a gateway (mobile or fixed)

A final security issue is related to the assignment of devices to users in order to avoid the risk that incoming measurements can be associated to a wrong user. There are several implications that we need to point out:

- A device has to be associated to a specific user during its operation. The association can cover a significant amount of time (patient holds/wears the device for a significant amount of time) or can be related just to the time necessary for acquiring a measurement (patient holds/wears the device just the time necessary for acquiring a measurement). In the first case the user directly operates the device without any doctor/nurse supervision, while in the second case the measurement is taken under the doctor/nurse supervision.
- When the user directly operates the device (e.g. a blood pressure meter), it's extremely difficult for the gateway to verify the user identity. Even in case of medical devices that allows for inputting an account, we cannot think to a scenario where each time the user input her/his identity

in the medical device. This operation is very tedious for the user and users are not willing to do it. Furthermore we have to take into account that several times low-cost medical devices do not allow any patient data input.

Once the medical device is held/worn by a patient, there are two different steps that have to be performed:

- Acquisition of a measurement (device-measurement association)
- Association of the measurement to the specific patient (device-patient association)

The recommended approach is to establish previously the device-patient association. Thus, the acquired measurement can be automatically associated to the specific patient without the need of a later acknowledgement. The device-patient association has to be done in correspondence with one of these two events:

- **Patient preparation**. Medical personnel in charge of properly installing the medical device on the patient will register (at the end of this phase) the device-user association also enabling the monitoring of the measurements. This approach is best foreseen when the medical device has to be worn by the patient for a significant amount of time and we like to avoid enabling each time the monitoring of the measurements and to re-associating each time the device with the user. The device is then statically associated with a user till when the medical personnel will de-install the device from the patient and through a specific application will remove the device-user association that had been previously created. According to HL7 terminology, this case produces "unsolicited" messages, because measurements are automatically acquired and immediate acknowledgment is not required. This is related to the home care environment, where the patient has to wear the medical device for a significant amount of time outside from the hospital premises and measurements will be automatically acquired without any doctor/nurse supervision.
- **Measurement enabling**. This is the case in which each measurement acquisition is controlled by the medical personnel (ambulatory set-up). In this case the patient can be retrieved through a web application by the medical personnel, associated with the medial device and then enabled for the measurement acquisition. At the end of the measurement acquisition if the device will be removed from the patient the device-user association will be removed as well. According to HL7 terminology, in this case we have "solicited" messages, having the doctor that immediately acknowledges the acquired measurements. This is related to the hospital/ambulatory environment, where the medical device is put on the patient just for the time necessary for acquiring a measurement under the supervision of a doctor/nurse.

8.4 Front End security

Organizations that use the Web to collect and transmit sensitive data to customers or other organizations need to secure their Web site. The general standard is the

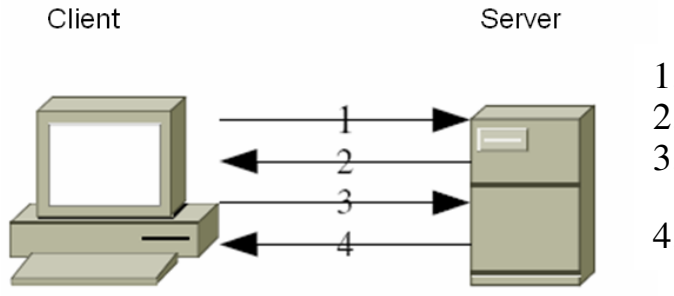
use of secure socket layers (SSL), which encrypts data transmitted via a Web site. Upon opening an Internet browser, an open or closed lock appears in the lower right hand corner of the Web site. If the lock is closed, it means the data transmitted over the Web site is secure, generally by SSL. This allows the transmission and collection of private data over a Web site, without worrying about a hacker accessing it. There is no such thing as security without risks, but the use of SSL and secure Web sites when transmitting data significantly reduces the risk of it being inappropriately intercepted. Secure Web sites can be established by using internal Web analysts/programmers or working with a vendor who has expertise in creating an appealing and secure Web presence.

Secure transmission helps solve the problem of illegitimate data interception, but there are further issues associated with accessing sensitive data. Authentication and authorization are two major subjects, especially for web applications; hence they are addressed in the context of the project's web-based portal. Unauthenticated users may only access the login page, which is used to enter and send to the server a set of credentials. Access to the portal may only be accomplished over SSL, therefore it is virtually impossible for "eavesdroppers" to obtain the credentials over the net. The server validates the user, whereupon the user gains access to further features of the web portal.

Security aspects within the platform is, at a first level, guaranteed through an authentication procedure. Each user that is allowed to access the platform services will be assigned with security credentials and with a profile. The credentials are used to authenticate the user upon logon while the profiling procedure, which is totally transparent to the user, will be used to assign the correct profile to the user itself, that is to identify the set of capabilities to access the services of the platform. According to profile assigned to the user that is performing the logging procedure, the system is able to exactly identify the services that can be accessed without restrictions, the services that can be accessed with some restrictions (to be defined by the Platform Administrator) and the services that cannot be accessed.

More adequate authentication procedure, for example based on smart cards, id cards, or even fingerprints, voice recognition, retina scan and so on, will be investigated apart since this goes beyond the objectives of the HF project.

The authentication schema that will be implemented is the *Local Authentication* (see image below). This is a simple schema where the client (in this case the final user but it can be also another information system) requires the provision of a service to the server, the server requires the user to provide a set of credentials, compares these credentials with a local copy if these data and, in they coincide, the identity of the user is considered *verified.* Afterwards, the authentication system is able to verify that the identified user has the rights to access the service required.



1. Service request
2. Request of credentials
3. Provision of credentials
4. Provision of service

In this schema the server is in charge to perform the procedure that are sequentially executed: authenticate, authorise and provide the access to the service. Therefore the authentication system should have information on the users and on their profiles, i.e. on the access capabilities/rights. The advantages of this approach are simplicity and the possibility to be implemented on any information system.
An important aspect to be taken into account concerns the access modalities of the different modules operating within the platform. In fact, as already described in other technical documents, the platform thanks to the interoperability and the integration middleware will enable the cooperation of different modules which are actually independent systems: the AmI framework, the image analysis tool, the CDSS, the Electronic Patient Record, the alarm system and so forth. Each of these systems is provided with its own authentication procedure and profiling mechanisms. How will the platform manage the accession procedures of all the underlying modules?
It is out of doubt that the platform should guarantee a *single sign-on* approach, that is the user will be authenticated only once and the platform will be in charge to activate all the authentication procedures of the modules involved in the services requested, and this activity should totally transparent for the user itself.
Concerning the first prototype, we will assume that all the cooperating systems providing services to the HF middleware will not be requiring any further authentication procedure. This way, the web portal will be the only system in charge to authenticate the user and all the other systems will rely on the authentication mechanisms of the portal. In a second stage the single sign-on mechanisms will be implemented to enable all the authentication procedures of the underlying systems.

As explained in section 3, many user profiles are supported by the software, with varying levels of access rights. Each user is associated to a certain user profile and the features that s/he may access are regulated according to that profile. As a general rule however, we could say that nurses and caregivers are mostly confined to the data management component of the application, i.e. the eCRF, while doctors and medical experts will be granted access to the data processing components, i.e. the DSS and the Knowledge Management. For each logged-in

user, a session is initiated and maintained on the server to facilitate access rights management and other functions.
Data integrity is one of the main concerns in any IT project of the healthcare sector. Establishing it in a web-based application presents many challenges, because a web-based application is by definition open to a large and diverse user base. Effort has been focused on displaying on the Graphical User Interface only the elements that are accessible to the user. Furthermore, each and every request is checked against the security model to establish that it is legitimate and that it can be satisfied. As mentioned previously, session information exists for every user that is logged in the web application. In case a request is found to conflict the access rights established by the security model, the processing is not carried through and the user is informed that s/he has been denied access to the application's feature, due to security constraints.

8.5 Security of HF services communication

Undoubtedly, any system that is based entirely on the Web for its functions is vulnerable to serious security threats. The most important threats, which we have to deal with in order to establish a secure medical environment, are briefly presented below.

- *Monitoring of communication lines*: By monitoring communication lines wiretappers may gain unauthorised access to medical data, thereby violating the patient's privacy.
- *Shared key guessing*: If one succeeds in guessing a shared key, that specific communication session can be decrypted by him and thus lead to a leak in of a patient's medical data.
- *Shared key stealing*: If one manages to steal the shared key, that specific communication session can be decrypted by him and thus lead to a leak in of a patient's medical data.
- *Unauthorised modification of information in transit*: Medical records may be modified on their course to their recipient. Modification may be performed in such a way that the receiving entity will not be aware of the modifications performed.
- *Forged Network Addresses*: If two or more healthcare organisations decide to trust the validity of data that is transmitted from one to the other, then a third party may transmit false medical information that will be accepted as valid by one of these organisations, by forging the network address of the computer that originated the data transmission.
- *Masquerade*: Users may masquerade as valid local or remote users, causing accountability problems. In addition an ingenious intruder may substitute a whole site with a masquerade one, creating thus a weak link in the trust model used by the communicating medical organisations.
- *Password stealing*: When passwords are used to authenticate medical personnel in a network and especially when they are not transmitted in encrypted form (which is usually the case), one may steal these passwords and therefore gain

access to the medical resources that are available to the legitimate owner of that password.

- *Unauthorised access*: unauthorised access from invalid users may cause the storage of false, corrupted or modified data, resulting the false diagnosis of a patient.
- *Repudiation of origin*: One may succeed in establishing a communication with a server holding medical data, having successfully forged the communication origin. In case, he will transmit, receive or modify medical records, these actions will be charged to the medical professional or organisation whose address is being forged, during that communication.
- *Private key stealing*: By stealing the private key of an entity, one may succeed in signing digitally an illegally modified medical record or diagnosis and thus validate the new, probably invalid, information contained in that medical record or diagnosis.
- *Private key compromise*: If the private key of an entity is compromised, one may use it in order to sign digitally an illegally modified medical record or diagnosis and thus validate the new, probably invalid, information contained in that medical record or diagnosis. [2]

9 Quality Assurance Process for the Prototypes

Health care procedures are not generally provided and consumed as an end in themselves, but as a means of improving the expected health status of those undergoing the procedures. Health technology assessment aims to provide objective information about the impacts of technologies, including safety, effectiveness, outcomes and costs, as well as social and ethical consequences, in order to assist in making health care decisions and setting health policy. Aging populations, changes in the incidence of diseases and the increasing expectations of populations associated with the rapid developments in medical research have all lead to increased pressures on health care systems. In response to this pressures, an increasing amount of literature has focussed on the evaluation of the quality of health care programmes and, more specifically, on the definition of measurable criteria for the assessment of the impact of information and communication technology to health care systems and programmes.

In this section, we will define and present the overall strategy for undertaking a quality assurance process for the prototypes devised and developed within HEARTFAID project, on the basis of which realize quality criteria for measuring suitable performance indexes of the resulting platform.

9.1 Quality of the Health Care Model

Heart failure is increasingly frequent in western world, carrying a high mortality rate and being responsible for a consistent increase in healthcare costs related to the multiple therapeutic interventions and the high frequency of hospital admissions required by these patients. There is therefore an increasing need for a better care, that might be provided not only by highly specialized centers, but also by small hospitals and by field cardiologists, a need that has to be matched with a policy of cost containment.

Progress in technology may offer an important support to make this possible, allowing adequate knowledge to be made available to all health care providers in this field. It might also offer new methods for regular and accurate collection of biological signals in patients living in their home environment, making use of sensors, either traditional or wearable, able to provide a continuous monitoring also through telemedicine facilities. More recent progress might further offer an advanced platform of services for the automated integration between the signals collected both at home and in the clinic environment on one side, and the available state-of-the-art knowledge on the other side, providing an intelligence support to clinical decision.

The proper adoption of these tools might help improving the daily care of chronic heart failure patients, through a prompt titration of treatment in response to early detection of even minor changes in clinical conditions, as well as through a reduction of diagnostic and therapeutic errors, by reinforcing the implementation of the most advanced recommendations provided by international clinical guidelines. Such an approach might also help improving the

cost/effectiveness of heart failure care facilitating the implementation of a disease management approach, in which therapy, education and follow-up are tailored for each patient by a multidisciplinary team constantly supported by an advanced platform of computerized services guiding the clinical decision through a continuous update of patient's clinical conditions allowed by advanced wireless telecommunication technology.

The HEARTFAID project, by suitable development and integration of a new health care model and the supporting technologies, is working to accomplish the final results of improve indices of health-related quality of life and control and reduce the overall economic and social costs of medical care.

In the deliverable D8, "Definition of the HEARTFAID model for the health care delivery", the proposal of an innovative health care management program, supported by the HEARTFAID platform, for patients with chronic heart failure has been described (Heart Failure Care Program: HFCP).

The development of the new management program has been carried out according to the following phases.

- Identification and formulation of the most important information relevant to the organization and management models for the heath care delivery within heart failure context. In particular, we underlined the differences between an ICT based HFCP and the more traditional ones, with also an analysis about economic issues of HFCP.

- Then two important issues have been analyzed:
  - the Heart Failure stakeholders;
  - the possible patients trajectories within the HEARTFAID platform levels.

  We observe that the above issues are logically necessary in order to design the HEARTFAID Care Management model. In particular, the Heart Failure stakeholders analysis was aimed to identify and group the principal "actors" (physicians, nurse, and so on) involved in the Heart Failure patient processes. A four groups clustering has been proposed in order to simplify and reduce the "actors" list.

- Then, we pointed out the guiding principles followed during the HEARTFAID care model design. The importance of Patient and Care Team empowerment has been particularly emphasized; these two principles have been subsequently used in the management model definition. In fact, two of the main aspects of HEARTFAID care model are the reinforcement of the coordination among care team members and the central role given to the patient during the care process.

- A general high level architecture of the care management model has been provided; in particular, three different levels have been identified, common to every care program:

- the macro level, related to the country health care policies;
- the meso level, regarding the medical management issues;
- the micro level, focused on the interactions between operators.

In relation to the HEARTFAID care model an analysis has been provided about the points of weakness and strength arising from each aforementioned level and from the intersections across distinct dimensions.

- The principal and new concepts introduced in the model were the Virtual Medical Team and the Care Coordinator. The Virtual Medical Team is the group of medical and non medical figures that are directly related to the care of the patient. It is "Virtual" because its members could belong to different health environments, and its functions will be assured and supported by ICT tools. On the other hand, the Care Coordinator is a medical figure in charge of follow all the phases of patient care process; compose and organize the virtual care team. The main idea is selecting a certain number of Care Coordinators in each health structure; new patients will be assigned to one of the care coordinators, that will decide the composition of the Virtual Medical Team, and will have the responsibility of the whole patient management process.

Through the HEARTFAID Care Management Program we wish to reach two objectives:

- effectively coordinate all the several care stakeholders. In fact, the Care Coordinator will have the responsibility and above all the capability to control every step of the patient care process. This possibility will be assured by the HEARTFAID platform functionalities and services;
- make systematic the assignment of each chronic patient to a specific physician; in fact, usually in hospital environments chronic patients are followed by the same medical doctor.

The effective accomplishment of the above objectives strongly affects the resulting "quality" of the HEARTFAID Care Management Program. On the other hand, the effective accomplishment of the above objectives is "enforced" and "supported" by the services and functionalities provided by the HEARTFAID platform.

The overall "quality" of the HEARTFAID Care Management Program will be tested and evaluated according to the comparison, in terms of outcomes, of the behaviour of the proposed model with respect to the current clinical procedures.

9.2 Goals: efficiency and effectiveness improvement

In general, in the health care delivery sector, advanced and innovative information technologies enable services to be delivered more efficiently and effectively, as well as new services that correspond to people's evolving needs and requirements. Typically, the application of quantitative methodologies and advanced ICT tools within medical and clinical settings may contribute to

considerable reduction of time and efforts for carrying out the relevant procedures.

For the HF medical and clinical domain, information technologies offer new solutions to meet the societal demands and solve societal problems. In fact, the strategic impact of the HEARTFAID platform mainly regards:

- the improvement, in terms of efficiency and effectiveness, of the overall medical and clinical activities and procedures within the relevant medical domain, with the final aims to guarantee a high level of quality of the health care service offered to the patients;
- the strong social impact of the obtainable results, by improving the functional status and the quality of life of the patients and decrease the social and economic costs.

From the medical and clinical impact point of view, it is worth while to remark that chronic diseases within cardiovascular domain are major causes of frailty and disability in late life. Age is the major risk factor for cardiovascular disease. Heart disease and stroke rise steeply after age 65, accounting for more than 40% of all deaths among people age 65 to 74 and almost 60% at age 85 and above. People age 65 and over are much more likely than younger people to suffer a heart attack, to have a stroke, and to develop coronary heart disease and high blood pressure leading to heart failure. Cardiovascular diseases are also major causes of disability, limiting the activity and eroding the quality of life of millions of older people each year.

Heart failure is primarily a disease of the elderly. Approximately 6% to 10% of people older than 65 years have HF, and approximately 80% of patients hospitalized with HF are more than 65 years old. Heart failure is the most common Medicare diagnosis-related group (DRG), and more Medicare dollars are spent for the diagnosis and treatment of HF than for any other diagnosis. The total inpatient and outpatient costs for HF in 1991 were approximately $38.1 billion, which was approximately 5.4% of the health care budget that year. In the United States approximately $500 million annually is spent on drugs for the treatment of HF.

A different type of epidemiological information comes from reports of HF related hospital admissions on a country to country basis. Hospitalisation for HF appears to be a growing problem on a global scale. In the USA, HF continues to be the most common cause of hospitalisation in people over the age of 65 years. HF is the reason for at least 20% of all hospital admissions among persons older than 65. Over the past decade, the rate of hospitalizations for HF has increased by 159%.

Hospital admission for heart failure is frequently prolonged and in many cases followed by readmission within a short period of time. For example, in the UK the mean length of stay for a heart failure related admission in 1990 was 11.4 days on acute medical wards and 28.5 days on acute geriatric wards. Within the UK about one third of patients are readmitted within 12 months of discharge, while the same proportion are reportedly readmitted within six months in the USA. Such readmission rates are usually higher than the other major causes of hospitalisation, including stroke, hip fracture, and respiratory disease. Moreover,

although there is evidence to suggest that an increasing number of heart failure patients are surviving a heart failure related hospital admission, there is a parallel decrease in the number of patients who are discharged on an independent basis to their own homes.

In any health care system, hospital admissions represent a disproportionate component of total health care expenditure. Not surprisingly, considering the high rates of hospitalisation for heart failure and the ongoing treatment and care it requires, the overall management of heart failure requires a significant amount of health care expenditure in industrialised nations. Heart failure is reported to consume 1-2% of health care expenditure in a number of industrialised countries.

Under this respect, the measurable benefits, in terms of efficiency and effectiveness, provided by HEARTFAID platform are basically related to:

- improve indices of healthy related quality of life. This is achieved by the possibility to personalize the therapy and have a continuous monitoring and assistance of the patient;
- control and reduce the overall economic and social costs of medical care, by decreasing the frequency of hospital admissions.

In fact, the application of HEARTFAID, by assuring process optimization, will bring an important increase of the treatment quality of the individual patient as well as a remarkable reduction of health care costs. Under this respect, it is expected that the highly innovative systems and services provided by HEARTFAID platform will have a high acceptance in targeted health care domains.

9.3 Quality criteria for the resulting platform

The overall quality assurance process of the prototypes developed during the HEARTFAID project running, is based on the definition of suitable quality criteria and on the relevant procedures for the quantitative evaluation of the related indicators. In the following, we define these criteria and provide some techniques for a quantitative assessment.

9.3.1 Reliability and Validity

Reliability and validity are the two basic properties of empirical measurements. Reliability concerns the extent to which an experiment, test, or any measuring procedure yields the same results on repeated trials. Validity is the degree to which an instrument measures what it purports to measure. Reliability is a necessary but not a sufficient condition for validity.

As far as the definition of appropriate criteria for estimate reliability and validity of the HEARTFAID platform, it is worth while to observe that the platform basically works according to the following phases:

- measurement and acquisition of biomedical and clinical data, signs and symptoms, qualitative information;
- integration, elaboration and computation of the acquired data and information;

- issue of the results, in terms of services and functionalities provided to the end-user.

In all these three phases, reliability and validity indicators can be estimated on the basis of the same approaches used for the case of empirical measurements.

Common approaches to examine reliability include test-retest, alternate forms, split-half, and tests of internal consistency. In the test-retest method, the same test is given to the platform after a period of time. The correlations between the scores in the two administrations of the same test are calculated, and the correlation between two parallel measures equals the reliability coefficient. A prerequisite for test-retest reliability is that the second administration be conducted within a small enough time frame so that the concept being measured (e.g. pain) does not change. This is, however, often a problem. Test-retest reliability is appropriate for traditional assessments that measure stable traits, but it is inappropriate for assessments of volatile concepts that change rapidly over time (e.g., how bothersome a symptom is).

The alternate form method requires two testing situations performed by the platform, but an alternate form of the same test is administered. The two forms are intended to measure the same concept. The correlation between the alternative forms provides the estimate of reliability. Similar to the test-retest method, the alternate form of the instrument must be given within a small enough time frame so that the concept being measured has not changed. Under these conditions, the alternate form approach can be appropriate for the estimate of the reliability of the functionalities provided by HEARTFAID platform.

In the split-half technique, items of the scale are split in two. To obtain a measure of reliability, the scores of the halves are correlated. This follows the same logic as in the test-retest technique, where the correlation between two parallel measures equals the reliability coefficient. The issue of how to split the items in half, however, is not clear cut.

By far the most popular approach is the internal consistency reliability coefficient Cronbach alpha. Among the reasons for its popularity is the fact that it, like the split-half technique, requires only a single test administration. It does, however, expand on that methodology of the split-half technique, and the calculation of alpha is based on the inter-item correlations among all the items of the scale. The higher the alpha, the higher the reliability.

The main methods to assess the validity of a test for a group of people under certain circumstances are content validity, criterion-related validity, and construct validity.

Fundamentally, content validity depends on the extent to which an empirical measurement reflects a specific domain of content and whether the items reflect the meaning associated with each dimension or sub-dimension of that measure. Content validity is crucial for all measurements, but unfortunately there is no rigorous way to assess it.

Criterion-related validity refers to the correlation of a measure with a criterion variable that is external to the measuring instrument itself. The higher the correlation, the more valid is the measure for the particular criterion. The measurements may be collected at the same point in time (concurrent validity), or

the measurement under study may be used to predict a future measurement (predictive validity). For example, the degree to which a test for college admission can predict later academic achievement reflects criterion-related validity of the test. The availability of a criterion measurement (i.e., a gold standard) is a prerequisite to examining criterion-related validity of any assessment, tailored or untailored. Because such a gold standard is often missing, measuring criterion-related validity is difficult.

In contrast to content validity and criterion-related validity, construct validity has a more generalized applicability and lends itself easier to empirical investigation. Constructs concern domains of variables. Construct validity is concerned with the extent to which a particular measure relates to other measurements consistent with theoretically derived hypotheses concerning the construct being measured. There are three major aspects of construct validation: (1) specifying the domain of observables related to the construct, (2) determining the extent to which observables measure the same thing, and (3) performing subsequent experiments to determine the extent to which supposed measures of the construct are consistent with "best guesses" about the construct.

A number of techniques for examining construct validity are applicable to the services and functionalities provided by HEARTFAID platform. For example, convergent and discriminant approaches, including known group differences, are based on hypothesized relationships between the measurement of concern and another variable. Convergent validity is demonstrated when two independent methods that measure the same variable or attribute are highly correlated. Divergent validity is demonstrated when measures of different attributes do not highly correlate. In their seminal paper on construct validation, Campbell and Fiske proposed the multitrait-multimethod matrix as an approach to examining convergent and discriminant validity. The multitrait-multimethod matrix includes two traits (one of primary interest) and two methods that are applied to both traits. The basic premise is that the measurements of a trait will converge across methods and diverge between traits. For example, measurements related to dyspnea severity should converge across paper-based and computer-based assessment methods, but the measurement of dyspnea severity should be less highly correlated with the measurement of nausea severity using the same method.

9.3.2 Safety

Generally, information technology contributes to reducing the risk of potential injuries and to minimising the possible harm to patients. Under this respect, there is now good evidence that knowledge based clinical decision support services, such as patient monitoring and reminder systems, prescribing systems, treatment management and workflow systems can make a significant contribution to quality and consistency of patient care. Interest in the use of such technologies is now growing rapidly, particularly in light of the recognition that human error in the delivery of patient care is a major source of avoidable mortality and morbidity.

Despite the potential of technology to help improve patient care we must also anticipate possible risks in their introduction. Most new medical technologies

entail new hazards (e.g. unanticipated side-effects of drugs) and even with our best efforts it will not be possible to avoid entirely the possibility that at some point in the future someone will suffer, in circumstances where the information technology is involved. Software developers clearly have a responsibility to ensure that avoidable hazards are anticipated and prevented, and that unavoidable ones are properly managed should they occur.

The goal of those developing knowledge based clinical decision support services must be to maximise the safety use of this new technology, thereby minimising the risk of adverse events and exposure to legal action. All technology developers would wish to see their work put to effective use for the benefit of patients, but since absolute safety can never be guaranteed with any technology, they should as a minimum be able to demonstrate that they have fully complied with commonly accepted best practice during all stages of development.

To this end, it is possible to identify four primary criteria to quality and safety for developing information technologies for health care delivery:

- the use of rigorous software engineering techniques to ensure the integrity, consistency and reliability of the technology platform;
- the adoption of systematic development life-cycles for creating and maintaining the medical content of an application and its associated scientific evidence base;
- the application of explicit safety and hazard management techniques within the applications where this is possible;
- the provision of comprehensive documentation to provide for quality and safety reviews by end users, in particular medical doctors.

9.3.3 Efficiency

Economic efficiency is a general term for the value assigned to a situation by some measure designed to reduce the amount of waste or "friction" or other undesirable economic features present. Economic efficiency is achieved when the cost of producing a given output is as low as possible. Production of a unit of good or services is termed economically efficient when that unit of good or service is produced at the lowest possible cost. In current usage, the term microeconomic reform refers to any policy that promises to increase economic efficiency (whether it does so or not).

In order to achieve economic efficiency the following need to occur: 1) Any product X is produced at the lowest cost. 2) The economy uses all the raw materials that in hand. Example: X and Y are produced by *a* and *b*. In efficient productivity, we use both *a* and *b* in a way that we cannot produce anymore X or Y with the *a* and *b* that had left.

Under this respect, information technology enables productivity to be improved, waste to be avoided, resource utilisation optimised and costs contained to budgets. Efficiency savings result when the same work is performed with fewer resources. If most hospitals and medical doctors' offices adopted information technologies, the potential efficiency savings for both inpatient and outpatient care could average over billion of Euro per year. The largest savings come from

reduced hospital stays (a result of increased safety and better scheduling and coordination), reduced nurses' administrative time, and more efficient drug utilization.

In order to evaluate the impact, in terms of efficiency, of the HEARTFAID platform, two specific methodologies will be implemented and tested: the Data Envelopment Analysis (DEA) and the Revenue Management.

Data Envelopment Analysis (DEA) is a Linear Programming methodology to measure the efficiency of multiple Decision Making Units (DMUs) when the production process presents a structure of multiple inputs and outputs. Some of the benefits of DEA are:

- no need to explicitly specify a mathematical form for the production function
- proven to be useful in uncovering relationships that remain hidden for other methodologies
- capable of handling multiple inputs and outputs
- capable of being used with any input-output measurement
- the sources of inefficiency can be analysed and quantified for every evaluated unit

In the DEA methodology efficiency is defined as a weighted sum of outputs to a weighted sum of inputs, where the weights structure is calculated by means of mathematical programming and constant returns to scale are assumed. A different model has been also developed with variable returns to scale.

The implementation of DEA within the HEARTFAID project will require the selection of the Decision Making Units (e.g., the clinical settings where the platform will be deployed), the identification and reliable measurement of the input and output values.

Revenue Management is the process of understanding, anticipating and reacting to consumer behavior in order to maximize revenue or profits. Other terms to describe this process are revenue optimization and demand management. Revenue management can result in price discrimination, where a firm charges customers consuming otherwise identical goods or services a different price for doing so.

The use of Revenue Management within HEARTFAID project could be finalized for the definition of the most profitable reimbursement scheme for the clinical management of chronic heart failure, by containing the production costs and making more efficient the clinical procedures in terms of using of the resources.

9.3.4 Effectiveness

In general, information technology enables healthcare to be developed, planned, scheduled and derived from evidence and provided consistently to patients who can, or may, benefit. On the other hand, healthcare professionals are enabled to work effectively in multi-disciplinary teams which share responsibility for the patient.

The well known procedure for measuring and assessing effectiveness is the cost-effectiveness analysis (CEA). CEA is a technique for selecting among

competing wants wherever resources are limited. Developed in the military, CEA was first applied to health care in the mid-1960s and was introduced with enthusiasm to clinicians by Weinstein and Stason in 1977: "If these approaches were to become widely understood and accepted by the key decision makers in the health-care sector, including the physician, important health benefits or cost savings might be realized." Regardless of whether this hope was realized, CEA has since become a common feature in medical literature.

CEA is a technique for comparing the relative value of various clinical strategies. In its most common form, a new strategy is compared with current practice (the "low-cost alternative") in the calculation of the cost-effectiveness ratio:

$$\text{CE ratio} = \frac{\text{cost}_{\text{new strategy}} - \text{cost}_{\text{current practice}}}{\text{effect}_{\text{new strategy}} - \text{effect}_{\text{current practice}}}$$

The result might be considered as the "price" of the additional outcome purchased by switching from current practice to the new strategy. If the price is low enough, the new strategy is considered "cost-effective."

It's important to carefully consider exactly what that statement means. If a strategy is dubbed "cost-effective" and the term is used as its creators intended, it means that the new strategy is a good value. Note that being cost-effective does not mean that the strategy saves money, and just because a strategy saves money does not mean that it is cost-effective. Also note that the very notion of cost-effective requires a value judgment—what you think is a good price for an additional outcome, someone else may not.

It's also worthwhile to recognize that CEA is only relevant to certain decisions. Table 1 delineates the various way a new strategy might compare with an existing approach. Note that a CEA is relevant only if a new strategy is both more effective and more costly (or both less effective and less costly).

TABLE 1
Conditions under Which CEA Is Relevant

	COST	
EFFECTIVENESS	**NEW STRATEGY COSTS *MORE***	**NEW STRATEGY COSTS *LESS***
New strategy is *more* effective	CEA relevant	Adopt new strategy
New strategy is *less* effective	New strategy is "dominated"	CEA relevant

As an example, consider two strategies intended to lengthen life in patients with heart disease. One is simple and cheap (e.g., aspirin and β-blockers); the other is more complex, more expensive, and more effective (e.g., medication plus cardiac catheterization, angioplasty, stents, and bypass). For simplicity, we will

assume that doing nothing has no cost and no effectiveness. Table 2 shows the relevant data.

TABLE 2
A CEA Examining Three Strategies

STRATEGY	COST	MARGINAL COST	EFFECTIVENESS	MARGINAL EFFECTIVENESS	CE RATIO
Nothing	$0	—	0 years	—	—
Simple	$5000	$5000	5 years	5 years	$1000/yr
Complex	$50,000	$45,000	5.5 years	0.5 years	$90,000/yr

Note that CEA is about marginal (also called incremental) costs and benefits. So the marginal cost of a simple strategy is the difference between the cost of that strategy and the cost of doing nothing. The marginal cost for the complex strategy is the difference between the cost of the complex strategy and the cost of the simple strategy (not the cost of doing nothing). The calculation is similar for effectiveness. The final outcome measure for the analysis is the CE ratio: the ratio of marginal cost to marginal effectiveness.

If a study is of interest and its primary outcome is a cost-effectiveness ratio, it is fundamental to seek answers to the following questions.

1. Are the relevant strategies being compared?

Because CEA involves marginal cost and benefits, the choice of which strategies to compare can drive the calculation and the conclusion of a CEA. Consider the effect of repeating the above analysis without the simple strategy (Table 3).

TABLE 3
A CEA Examining Two Strategies

STRATEGY	COST	MARGINAL COST	EFFECTIVENESS	MARGINAL EFFECTIVENESS	CE RATIO
Nothing	$0	—	0 years	—	—
Complex	$50,000	$50,000	5.5 years	5.5 years	$9091/yr

By excluding the simple strategy, the CE ratio for the complex strategy falls from $90,000 per life-year to $9091 per life-year. Thus, CEA is very sensitive to the choice of strategies being compared. Readers need to carefully consider whether the choice being presented is really the choice that interests clinicians.

2. How good are the effectiveness data?

It's hard to get too excited about cost-effectiveness if the effectiveness of the strategy is really unknown. So as a first step, the critical reader should examine the information used for effectiveness. Ideally, the data should come from randomized trials. If they don't, you'll want to scrutinize the face validity of the assumptions. Unfortunately, sometimes the analyses get way ahead of the data

(one CEA was published on autologous bone marrow transplantation in metastatic breast cancer 8 years before a randomized trial showed no benefit).

3. Do the effectiveness data reflect how the strategy will be used in the real world?

Even if the effectiveness data are from randomized trials, it's important to ask whether they really pertain to the population and setting in which the strategy is likely to be applied. Consider a CEA of carotid endarterectomy in asymptomatic patients with more than 70% stenosis. If the trial data represent the best surgical practice while broad implementation of the strategy would involve community providers, then effectiveness is being overestimated—as is cost-effectiveness. A similar problem may occur if the trials involve patient selection criteria that are not easily replicated in practice. A critical reader of CEAs should carefully consider the generalizability of the effectiveness data.

4. Where do the cost data come from?

The basic question here is, "Was resource use modeled, or was it measured in real practice?" In modeling, investigators have to make assumptions about which services are likely to be utilized differently—thus driving the difference in cost. The measurement of resource use in practice has the advantage of capturing utilization that may not be anticipated by investigators (e.g., extra testing, extra visits, readmissions). In either approach, there can be considerable debate about how to attach dollar amounts to utilization counts (debates that can get very tedious very quickly). Critical readers should look at the utilization counts themselves and have some confidence about the face validity of the dollars attached to them (probably the most practical standard being the Medicare fee schedule/allowed charges). If more utilization doesn't equal more money, something's wrong.

5. Did we get anywhere?

Finally, users may want to consider whether the entire exercise somehow helped them with a decision. Although some CEAs have extremely high CE ratios (i.e., > $200,000 per quality-adjusted life-year—a poor value) and other have very low CE ratios (i.e., < $10,000 per quality-adjusted life-year—a good value), most fall somewhere in the middle. Analyses with CE ratios of $50,000 per quality-adjusted life-year may conclude with an assertion that the analyzed strategy is "cost-effective." Whether or not this helps anyone make a decision is hard to know.

9.3.5 Utility

Cost-utility analysis (CUA) is a form of economic analysis used to guide procurement decisions. The most common and well-known application of this analysis is in pharmaco-economics, especially health technology assessment (HTA).

In health economics, the purpose of CUA is to estimate the ratio between the cost of a health-related intervention and the benefit it produces in terms of the

number of years lived in full health by the beneficiaries. Hence it can be considered a special case of cost-effectiveness analysis, and the two terms are often used interchangeably.

Cost is measured in monetary units (Euro). Benefit needs to be expressed in a way that allows health states that are considered less preferable to full health to be given quantitative values. However, unlike cost-benefit analysis, the benefits do not have to be expressed in monetary terms. In HTAs it is usually expressed in quality-adjusted life years (QALYs).

If, for example, intervention A allows a patient to live for three additional years than if no intervention had taken place, but only with a quality of life weight of 0.6, than the intervention confers 3 * 0.6 = 1.8 QALYs to the patient. If intervention B confers two extra years of life at a quality of life weight of 0.75, then it confers an additional 1.5 QALYs to the patient. The net benefit of intervention A over intervention B is therefore 1.8 - 1.5 = 0.3 QALYs.

The incremental cost-effectiveness ratio (ICER) is the ratio between the difference in costs and the difference in benefits of two interventions. A threshold value is often set by policy makers, who may decide that only interventions with an ICER below the threshold are cost effective (and therefore should be funded).

In the United Kingdom, as of January 2005, the National Institute for Health and Clinical Excellence (NICE) is believed to have a threshold of about £30,000 per QALY, although a formal figure has never been made public. Thus, any health intervention which has an incremental cost of more than £30,000 per additional QALY gained is likely to be rejected and any intervention which has an incremental cost of less than or equal to £30,000 per extra QALY gained is likely to be accepted as cost-effective.

In North America, US$50000 per QALY is often suggested as a threshold ICER for a cost-effective intervention.

A complete compilation of cost-utility analyses in the peer reviewed medical literature is available at the CEA Registry Website.

9.3.6 Usability

In general, usability is a term used to denote the ease with which people can employ a particular tool or other human-made object in order to achieve a specific goal.

In human-computer interaction and computer science, usability usually refers to the simplicity and clarity with which the interaction with a computer program or a web site is designed. The primary notion of usability of a tool or object is basically related to the following issues:

- more efficient to use: it takes less time to accomplish a particular task;
- easier to learn: operation can be learned by observing and using the object;
- more satisfying to use.

The document ISO 9126 (1991) Software Engineering Product Quality, issued by the International Organization for Standardization, defines usability as “a set of attributes that bear on the effort needed for use, and on the individual assessment of such use, by a stated or implied set of users”. Further, the document ISO 9241-11 (1998) Guidance on Usability, also issued by the International

Organization for Standardization, defines usability as "the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use".

Usability is an example of a non-functional requirement. Under this respect, usability cannot be directly measured but must be quantified by means of indirect measures or attributes such as, for example, the number of reported problems with ease-of-use of a system.

"It's usable" or "it's user friendly" are phrases that are used without too much thought as to the detailed nature of usability. Five technical distinctions have been proposed between uses of the term. This distinction helps in the identification and specification of systems in terms of their non-functional requirements.

Usability 1 = Utility - the thing can be used to complete the desired task.
Usability 2 = Goal / Task support - the thing is designed to help you complete your task.
Usability 3 = Accommodation – the thing is designed to accommodate different user populations.
Usability 4 = Adoption – the thing exhibits significantly more usability than its competitor designs – and therefore will be adopted by users.
Usability 5 = Extensibility/ Adaptability – the thing has features that allow it to be adapted or extended to suit a new (unpredicted) task or goal.

It is possible to devise a framework of system acceptability, where usability is a part of "usefulness" and is composed of:

- Learnability (e.g. intuitive navigation)
- Efficiency of use
- Memorability
- Few and noncatastrophic errors
- Subjective satisfaction.

Usability includes considerations such as:

- Who are the users, what do they know, and what can they learn?
- What do users want or need to do?
- What is the general background of the users?
- What is the context in which the user is working?
- What has to be left to the machine? What to the user?

Answers to these can be obtained by conducting user and task analysis during the project life.

- Can users easily accomplish their intended tasks? For example, can users accomplish intended tasks at their intended speed?
- How much training do users need?
- What documentation or other supporting materials are available to help the user? Can users find the solutions they seek in these materials?
- What and how many errors do users make when interacting with the product?

- Can the user recover from errors? What do users have to do to recover from errors? Does the product help users recover from errors? For example, does software present comprehensible, informative, non-threatening error messages?
- Are there provisions for meeting the special needs of users with disabilities? (accessibility).

Examples of ways to find answers to these and other questions are: user-focused requirements analysis, building user profiles, and usability testing.

9.4 Validation and evaluation procedures

The performance evaluation and validation procedures will be organized and developed according to main phases:

- The deployment of the prototypes in the clinical settings provided by the clinical partners;
- The development of clinical testing.

Within an appropriate and pre-defined referential territory for each clinical partners (e.g., Calabria region for UNICZ, Lombardia region for UNIMIB and AUXOL, and Krakow region for JUMC), suitable clinical settings and health care environments will be selected with the aim to deploy and integrate the systems prototypes into the every day medical activities. In Hospital the systems prototypes will be tested by comparison with the routine clinical protocols developed for the management of heart failure patients. At Home, the systems prototypes will be tested by collecting clinical data through the data acquisition and transmission infrastructure.

The clinical testing procedures are devoted to validate and clinical assess the system prototypes in suitable clinical settings, with the support of the health care operators and final end-users. In hospital testing will be based on the comparison between the clinical decision taken by cardiologists on the background of the relevant biomedical and clinical parameters, and the indications provided by the systems prototypes, fed with the same inputs. The systems prototypes testing will continue after discharge of patient from the hospital, through remote monitoring of clinically relevant parameters in the hone care and on the move environments. The decision taken by the cardiologists and nurses dedicated to their remote home care will be compared with the indications provided by the systems prototypes, fed by the same teletransmitted information.

More specifically, the basic steps will be:

Step 1: To test the platform, a suitable set of outpatients will enrol with clinical evidence of chronic and stable heart failure (NYHA class II-IV). After signing the informed consent, patients will have a full physical exam and the clinical and laboratory data will be reviewed. Then, the general practitioner will be contacted to assure an integrated management and continuous therapeutic strategy of a suitable subset of heart failure patients, especially within the home environment. In this way every earlier

symptoms or signs of heart failure will be detected by the telemonitoring system, assembled to detect few simple clinical parameters (heart and respiratory rate, blood pressure, body weight, etc.) and sent to medical staff.

Step 2: Validation of acquired clinical data. This will be done by a clinical and laboratory control that will verify the accuracy of parameters automatically detected. Data obtained both from physician and from the telemonitoring system will be acquired by the platform for a successive evaluation.

Step 3: Modification of therapeutical strategy and clinical application. After evaluating the accuracy of acquired data, the physician will modify a pharmacological treatment according to clinical findings in order to improve Heart Failure, to increase the free hospitalization time and/or to reduce hospitalization days. This approach will consent to reduce the social and economic costs. The overall patients management will be performed jointly by the clinical partners.

In terms of benchmarks and metrics of success, the main benchmark will be considered the standard behaviour of expert cardiologist, who applies accurately the guide lines and clinical protocols related to HF. In particular errors of commission and errors of omissions will be registered and used to improve the performance of the system prototypes. Moreover, the quality of the data collected through telemonitoring will be compared with the quality reached in the measurements carried out on the inpatients.

In terms of metrics of success, different groups of indicators will be considered suitable indices for measuring the quality criteria above defined.

An indicative list is the following:

- patient centered indicators:
  - registered outcomes
  - clinical stabilization at home of the HF patients
  - generic and condition-specific quality of life
  - satisfaction with care and acceptance of the new ICT based care model
  - incidence of acute exacerbations at home

- physician centered indicators:
  - adherence with the recommendations given by the system prototypes
  - physicians' attitudes toward guidelines

- indicators about costs and productivity
  - health care costs per patients
  - number of unplanned hospitalizations
  - number of home visits needed

10 Conclusions

In the rapidly changing health care industry, technological advances have made many new procedures and methods of diagnosis and treatment possible. Clinical developments, such as organ transplants, less invasive surgical techniques, skin grafts, and gene therapy for cancer treatment, continue to increase the longevity and improve the quality of life of many people. Advances in medical technology also have improved the survival rates of trauma victims and the severely ill, who need extensive care from therapists and social workers as well as other support personnel. In addition, advances in information technology continue to improve patient care and worker efficiency with devices such as hand-held computers that record notes on each patient.

Recent studies and experiences have demonstrated that accurate heart failure management programs, based on a suitable integration of inpatient and outpatient clinical procedures, might prevent and reduce hospital admissions, improving clinical status and reducing costs.

HEARTFAID aims to devise, develop and validate an innovative knowledge based platform of services, able to improve early diagnosis and to make more effective the medical-clinical management of heart diseases within elderly population.

HEARTFAID aims at defining efficient and effective health care delivery organization and management models for the "optimal" management of the care in the field of cardiovascular diseases. The HEARTFAID innovative computerized system will improve the processes of diagnosis, prognosis and therapy provision, providing the following services:

- electronic health record for easy and ubiquitous access to heterogeneous patients data;
- integrated services for healthcare professionals, including patient telemonitoring, signal and image processing, alert and alarm system;
- clinical decision support in the heart failure domain, based on pattern recognition in historical data, knowledge discovery analysis and inferences on patients' clinical data.

One of the most important advantages of electronic records is information online delivered on time. The future will certainly demonstrate the advantages of using not only electronic records but a whole framework of information services and support for citizens and clinical practice. Information on vital signs and orders for tests are transferred electronically to a main database; this process eliminates the need for paper and reduces recordkeeping errors.

The initial costs of implementation of such networks will be meaningless compared with the resulting efficiency and quality of service.

The formalization of the pre-existing clinical knowledge and the discovery of new elicited knowledge represent the core of the HEARTFAID platform.

In particular, HEARTFAID provides healthcare professionals with access to timely relevant information at the point of need (i.e. different types of health care delivery environments), with a set of functionalities and services for acquiring up-to-date relevant medical knowledge that will provide a reliable support to healthcare

professionals in their daily medical and clinical operations, enabling new ways of working as well as improved patient quality.
Operations that are currently hard to handle like research and analysis will strongly be empowered by interoperable records and devices thus resulting more efficiency, better follow up of distributed information and reduction of costs by avoiding loses or repetition of exams. This interoperable environment will ease clinical practice, help research procedures and deliver more efficient support decision tools. As a corollary of all this , it will be unavoidable to have a more efficient health care systems and better health care for citizens.

11 References

[1] Health Information Standards Organisation. (n.d.). Why standards? [Online]. Available http://www.hiso.govt.nz/whystandards.htm

[2] S. Kokolakis, D. Gritzalis, and S. Katsikas, "Why we need standardisation in healthcare security," in Security standards in healthcare information systems: A perspective from the EU ISIS MEDSEC project, vol. 69, F.-A. Allaert, B. Blobel, K. Louwerse, and B. Barber, Eds. Amsterdam, Netherlands: IOS Press, 2002, pp. 7-12.

[3] The Role of Standards in Medical Information Security: An Opportunity for Improvement. P. A. H. Williams School of Computer and Information Science Edith Cowan University, Joondalup, Western Australia

[4] ISO/IEC 17799:2005 Information technology - Security techniques - Code of practice for information security management, International Standards Organization, 2005.

[5] ISO/IEC 27001:2005 Information technology -- Security techniques -- Information security management systems – Requirements, International Standards Organization, 2005.

[6] Information security management— Implementation guide for the health sector, Standards Australia HB 174—2003, 2003.

[7] Health Informatics—Requirements for an electronic health record architecture Standards Australia ISO/TS 18308:2004, MOD, 2005, pp. 32.

[8] J. S. Hooda, E. Dogdu, and R. Sunderraman, "Health Level-7 compliant clinical patient records system", in Proc. 2004 ACM symposium on Applied computing, 2004, pp. 259-263.

[9] International Standards Organisation ISO/TC97 7498-2 (1988) Information Processing Systems – OSI Reference Manual Part 2: Security Architecture (Geneva: ISO)

[10] Developing Secure Web-based Medical Applications*+ S. Gritzalis, J. Iliadis, D. Gritzalis, D. Spinellis, S. Katsikas

[11] CEN TC 251, NC 98-106: “First Working Document of Safety and security related software quality standards for healthcare”, 1998.

[12] CEN TC 251, ENV 12924: “Medical Informatics - Security Categorisation and Protection for Healthcare Information”, 1997.

[13] CEN TC 251, ENV 13608-1:2000, Health informatics – Security for healthcare communication – Part 1: Concepts and terminology, 2000.

[14] CEN TC 251, ENV 13608-2:1999, Health informatics – Security for healthcare communication – Part 2: Secure data objects, 1999.

[15] CEN TC 251, ENV 13608-3:1999, Health informatics – Security for healthcare communication – Part 3: Secure data channels, 1999.

[16] ISO/ TC 215, Health Informatics, Privilege Management and Access Control -- Part 2: Formal models, Under Development Standard ISO/CD TS 22600-2, August 16, 2005.

[17] ISO/ TC 215, Health Informatics, Trusted end-to-end information flows, Published Standard ISO/TR 21089:2004, June 15, 2004.

[18] Robert Hoyt MD, Melanie Sutton PhD, and Ann Yoshihashi MD - Medical Informatics: Practical Guide for the Healthcare Professional, Lulu.com, Jun 7 2007

[19] http://www.securityfocus.com

[20] http://www.medcom.dk/

[21] http://info.med.yale.edu/diagrad/teach_link.html

[22] http://www.infobiomed.org/