Cyclic and person-centric **H**ealth management: **I**ntegrated app**R**oach for h**O**me, mobile and clinical e**N**vironments – Grant Agreement no. 100228

ARTEMIS JOINT UNDERTAKING

Title of the deliverable:

Overall assessment of the project and set of guidelines for further developments

Deliverable No.		D7.6.1	
Workpackage No.	WP7	Workpackage Title:	System Integration and Verification of the Project outcomes
Authors (Partner) (per company, if more than one company provide it together)		Silvio Bonfiglio (FIMI), Paolo Emilio Puddu (UOR) with the contribution of all the CHIRON Partners	
Status (F: final; D: draft; RD: revised draft):		F	
Dissemination level: (PU = Public; PP = Restricted to other program participants (including the JU);RE = Restricted to a group specified by the consortium (including the JU);CO = Confidential, only for members of the consortium (including the JU).		PU	
File Name:		D7.6.1 Overall assessment of the project v1.0.doc	
Project start date and duration		01 March 2010, 45 months	

CONTENTS

INTRODUCTION

This deliverable is intended to provide an overall assessment of the CHIRON project in terms of degree of achievement of its various objectives i.e.

- Scientific & technological objectives,
- Medical objectives,
- Socio-economic objectives.

The assessment is based on the analysis of the uniqueness and added values generated by the project; furthermore we performed – with the involvement of all the CHIRON Partners - a self assessment for rating the level of achievement of the initial objectives of the project and for identifying the best outcomes of the CHIRON work.

In the scientific & technological assessment we addressed two key aspects:

a. The design of a reference architecture and of solutions able to allow the achievement of the CHIRON objectives and to reduce time and costs for new developments and for products certification / qualification;
b. The technological advance in specific research areas.

Also with regard to the medical perspective multiple objectives were considered:

a. A contribution to a better knowledge in Congestive Heart Failure,
b. A support to the doctor for a better diagnosis and assessment of the health status of the patient through the availability of a rich set of aggregated information / data and the availability of advanced solution of signals and image processing for accurate features extraction;
c. The realization of a “continuum of care” and a person-centric healthcare able to prevent or at least to reduce the occurrence of degenerative trends.

The socio-economic assessment will assess the enhancement in quality of life of the patients and their informal carers (family members), the reduction in the overall healthcare costs, the level of acceptance of the solution by the patients and by the main stakeholders. Furthermore from an economic perspective we considered also the contribution given by CHIRON to the uptake of the e-health market and to the competitiveness of the European industry in such sector.
We will use a “societal perspective” in defining the economic effectiveness where we will include all the costs and benefits no matter who bears the costs and who receives the benefits.
On the basis of the outcomes of the overall assessment of the Project, the final section of this document is devoted to the compilation of a set of guidelines for further development.

The project' s objectives

Here below we summarize the objectives of the project as indicated in the Technical Annex:

Type	Description	Notes
A. *ARTEMIS JU HIGH LEVEL OBJECTIVES* *(as reported in the* section 3 of the ARTEMIS Annual Work Programme (AWP 2009))		
SCIENTIFIC & TECHNOLOGICAL OBJECTIVES	Reduction of the cost of the system design; reduction in development cycles, Reduce the effort and time required for re-validation and recertification after change	section 3 of the ARTEMIS Annual Work Programme (AWP 2009))
	Achieve cross-sectorial reusability of Embedded Systems devices developed using the ARTEMIS JU results	
	Reference designs and architectures that offer common architectural approaches for given ranges of applications.	section 3.1 of the ARTEMIS Annual Work Programme (AWP 2009))
	Create an open system architecture capable of seamlessly connecting heterogeneous devices and systems in widely dispersed domains (Cross domain connectivity and communication capabilities)	
	Seamless connectivity and middleware with : a. Resource management to ensure seamless connectivity, b. Dynamic adaptability to a changing environment	
MEDICAL OBJECTIVES	To move away from "health care" to "health management" i.e., from "how to treat patients" to "how to keep people healthy" "In this way Europe may optimize the use of its expenditure on healthcare, which is at present rising from a recent figure of about 8% of GDP – or about 600 billion Euro p.a."	sub-programme ASP2 (Person-centered healthcare management)
B. SPECIFIC CHIRON OBJECTIVES		
SCIENTIFIC & TECHNOLOGICAL OBJECTIVES	Design and develop new sensor nodes with enhanced features and proved networking capabilities	
	Develop high-speed electronics and embedded software for medical images processing and visualization for a fast and more accurate diagnosis.	
MEDICAL OBJECTIVES	Contributing in promoting a paradigm shift from diagnosis and treatment of patients based on symptoms to diagnosis of patients based on risk assessment of healthy persons.	
	Reduction in hospitalization, Reduction of the mortality in CHF class III patients,	
	availability of a larger quantity and variety of data for a better accuracy of the diagnosis and for the effectiveness of the therapy	
	Enhanced accuracy of the diagnosis through medical images	
	Introduction of innovative solutions in health monitoring at home	
SOCIO-ECONOMIC OBJECTIVES	Enhancement of the quality of life of the patients	
	Acceptance of the solution by the patients and by the main stakeholders	
	Reduction in the overall healthcare costs	

PART 1 – TECHNOLOGICAL AND SCIENTIFIC ASSESSMENT

CHIRON represents a complete, strongly integrated, multi-functional system; in our opinion the most important achievement of the Project's Team is not related to a specific component of the designed system, but rather to the overall outcome of the ensemble. The Group was able to develop a very complex system made up of several interacting components coming from a very wide range of disciplines: medical devices, telecommunication systems, data analysis and processing, imaging systems. The joint work of several scientists produced scientific, technological and medical results in multiple disciplines and an important effort was that devoted to the connection and inter-operation of different subsystems.

1.1 THE CHIRON ARCHITECTURE

The following diagram shows the CHIRON architecture:

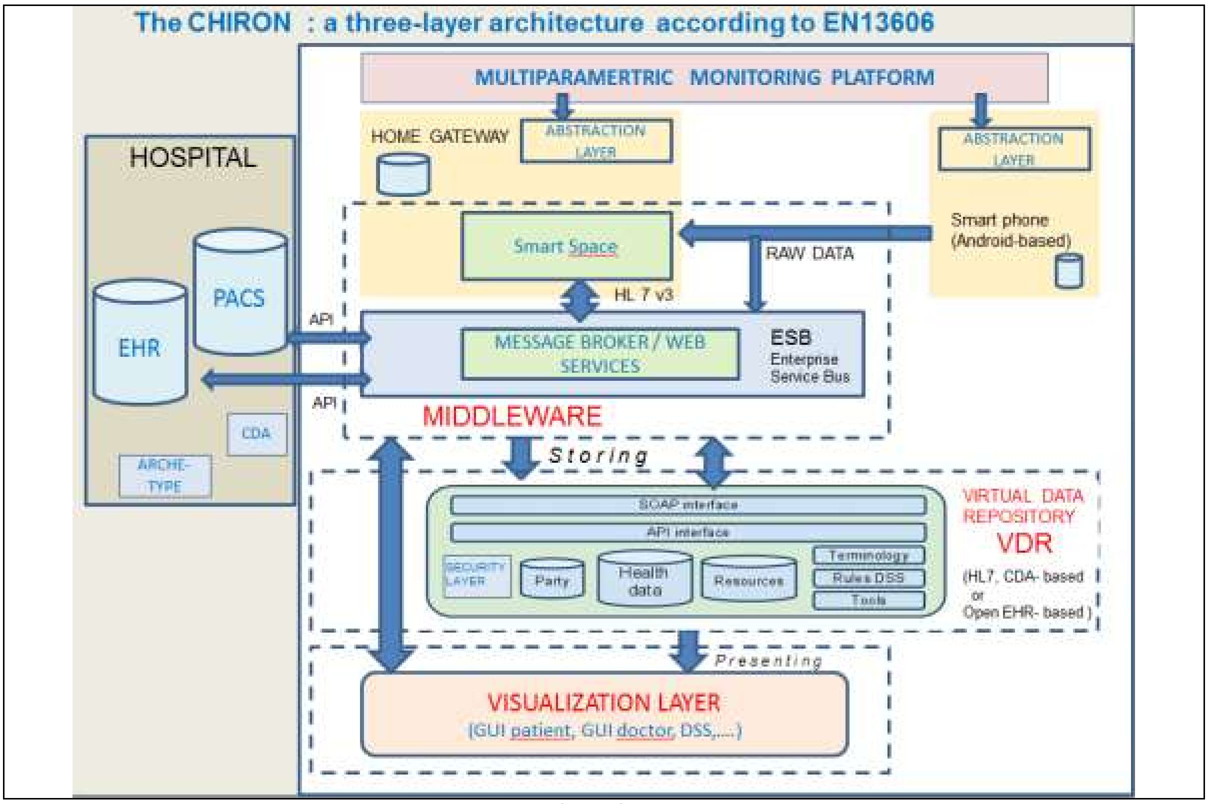


Fig. 1: The CHIRON architecture

It realizes the objectives of designing:

- *A reference architecture that offers common architectural approaches for given ranges of applications;*
- *Seamlessly connectivity of heterogeneous devices and systems in widely dispersed domains (Cross domain connectivity and communication capabilities)*

Due to the lack of an even de-facto standard, nowadays Wireless Sensor Networks rely on different and heterogeneous platforms and protocols, thus requiring a suitable abstraction layer to make them accessible.

Environmental sensors are based on different hardware/software solutions; on the other side, the monitoring of patient's vital parameters is demanded to specific commercial devices that are able to communicate via standard technologies (e.g. Bluetooth, ZigBee) being part of the so called Body Area Network (BAN). These devices cannot be integrated off-the-shelf in the CHRON architecture; for this reason we developed an abstraction layer acting as a bridge between the BAN and the CHIRON middleware (the Smart Space).
The Abstraction layer gets the data (physiological and environmental data) coming from different sources and hides the heterogeneity of their nature.
It exposes a generic device profile to the application layer and provides a standard mechanism to access data and services of heterogeneous networked embedded devices independently from the hardware of the nodes and from the specific solution adopted at network and communication layers.

The middleware used in CHIRON allows the interoperability between the home-based subsystem (user plane) and the clinical domain (medical plane).
The CHIRON architecture addresses issues such as:
- Integration of multi-source medical information;
- Heterogeneous nature of the sub-systems to be combined (different sensor networks) and integration of personal health into the clinical workflow;
- Different communication modes combined with each other (WiFi, Bluetooth, ZigBee, etc.) and all carrying high level healthcare protocols (HL7);
- Different types of data analysis, data repository and data access.

In such way the system ensures a continuum of care through clinical and non clinical settings (nomadic environments, people's homes). A common standard (HL 7 v3 based) for medical information exchange among the Chiron architecture layers and among interconnected devices was used.
A specific Knowledge Processor, "HL7 Observation Dispatcher", was developed. This KP in addition to the other KPs allows to Smart Space platform to:

- Collect and semantically organize information derived from the heterogenic sensors and devices network (User Plane);
- Automatically create HL7 v3 Observation codified using the standardized medical vocabularies LOINC and SNOMED;
- Automatically insert these HL7 v3 Observation in a complete HL7 v3 CDA R2 and send it to WCF Service.

The WCF Service (based on CDA R2) successfully connect with a Virtual Data Repository (VDR) (designed according to OpenEHR standard) thanks to an additional module that automatically and bidirectionally translate HL7 v3 CDA R2 Observations in OpenEHR Compositions (HL7 v3 CDA R2-OpenEHR converter).
In particular, this converter is a WCF Service which is called by Smart Space to update the VDR content or by HL7 Web Service to present all observations stored in VDR via HL7 v3 CDA R2.
This solution allows to present all information stored in the VDR in both approaches indicated in EHR.com standard: openEHR and HL7 v3 CDA R2.

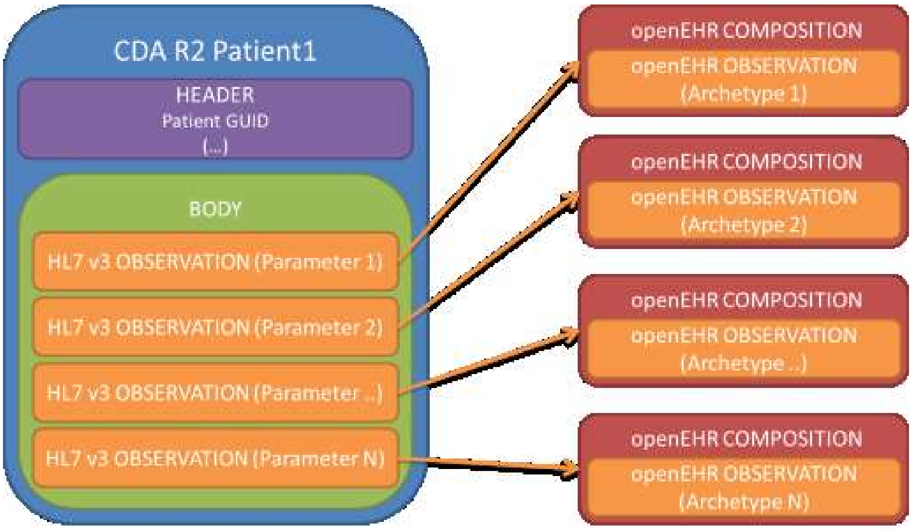


Fig. 2: HL7 v3 CDA R2-OpenEHR Converter: from HL7 v3 Observations to openEHR Compositions-Observations

This represents also the contribution of CHIRON to the achievement of another ARTEMIS JU objective:

to reduce the cost of the system design and of the development cycles through standardization and even through the adaptability to different standardized options (in our case CDA R2 and openEHR both HL7-based). CHIRON realized a 100% standardised system using both HL7 v3 CDA R2 as well as openEHR archetypes approaches. The openEHR based archetype (the information model used in CHIRON to collect and show all data) was the result of a continuous cooperation between the ICT system architects and the medical professionals of the CHIRON Consortium.

The SmartSpace middleware is ready to be integrated within the Landscape Reference Architecture proposed by the Healthcare Services Specification Program (HSSP) as Health Record Management Service. It realizes the main objective of HSSP i.e. to use SOA approach to provide and guaranty an effective interoperability between applications and distributed and heterogeneous devices, which belongs to independent socio-health system organizations.

The adopted middleware, the SMARTSPACE (SS) was developed in another ARTEMIS project (SOFIA, call 2008) for applications in domains other than the healthcare one; its adaptation and use in CHIRON represents the result of a co-operation the CHIRON Consortium established with other European Projects.

Once again it is an example of the multi-domain compatibility, interoperability and even communality the ARTEMIS strategy is realizing by promoting

"cross-sectorial reusability of Embedded Systems devices developed using the ARTEMIS JU results".

Multi-domain interoperability is highly important in the CHIRON solution: in a person-centric healthcare approach – such that fostered by the European Commission and among the key objectives of the CHIRON project – healthcare services have to consider the citizen as a person more than simply as a patient and to take into account information, situations, behaviors, contexts of his/her daily life even if apparently outside the specific "health" and "wellbeing" domains.

The “reusability” of the CHIRON research work in other application domains has a clear proof in the solutions developed for the “management of heterogeneous and multisource information” . By partially using the outcomes of the CHIRON work, WLAB created DISSense, a novel and open source energy efficient collection protocol that was successfully used in a testbed for monitoring the construction of a new tunnel of the new B1 line of the Rome Underground.

CHIRON makes use of a semantic approach in the management of the huge quantity of data and knowledge exchanged among the different layers of the CHIRON system. We developed congestive heart failure (CHF) ontology that represents a precise and upgradable representation of the Heart Failure domain and a useful framework for building knowledge based systems in the HF domain, as well as for unambiguous communication between professionals.

The proposed HF ontology was derived by using the work done in a previous European project (Heartfaid project of the FP6 Program (IST-2005-027107)[1]) and was implemented by using Ontology Web Language (OWL) and Protégé editing tool. Once again an example of continuity and synergic integration in the research work promoted by the European Commission.

The CHIRON project addressed also an objective of another Artemis sub-programme, the ASP5 (Computing environments for embedded systems) and more specifically the objective of

“enabling massive, real time data processing in multiple domains (image processing, signal processing, etc.)”

In CHIRON a key aspect is the integration between personal healthcare (home-based and nomadic scenarios) and the clinical workflow, between personal information / data captured at home and the “medical” information generated in a clinical setting and included in the Electronic Health Record, between value-based data and alphanumeric information and medical images (acquired on real time or stored in the hospital PACS system).
In CHIRON a correlation is established between the monitoring at home and the medical imaging chain in the hospital (see figure 2): the imaging modality can indicate which functions/parameters should be measured by sensors on the patient for the monitoring at home and the sensors can generate alarm and define more precisely what to look for at the hospital with the medical imaging chain.

[1] It was developed by the Ruđer Bošković Institute and published in http//lis.irb.hr/heartfaid/ontology/ and originally it was requested by Stanford University Medical Center for research in the study on risk factors for CHF.

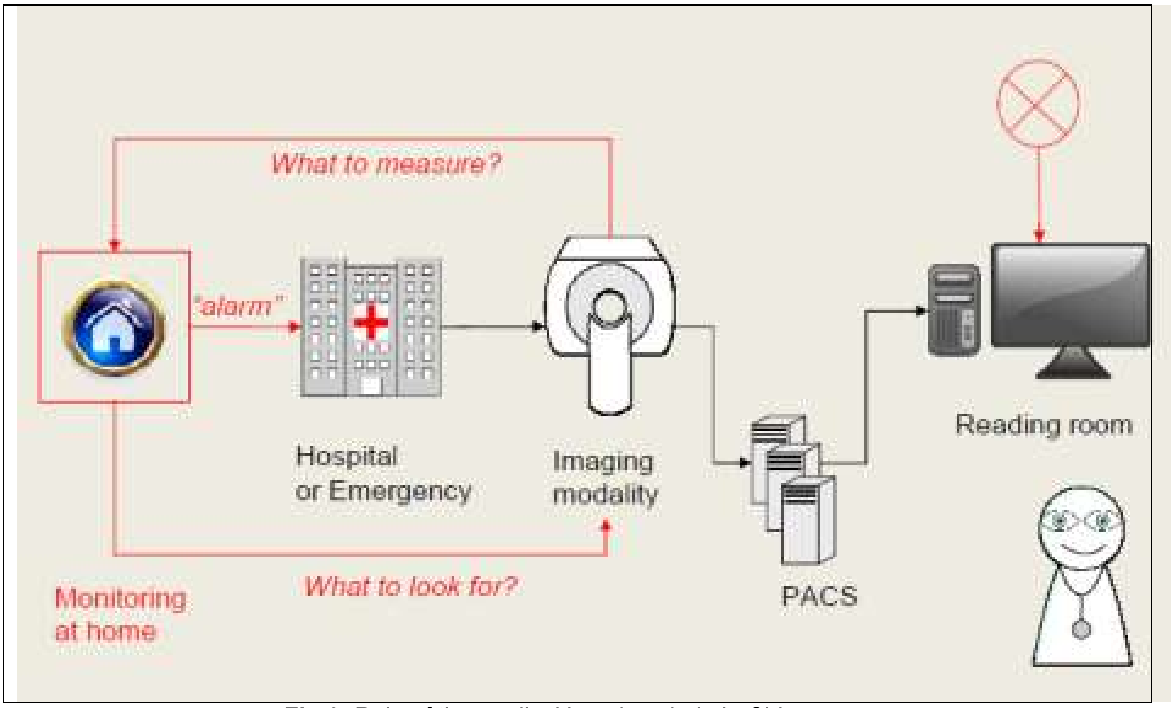


Fig.2: Role of the medical imaging chain in Chiron

Integration of medical images with EHR data was realized also in the cathlab environment of the hospital to combine previous and relevant patient's data (EHR) with the images of the X-ray system.

Furthermore CHIRON succeeded in making the first attempt to support a knowledge-based healthcare system integrating past and current data of each patient together with statistical data related to the whole community. It was done by developing the LITERATURE SEARCH module. It allows doctors to search automatically contents of different publications to get support for a more accurate and knowledge-based diagnosis. The module generates summaries in a semantic context and allowing doctors to get answers to complex questions. It works on plain text, extracting the relevance of certain medical paper using Medical Subject Heading (MeSH) codes and summarizes the publication's content into a few annotated sentences using Natural Language Processing (NLP) techniques.

The CHIRON architecture succeeded in matching other two ARTEMIS JU objectives:

a. "resource management to ensure seamless connectivity",
b. "dynamic adaptability to a changing environment".

"Resource management to ensure seamless connectivity"

In contrast to the typical architectures and keeping in mind the energy constraint of a sensor node, specialized low-complexity algorithms were developed for on-board signal denoising, artifact removal, intelligent classifier and feature extraction for each of the electrophysiology sensors without compromising the medically trustworthiness quality of the captured signals.
Focus was on adaptive energy management and harvesting capabilities in the sensor networks, ultra low power architectures and protocols.
CHIRON succeeded in the design and realization of innovative, autonomous, efficient, secure, long lasting sensor networks, able to draw energy from the environment and optimally use it through accurate energy prediction models.

1.2 OTHER TECHNOLOGICAL ACHIEVEMENTS

1.2.1 NEW SENSOR NODES WITH ENHANCED FEATURES AND PROVED NETWORKING CAPABILITIES

Energy harvesting, power management, local processing and local storage capabilities, privacy/security provisions realized at BAN level are among the features of the advanced sensor nodes developed in CHIRON.

The CHIRON sensor platform is the first attempt of integrating all necessary physiological sensors into a single non-invasive wearable package.
Furthermore we succeeded to integrate all required signal processing routines – together with friendly user interfaces - into a smartphone application.

The validity of the CHIRON research work in the area of m-health was recognized by the award of Bluetooth "App of the Month" assigned by Bluetooth SIG Organization to Mobilis SenseView solution that shares same roots with CHIRON eHealth mobile application; more than 50 different *Bluetooth*®, Bluetooth Smart technology and internal sensors can be connected to SenseView.

Main achievements of the CHIRON project were:

A. Energy harvesting and power management

- New protocols for data gathering in sensor networks that use adaptive duty cycle and data aggregation (One of the two protocols was implemented on sensor nodes and tested on a real test-bed).
- Accurate energy prediction models to estimate the variable energy intake of energy harvesting equipped wireless sensor nodes, as a needed step towards global system optimization.
- Smart Battery Device using solar and piezoelectric harvesters.
- Integrated Temperature / Sweat Index Sensor module **with very low power consumption** in both active and sleep mode (average measured power consumption of the complete system is less than 150nW for a measurement rate of 10 samples/s which is one of the lowest power consumption compared to the state-of-the-art).

B. Advanced wireless communication and monitoring

B1. A new area of research and technical development of Bluetooth Low-Energy standard 4.0 (BLE4) resulting in the development of new types of services and new ways of monitoring environment and patient's' activities. Based on BLE4 an advanced solution for positioning and ambient environmental monitoring was developed by INTRACOM; it allows an accuracy even better than that achievable with RFID tags while maintaining similar power consumption (i.e. operational time measured in years).

B2. Data Security and privacy

- an extremely fast ECDSA implementation for sensor node and a framework exploiting harvested energy, energy prediction and precomputation of cryptographic primitives to significantly increase the number of digital signatures that can be performed per day;

- an extremely powerful fine-grained data-centric access control mechanisms based on multi-authority Ciphertext Policy Attribute Based Encryption (CP-ABE);

- New algorithms for traffic analysis attacks in wireless body area networks;

c. ULTRA LOW ENERGY FEATURE EXTRACTION ALGORITHMS

It is envisioned that the methodologies developed in CHIRON – even if focused on ECG - can be applied in the analysis of additional physiological signals and can provide novel processing techniques for the extraction of critical medical information. Furthermore, the knowledge on designing low-complexity algorithms, acquired under CHIRON, will facilitate the development of ultra-low power, application-specific wireless sensor platforms where all data processing takes place in application specific integrated circuits (ASIC). This novel approach in wireless sensing differentiates from the traditional approach of employing general purpose microcontrollers, which are much more energy demanding, for processing and is expected to play a key role in future technologies (e.g. internet of things, cloud computing) that will be part of next-generation healthcare systems.

- Algorithms for the analysis of the ECG Signal (FALCON module)

the ECG signal is automatically positioned into individual heartbeats and the ECG fiducial points are extracted from every single heartbeat, in a process known as ECG delineation; subsequently every medical ECG parameter (QRS-duration, R-R interval, PQ-interval etc...) can be calculated.
The innovative aspect of FALCON is its hybrid nature, where time-domain and frequency-domain signal processing techniques are combined to produce a low-complexity feature extraction algorithm. The performance of FALCON was evaluated against the state-of-the-art ECG delineators using ECG samples from publicly available databases (QTDB and PTBDB in Physionet). The obtained results reveal that FALCON achieves a comparable level of accuracy with the state-of-the-art delineators and satisfies the CSE (Common Standards of Electrocardiography) tolerance limits when tested in standard 12 lead ECG databases. On the other hand by analysing the computational complexity of FALCON , it requires approximately 8 times less mathematical operations (additions, multiplications, etc..) than the state-of-the-art ECG delineators. This particular feature renders it ideal for low-power VLSI implementation, facilitating the continuous CVD monitoring scenario demand for low-power signal processing. In addition the FALCON algorithm is augmented by a lossless compression scheme, implemented in parallel, which minimizes the amount of ECG data that need to be stored.
To develop FALCON we explored Independent Component Analysis (ICA) method for denoising and artefact separation and Wavelet Transform and in particular its discrete counterpart (DWT) for the analysis of the ECG. The FALCON algorithm package, developed under CHIRON for the real-time feature extraction of ECG parameters is heavily based on the DWT.

The DWT also served as the basis for the formulation of an algorithm for the automated calculation of the Selvester QRS score from the ECG signal.

- Algorithm for the arrhythmia prediction

It employs phase-space reconstruction techniques in order to study the level of synchronization of the ECG signal and from there attempt to predict the onset time of life-threating arrhythmias.

- An integrated system for inferring the user's-patient's activity and calculating the equivalent metabolic energy during activities.

The system – developed by JSI - won the EvAAL Competition with a final score of 8.36, the highest score achieved by any competitor. Evaluation criteria included Accuracy, User Acceptance, Recognition delay, Installation complexity and Interoperability with AAL systems. The solution by JSI was accurate and had a low recognition delay, uses accelerometers integrated into clothing which the evaluators considered user-friendly, and is open-source.

1.2.2 MEDICAL IMAGES PROCESSING AND VISUALIZATION

One of the objectives of the CHIRON project was to develop

high-speed electronics and embedded software for medical images processing and visualization for a fast and more accurate diagnosis.

We succeeded in achieving this result by realizing:

- solutions for computer aided analysis of medical images allowing a first, automated detection of suspicious regions and
- new, advanced visualization solutions and medical display calibration methods.

Moreover – as mentioned in the section 1.1 – the integration of the imaging chain into the overall CHIRON architecture was realized too.

A. IMAGE PROCESSING

Main achievements in the image processing area were:

- A framework for cardiac scar detection and segmentation in MRI
- Elasticity analysis on US3D images to differentiate patients

1) Technique for near-automated segmentation of Cine Cardiac Magnetic Resonance Images

- Comprehensive segmentation of both RV and LV cavities by means of the same algorithm
- 3-Dimensional segmentation for higher accuracy
- Multiscale approach for higher computing speed
- Technique initialization limited to the positioning of two seed points in the first frame
- LV and RV volumetric curves estimation without further processing

2) Elasticity analysis on Ultrasound 3D cardio images

The strain analysis of cardiac tissues from 3D ultrasound images through speckle tracking was an extremely important achievement. It was the result of a cooperation between an Engineering Team from the University (the University of Bologna) and a Medical Team (the Policlinico Umberto I of the University La Sapienza of Rome) and the validity of the achieved results is demonstrated by the decision of La Sapienza University of Rome of funding a 3-year research project on this topic to continue the activity done in CHIRON.

B. VISUALIZATION SOLUTIONS

Generated innovations:

3) HDR display and image processing

- New grayscale mapping,
- New high brightness backlight based on matrix color LEDs and combined optical stack[2],
- Real-time image processing implementation on multi core CPU and GPU based on OpenCL,
- Methodology to drive multiple layers image sources: dual LCD and matrix backlight,
- Modeling of multi layer displays to control alignment, parallax and veiling glare.

4) Solutions for enhancing subtle details in mammographic images *("Virtual Moon")*

The virtual moon is a solution for enhancing subtle details by highlighting a region of interest on the screen. By doing that the observer will locally optimize his perceived contrast by adjusting his white point to the maximum white point in the area is looking.

5) **Personalized display GSDF calibration** in mobile applications (i-pad calibration) and in stationary applications where personalized GSDF calibration methods adapted to the age and the vision capability of the user were introduced.
The iPad application developed by BARCO calibrates the display of the tablet PC according to the DICOM standard to allow the review of medical images. The application is now available on the Apple store and can be downloaded for free. The iPad was approved by the FDA.
Barco was the first and only medical display company to launch an iPad application for the calibration according to GSDF DICOM standards of commercial tablets PC.

6) New dynamic QA checks for medical displays,
A database has been constructed with medical thorax images in which nodules are inserted. To do it a software tool was developed to simulate the properties of real life nodules such as the correct contrast, diameter, luminance function, position, etc.

7) Tracking of displays in the hospital and "personalized and task-oriented calibration"
Near Field Communication and Bluetooth technologies were used for medical display localization and user identification to realize customized calibration of the display.

---

[2] The results of the work on the new direct led backlight will be used also by Barco and FIMI in the new generation of high-end medical displays for the primary diagnosis market.

C. OTHER ACHIEVEMENTS

8) **Integration of X-ray and Ultrasound images**

The solution represents the world-first solution helping interventional cardiologists and cardiac surgeons to perform minimally-invasive structural heart disease repairs by providing an intelligently integrated view of live X-ray and 3D ultrasound images. The product (the Philips EchoNavigator) was already introduced in the market and got the FDA approval.
CHIRON contributed to the development of the product (at least for an estimated 25%).

9) **Integration of patient's data with medical images** in the cathlab environment of the hospital.

All these solutions have been validated in terms of clinical added values (see section 2).

PART 2 – MEDICAL ASSESSMENT

INTRODUCTION

CHIRON aims at contributing in promoting a paradigm shift from diagnosis and treatment of patients based on symptoms to diagnosis of patients based on risk assessment of healthy persons. This is in line with the ARTEMIS JU objective in the Sub-Programme ASP 2 (Person-centered healthcare management):

"to move away from "health care" to "health management" i.e., from "how to treat patients" to "how to keep people healthy" In this way Europe may optimize the use of its expenditure on healthcare, which is at present rising from a recent figure of about 8% of GDP – or about 600 billion Euro p.a."

In currently applied healthcare practice, a disease is commonly discovered after symptoms have emerged. Only then, people become patients and apply for medical care; a diagnosis is made and a treatment is proposed and initiated. As shown in the graph below, diagnostic equipment (e.g. X-ray imaging) are employed at a certain state of progression of a given disease.

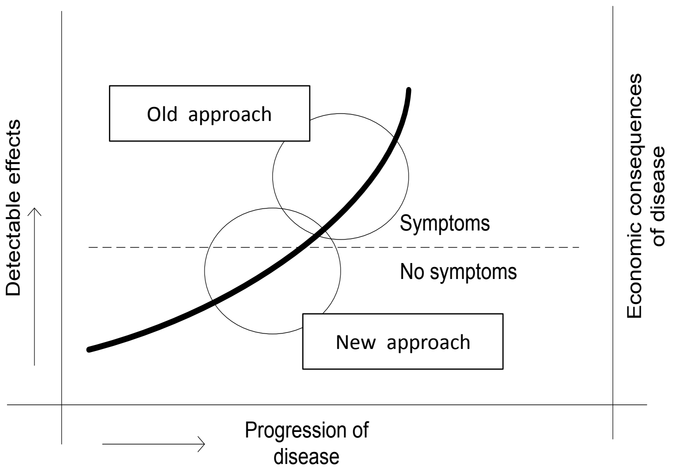


Fig. 3: A shift from diagnosis and treatment based on symptoms to diagnosis based on risk assessment of healthy persons

On the contrary diseases need to be detected earlier and subsequent diagnosis and treatment need to be carried out earlier. Obviously, the benefit will be better quality of life and, on a global scale, a more healthy and cost-effective economy

Monitoring programs, screening plans or regular check-ups help to detect diseases in an early stage, before symptoms have occurred.
To be effective these approaches need to provide accurate information i.e. to provide early detection and – at the same time – to avoid an excessive percentage of "false negative" causing useless further studies and to avoid additional costs.
CHIRON aims at contributing to this new approach in healthcare.

CHIRON contributed to the achievement of this medical objective in three ways:

a. By providing innovative ICT-based solutions for a continuous, unobtrusive monitoring of the patient (prevention),
b. By supporting the doctors with advanced tools for diagnostics, treatment planning and intervention,
c. By enriching the medical knowledge in the area of Congestive Heart Failure (CHF) and more specifically in the identification of early indicators of degenerative trends.

It is important to notice how all the research work in CHIRON was driven by the "medical needs" with the two Medical Partners and the "medical members" of the CHIRON Scientific Advisory Board playing a fundamental role in this regard.
It was a key commitment of the project to avoid the typical risk of all the research projects in the area of e-health i.e. to be "too technologically driven".
The innovative solutions developed in CHIRON not only represent an advance in the area of Computer Science and Information & Communication Technology but have all a "clinical validity" verified with an accurate and intensive experimentation.

2.1 MEDICAL BENEFITS OF THE CHIRON SOLUTION

2.1.1 INNOVATION IN REMOTE PATIENT MONITORING

A. An integrated, unobtrusive multi-sensorial platform

Most of the state-of-the-art ambulatory ECG modules use conventional "wet" ECG sensors. For data sampling and wireless transmission, they use either existing standard wireless interfaces or general-purpose wireless sensor nodes. This combination results in many system-level drawbacks such as big form factor, low transmission speed, short battery lifetime and lack of "wearability".
Wearable 1 lead ECG meters are available in the market but key issues remain in terms of accuracy and "medical validity" of such solutions outside a generic application for wellbeing or fitness.
The CHIRON solution incorporates an appropriate set of advanced techniques resulting in an unobtrusive and "medically reliable" device for the remote monitoring of patients with cardiac problems. Tests of the ECG module performed outside the hospital, at home, during physical exercise and during a marathon demonstrated that the chest strap recordings has excellent sinus rhythm visualization and a negligible number of artifacts. At the same time it is unobtrusive and with low power consumption: when transmitting real-time ECG (at 500Hz), the entire system runs continuously for 10 hours on a 450mAh Li-Po battery and when saving ECG data the autonomy is about 100 hours.
A comparison with holter ELA as gold standard equipment shows how the module (hardware and feature extraction algorithms) allows to detect reliable QRS complex and has very good results in terms of R peak detection. A negligible number of artifacts and comparable results for the analysis of HRV parameters were obtained, allowing to gain high correlation values around 98% (further analysis is in progress).

B. Measurement of serum potassium concentration in the blood from the ECG

The ECG effects of potassium are well known since many years: the earliest electrocardiographic manifestation of hyperkalemia being the appearance of narrow-based, peaked T waves.

Nevertheless, qualitative evaluation of ECG changes for the diagnosis of potassium level resulted in poor sensitivity and specificity whereas, in spite of preliminary positive observations, quantitative measurement of the height of T waves did not correlate with K, even if normalized to QRS. In the subsystem designed in CHIRON we looked for an amplitude-invariant measurement of the sharpness of T-wave, the ratio of the T wave slope to amplitude (TS/A) and we developed an algorithm to estimate blood potassium concentration [K+] from automatic measurements of TS/A.
The measurement of the serum potassium concentration in the blood by using the ECG signal is a completely innovative research that could have a strong impact for the diagnosis and treatment of several pathologies including, for example, cardiovascular diseases and chronic kidney diseases. Nowadays, the only available measurement for serum potassium is laboratory-based through blood samples; consequently this measurement is not real time, it is invasive and requires the presence of expert personnel.
Within the treatment of patients with acute and chronic heart failure, maintenance of normal potassium homeostasis is an important clinical requirement. In these patient populations, mortality and morbidity can be reduced by the administration of drug therapies that modify potassium homeostasis. These therapies based on pharmacological agents may improve clinical outcomes and, at the same time, enhance the risk of potassium-related adverse events. Consequently, adequate monitoring of serum potassium level should be performed to control the benefit and risk of drug therapies. Therefore, a noninvasive monitoring of serum potassium would be of great importance and useful especially in patients already undergoing specific monitoring, including home monitoring using wearable devices for ECG acquisition.
The main innovative aspects of the measurement of the serum potassium concentration in the blood by using the ECG signal rely in real-time and non-invasive monitoring of patients at risk for hyper- and hypo-kalemia which are among the main risk factors for cardiac arrhythmias as well as being indicators for worsening of heart or kidney conditions.

2.2 SUPPORTING DOCTORS IN DIAGNOSIS AND TREATMENT PLANNING AND INTERVENTION

A. Enhanced visualization solutions for a more accurate diagnosis

We reported in the Section 1 of this deliverable the CHIRON innovations in the area of visualization of medical images. It was a precise task of the project to validate their medical validity by involving the doctors. A clinical study based on real medical images was performed to evaluate the clinical benefit of the High Dynamic Range Display vs a Low Dynamic Range Display. Results show how in the detection of difficult and very difficult nodules, the High Dynamic Range makes definitely the difference in terms of detection and productivity (search and detection time).

Furthermore the project allowed to gain notions about the characteristics of the human visual system (HVS) and about the theoretical and practical characteristics of the clinical environment where diagnostic imaging equipment is used. These notions are the basis for the ongoing study about models for the HVS, in cooperation with foreign universities and research centers, and for their exploitation in determining suitable properties for advanced medical displays.

B. Advanced solutions in the cardiovascular intervention

The best achievement was the integration of live 2D X-ray and live 3D Ultrasound images based on a 2D/3D registration algorithm. Based on this integration, a prototype application has been built to support structural heart disease procedures. The research work performed in CHIRON was the basis for the development of the Philips “EchoNavigator.

Validation tests with positive results were executed in the hospitals of Denver, Zurich and New York.

2.3 ENHANCING THE MEDICAL KNOWLEDGE WITH REGARD TO CHF

New insight with regard to CHF class III was acquired.
A survey involving doctors and cardiac experts allowed to identify a list of 67 parameters as potential indicators of the health status and of the risk profile of the CHF patients.

In the context of personalized Medicine the CHIRON's objective was the collection of simple but high quality data, from heterogeneous sources, that could improve the knowledge of CHF and therefore the effectiveness in diagnosis and therapy. However, there were many questions about which markers are diagnostic, prognostic, or pathologic and there was a lack of medical knowledge with regard to the impact some of the monitored parameters could have in the evolution of Congestive Heart Failure.
This uncertainty was also confirmed by the lack of consensus in the answers given by Opinion Leaders in Cardiology to the above mentioned Survey conducted by the CHIRON Project[3].
For this reason the CHIRON Consortium decided to replace the originally planned "randomized clinical trial" with an "observation study". In fact a RCT with the sufficient power to disclose outcome differences (treated vs untreated) should involve hundreds (or thousands) patients for several years and this was beyond the budget and the timeframe of the project.
On the contrary an Observation Study was judged useful to provide the missed knowledge by catching the relationship between the simple parameters looked for continuously by CHIRON system and outcome.
The CHIRON Observation Study was executed in Italy and in United Kingdom.

CHIRON could offer a potentially new paradigm for risk assessment at short- and very-short- term in CHF patients based on concomitant measurements of several parameters just around the patient to foresee in advance changes in well being or keeping of an healthy status.

Due to the limited number of involved patients and the relatively short length of the experimentation, the outcomes will not allow to get statistically relevant data and arrive at firm conclusions but in any case will give qualitative indications and useful information on the potential benefits of the CHIRON solution.
Furthermore the Observational Study allowed to understand

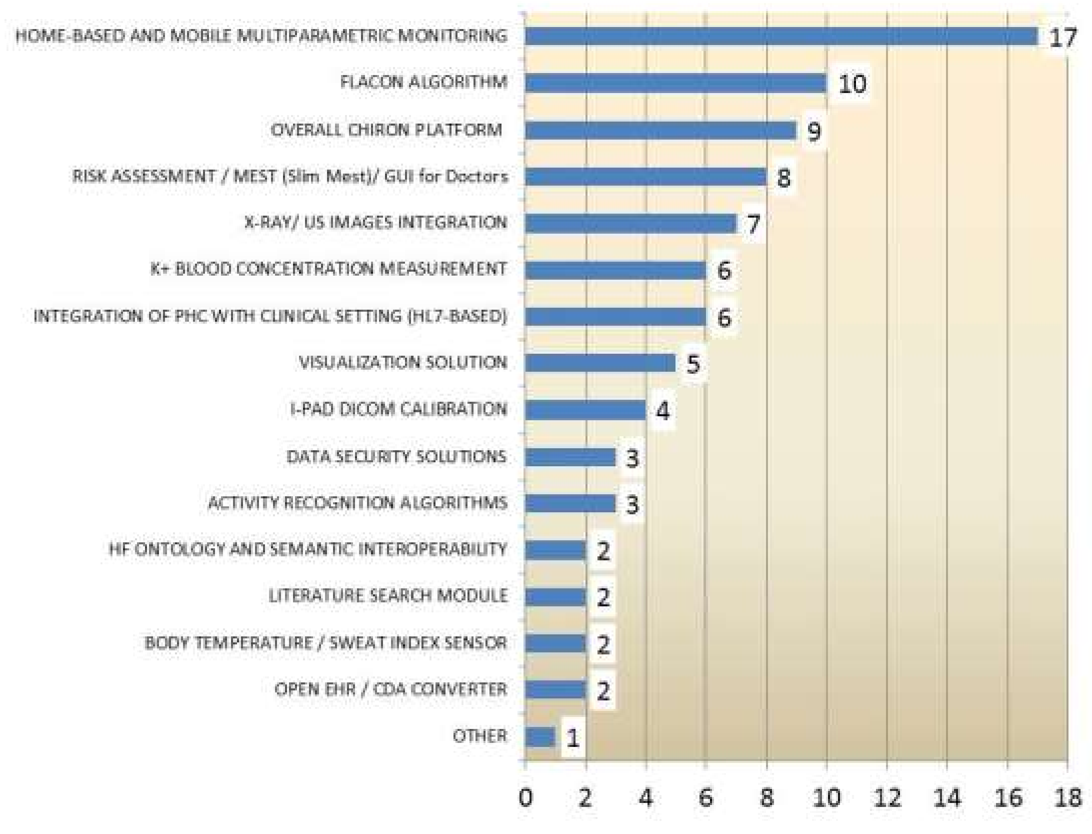
- Patient acceptance of tele-monitoring including wearable sensors and smart phone;
- Medical feasibility of long-term monitoring including its seasonal variability;
- Relevance and long-term variability of the measured parameters (ambient and skin temperatures and humidity, daily systolic blood pressure and electrocardiographic variables including QT, heart rate and QRS duration along with metabolic equivalents, all assessed by specific activities of the patients);

[3] We built a list of potentially critical parameters having a possible impact on CHF (NYHA class 2 or above); the panel of Cardiologists was requested to rank the relevance of the information.

- Medical impact of short term changes of these parameters and their short-term relationship with the perceived wellbeing of the CHF patient;
- Potential modification of the “standard” approach of assessing long-term risks in CHF patients in favor of a short-term time-varying approach in which closer to the patient monitoring might present a central paradigm.
- Medical perspective of the obtained information in the CHIRON Observational Study in the context of the presently available information in this highly technological and multidisciplinary domain, in order to look for potential, future implementations also for different case studies.

2.4 SELF ASSESSMENT

The CHIRON Partners were requested to select the three more innovative solutions generated by the Project; the result of this self-assessment is reported in the following graph:



Other includes: Integration of images with EHR data, SCAR MRI analysis, Heart tissue elasticity analysis, Bluetooth Low Energy-based Localization system.

Fig.4: Best innovation in CHIRON – Self assessment of the Consortium Partners

PART 3 - SOCIO-ECONOMIC ASSESSMENT

INTRODUCTION

The CHIRON project was developed by having in mind the interests of all the involved stakeholders: the patients in the first place, their families, the doctors, the National Health Service and the overall community and the industry and the business community. The objective was to include and harmonize the interest of all of them by bringing benefits to the whole chain.

Fig. 5 : Addressing the interests of all the stakeholders

As highlighted by some reports[4] these requirements are sometimes different from each other:

- ✓ citizens generally want fast, safe and effective delivery of health services at reasonable cost; additionally continuous home health monitoring is required to be as unobtrusive as possible to achieve a high acceptance rate;
- ✓ administrations might want safe, efficient and measurable delivery of health services at lowest possible cost;
- ✓ care professionals might seek assistance to deliver safe and effective delivery of health services regardless of the cost.

Also industrial players have sometimes different objectives with regard to standardization, interoperable systems vs proprietary systems.

[4] See – as an example – the " e-health INTEROP Report- Phase 1" issued by CEN/CENELEC/ ETSI in February 2009

3.1 PROVIDING BENEFITS TO THE PATIENTS AND TO THEIR FAMILY MEMBERS

The objective was to bring tangible and intangible benefits to the main stakeholder of the healthcare process i.e. the patient and indirectly to his/her family members.
Tangible benefits are clearly related to his/her physical health status and to the reduction of the costs and the burden for the patient and the family caused by the disease.
Intangible benefits are linked to the “quality of life”, to the reassurance of the patient, to the “peace of mind” of the family members.

3.1.1 TANGIBLE BENEFITS

Reduction in hospitalization

CHIRON aims at preventing the occurrence of degenerative episodes and in such way to reduce the need of hospitalization in patients suffering from chronic diseases and in any case to reduce the days of hospitalization.
One of the main advantages of Remote Monitoring is represented by the availability of continuous rather than sporadic data to enhance understanding of the dynamic disease state.

Reduction of the mortality in CHF class III patients

Mortality in CHF is related to the severity of the disease, in turn related to the severity of left ventricular dysfunction (which might be assessed by left ventricular ejection fraction by imaging techniques, also relatively non-invasive). If one concentrates on class III a high proportion of death (>40%) might be anticipated in 12 months, particularly in the elderly population.
The goal of CHIRON is to contribute to reduce this percentage.

Reduction of the burden and costs for the patient and his/her family

The benefits are linked to the reduction of the lost working days (both for the patient and the informal carers), to the reduction of the frequency of the transfers to the clinical centers for hospitalization or for medical checks. We will analyze them in the section related to the socio-economic assessment of the project.

The lack of medical knowledge with regard to the impact some of the monitored parameters could have in the evolution of Congestive Heart Failure obliged the Consortium to change the approach of the “medical assessment” of the project from the originally planned “clinical trial” to an “observation study” intending to provide such knowledge.

No special intervention was executed during the observational study other than those already planned in the therapeutic program of each patient participating to the study; the doctors analyzed the data on a periodic basis and only for the patients for which an *“event”* (e.g. unscheduled office visit, urgent care visit, emergency department visit or hospitalization) occurred[5] or when a worsening of the health status (“today vs. yesterday”) was perceived by the monitored patient (*“surrogate event”).*
Due to the missed intervention and to the “a posteriori” analysis, the study was not powered to detect a clinically-meaningful reduction in all cause mortality and cardiovascular hospitalization but the results were intended to provide very useful information for the design of a later multicenter study powered to do so.
The study is peculiar since it monitors newly envisaged parameters (among them humidity, both on skin and ambient, patient movements and location, derived potassium levels) in addition to more

[5] We did not report any of such events in the patients participating to the observational study (both in UK and in Italy).

standard ones such as ECG whose interpretation is however receiving a fresh look in both time and frequency domains. These parameters are closely interplayed since one major issue is integration to look for very short signals of outcome in monitored patients.

In this new approach (where we missed the early intervention as a countermeasure to a detected situation) the "medical validation" did not allow to make a comparison between "CHIRON-based treatment" and "conventional treatment" and to assess the "tangible benefits" of the remote monitoring.

For them we have to take for granted the outcomes of similar, recent analyses reported by the literature.

3.1.2 INTANGIBLE BENEFITS

In the CHIRON project we devoted a lot of attention to the "intangible benefits" of patients and family members.

Acceptance of the solution by the patients and by the main stakeholders

The acceptance of new technological solutions by the users (mainly if elderly persons) is not so obvious; It is often linked to the perception of the benefits they bring; the unobtrusiveness of continuous home-based monitoring solutions has a high impact on the overall acceptance. Moreover concerns about privacy and personal data security could be a serious obstacle.

Enhancement of the quality of life of the patients

The patient is at the centre of the health system; he is the master of his/her health status, rehabilitation, and care plan and can rely on a continuous medical and psychological support from physicians, caregivers and the overall community. He/she will get reassurance by knowing that his/her health is under continuous monitoring.
Quality-of-Life (QOL) is a subjective, psychosocial index used to evaluate the wellbeing of individuals: it is a general term summarizing the main aspects of one's life and focusing on his/her overall health. It is calculated by using surveys; in healthcare the indicator of "Health-related Quality of Life (HRQOL)" was introduced[6]
During the CHIRON Observational Study Quality of Life assessments at baseline, 3, 6 and 9 months were measured.

A. Acceptance of the CHIRON solution

Various meetings were organized with the users to verify the "acceptability" of the CHIRON system and of its approach. The discussions with the patients was focused on four main attributes:

a. the perception of the usefulness of the solution,
b. the size of expected improvement of the health status as a result of the use of the CHIRON applications,
c. the confidence on the robustness and reliability of the solution,

[6] Popular tools of Health-related Quality of Life (HRQOL) are the following ones:
- Short form health survey (SF-36) (1993),
- Sickness Impact Profile (1975),
- Symptom States Scales such as the Faces Pain Scale (1988), the Fatigue Scale (1993) or the
- Functional Independence Measure Scale (1987).

d. the concern about data security and privacy.

The following diagrams show the results (the judgment of the users was in a scale of 1 to 5 with 1= poor judgment and 5= excellent judgment); for the “acceptance” attribute we involved also the doctors and the graph reported here below shows the differences in the received answers.

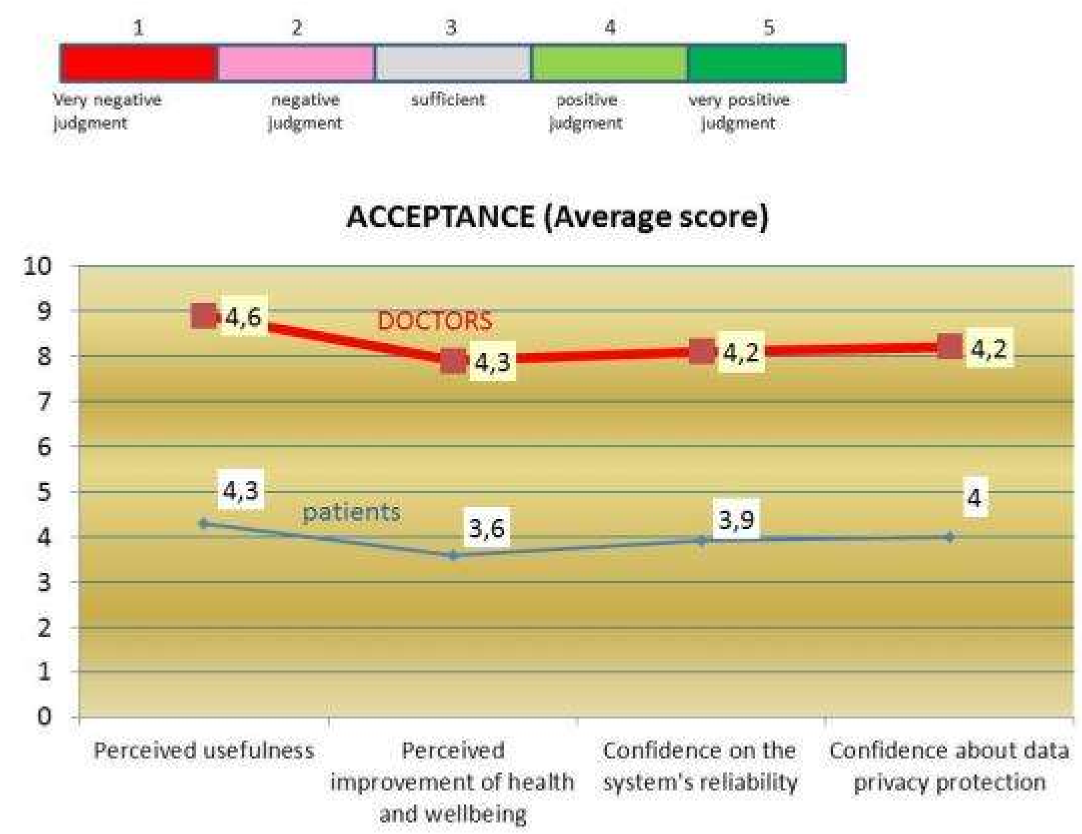


Fig. 6 : Acceptance of the CHIRON solutions

We took into consideration the four main factors building the acceptance i.e. the perceived usefulness, the perceived improvement of the health and wellbeing, the confidence on the reliability of the system (i.e. the accuracy of the measurement of the monitored parameters and a low incidence of false positive or false negative), the trust on the capability of the system to protect the collected data and the privacy of the user.
In all the four parameters the judgment of the primary users was positive (between 3.5 and 4.5) and it is interesting to notice how the medical professionals (the secondary users) expressed a better judgment in all the 4 parameters (from 4.2 to 4.6).

<u>During the Observational Study both in Italy and UK the Medical Partners coordinating the study noticed “ a total acceptability of close to the patient monitoring even for relatively long time spans,</u>

going well beyond the expectations and the state of the art in the domain of telemedicine and e-health”[7].

All patients enrolled in Italy were extremely happy with the CHIRON systems and their families communicated, during follow-up visits, a high level of acceptability and confidence also in cases of relatively low social status.
Most probably the good level of acceptance achieved by CHIRON is justified by the usability of the system that was very well appreciated by the users as indicated in the following diagrams. We differentiate the judgment related to the overall monitoring system (the multi-sensorial platform) from the usability of the smart phone i.e. of the interface allowing the user to interact with the system.
With regard to the monitoring platform three parameters were considered: the “learnability” of how to use the devices, the “easiness to start to use” and the “ease of use” (achieved score of approx.. 4 for all of them).

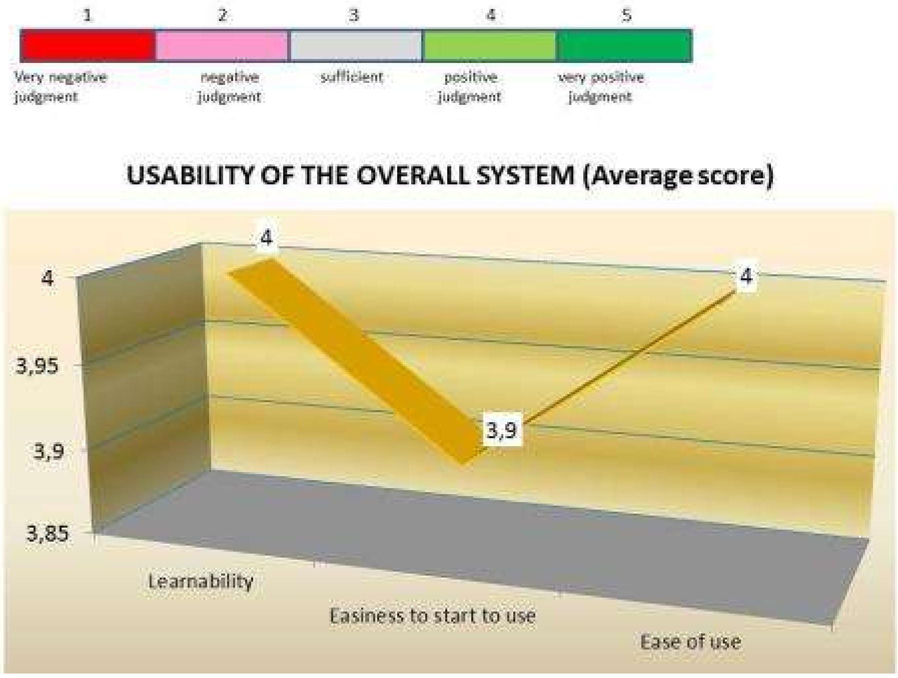


Fig.7: Usability of the CHIRON system

A similar positive result was achieved for the usability of the CHIRON smart phone where the considered parameters were related to the Graphic User Interfaces (clarity of the overall layout, colour contrast, readability of the texts, easiness to find or to locate the needed information); the score for these parameters was in the range of 3.7 to 4.1).

[7] This result is in line with the outcomes of a study done in UK in 2007 and reported in the European Journal of Heart Failure (Nov. 2007). The adherence to the telemonitoring program of elderly patients with chronic heart failure was 92.3% and the programme acceptability rate was 76.45%.

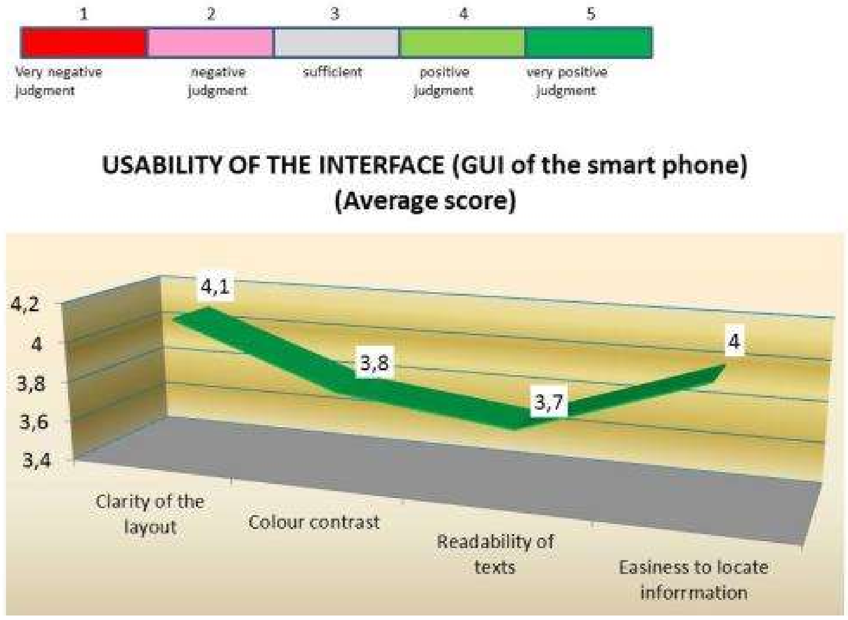


Fig. 8: Usability of the GUI of the smart phone

Finally we checked the "willingness to use the CHIRON system"; here – as expected – the answers of the users were conditioned by the cost they have to pay:

- In case of no cost involved approx.. 80% of the users indicated their willingness to use the system and only 7% expressed a convinced refusal (while 13% showed to be uncertain);
- In case of payment only 25% confirmed their willingness to use, 40% was uncertain and 35% gave a clearly negative answer.

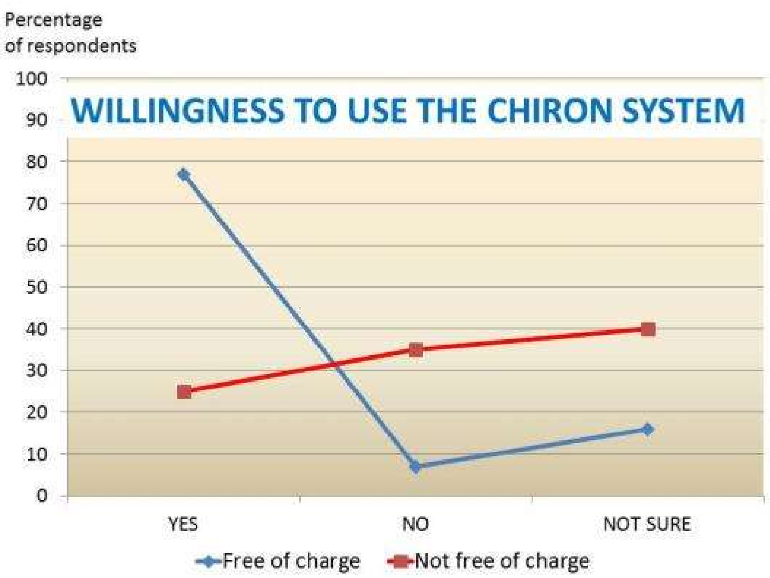


Fig. 9: Willingness to use the CHIRON system

3.2 SOCIO- ECONOMIC ASSESSMENT

A critical question is related to the ultimate goal of the healthcare policies: better services (such as a wider access to healthcare) or better finance (i.e. overall cost benefits and better financial efficiency)?
It is important to highlight that the outcomes of some previous studies show that – through the use of new technologies and mainly ICT– both objectives could be pursued.

Cost-benefit analysis (CBA) and cost-effectiveness analysis (CEA) are techniques widely used in various sectors to support decision making processes[8]. In healthcare CEA and CBA are used to assess and control resources allocation. Given current problems the continued interest in this matter would not be surprising; in the period of a decade, the society's principal goal for the health system has shifted from increasing the access to healthcare to controlling the rapidly inflating costs of care.
The dilemma today is in containing costs without compromising the desired benefits.
Another important indicator is the "opportunity cost". Due to the limitation of the available resources, the investment in a program causes often the missed opportunity of getting the benefits offered by another program i.e. causes the loss of a different opportunity. The objective is to minimize the "opportunity cost" or to maximize the benefits of the chosen program.

Moving the healthcare from the hospital to home through the use of the technology represents a promising and important step for a sustainable healthcare system. In health care benefits are frequently gained from cost avoidance, cost reduction, control of resource allocation, improvement in service quality rather than from revenue enhancement activities.
The economic impact or the 'savings' that can be attributed to various ICT interventions are of considerable interest to both policy makers and industry.

In 2005 Tsai, Chen and Yin introduced the concepts of "effectiveness score" and "cost-effectiveness ratio (c/e ratio)" to compare home healthcare with usual, hospital-based care. The effectiveness score has a multi-dimensional perspective (social interaction, satisfaction, outcome indicators of the disease, etc.).
Tsai, Chen and Yin estimated a c/e ratio of 4.3 for home healthcare (cost= 1420 $; effectiveness score of 320.8) and 13.5 for the usual (hospital-based) care (cost = 3,209 $; effectiveness score of 238.0).

---

[8] In CBA and CEA the outcomes of a project/program are compared with the involved costs; in CBA benefits and costs are both measured in money, while in CEA the outcomes are evaluated in non-monetary terms (e.g. in years of life saved, degree of blood pressure lowered, etc.). Cost-Benefit Analysis methods were preferred up to 1975; more recently Cost Efficiency Analysis is becoming more popular. It is a preferred approach in healthcare since researchers have not yet been able to quantify the social benefits such as quality-of-life in monetary terms.
A specific case of CEA is the Cost Utility Analysis (CUA) where the costs are compared with benefits in terms of their utility to the patient usually evaluated in quality of life measures quality of life including emotional, social and physical well being.
Typically the measurement of utility generated by an assistive device should include at least two dimensions: the increase of quality of life and the period in which such increase is maintained (Quality-adjusted Life Years (QALY)).
Quality-adjusted life years (QALY):
In QALY the number of life years are weighted according to a quality index (0= death; 1= healthy life); the weights are defined by considering statistical data in groups of people with similar problems and are objective, i.e. take into account objective criteria rather than a personal perception of quality-of-life. On the contrary Quality-of-Life (QOL) is a subjective parameter and is calculated by using surveys.

In a similar way Intel and the Center for Aging Services Technologies CAST) highlighted the cost reduction combined with a better quality of care by moving from acute care at the hospital to residential care and finally to home care.

In CEA and CBA applied to healthcare a challenge is to measure the quality of life of users and the socio-economic benefits of the care systems in a more scientifically acceptable way. There is no clear and formal identification of specific socio-economic indicators of outcomes (both quantitative and qualitative). No consistency was found within and between studies; often comparison of results of one study with another can be misleading.

The following diagram shows the overall process for the socio-economic assessment used in CHIRON:

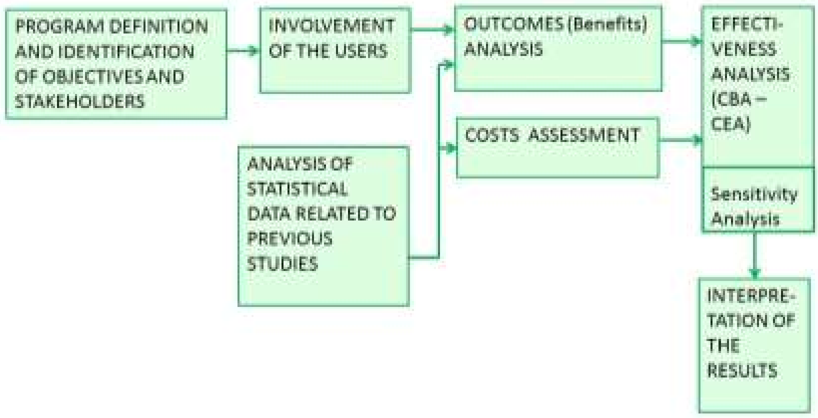


Fig.10: The process of the socio-economic assessment

The **Cost Analysis** included direct costs and indirect costs.
Direct Costs we considered were the costs of the healthcare service, of the equipment / devices (purchasing cost, amortization, technical duration of the equipment vs. the clinical duration of its use), the communication costs (Internet access), the service fee, the installation, training and maintenance costs.

As an indirect cost we focused on the time lost for undertaking the treatment and we considered also the "intangible costs" i.e. the induced costs deriving from the psychological status of the patient and his/her family such as those generated by pain, anxiety, lower quality of life. These costs – even if difficult to quantify – are no less real for the persons with chronic diseases and their families.

Discounting was performed to adapt the costs to their evolution in time; moreover we analyzed the uncertainties and performed a "sensitivity analysis"[9].

For both the **Costs and Benefits Analysis** we identified all the stakeholders and identified the benefits each one of them will get from a remote monitoring of CHF patients as that proposed by CHIRON.

[9] Sensitivity analysis is the examination of an uncertain event under different assumptions; applied to CEA it assesses the impact on the cost-effectiveness ratio of varying the baseline assumptions across a range of plausible values. Sensitivity analysis thus provides insight into the stability of the cost-effectiveness ratio, identifies those baseline assumptions that have the greatest impact on the overall costs and defines boundaries beyond which a specific project / program may no longer be cost-effective.

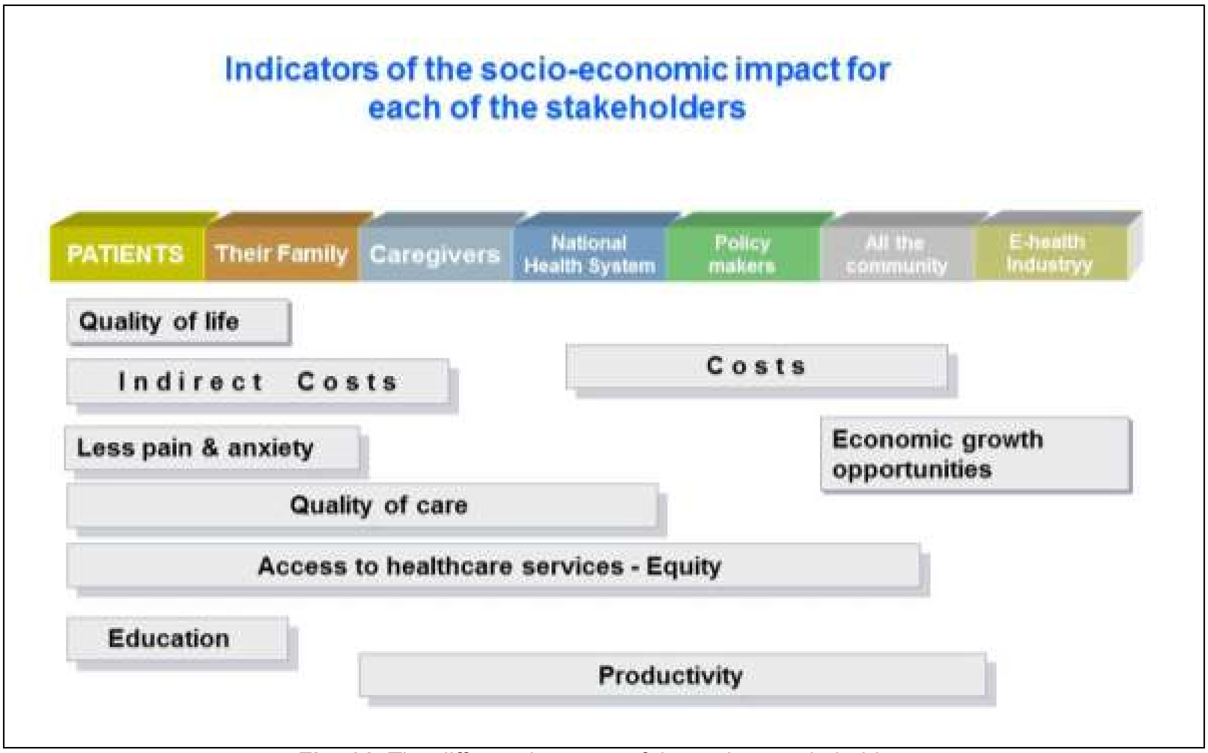


Fig. 11: The different interests of the various stakeholders

For the final assessment we followed a "societal perspective" i.e. we included all the costs and benefits no matter who bears the costs and who receives the benefits[10].

In this regard the main identified contributors of the overall "societal" benefit are:

a. The saving in the time spent by the patients, the family members and by the medical professionals (reduced visits and reduced time per visit linked to the beneficial effect on the health status of the patient, his/her psychological wellbeing and his/her commitment to healthier lifestyles). The time saved by the doctors can be used to provide healthcare services to more people i.e. to allow – at equal overall cost – the access to the healthcare services to a larger portion of the population.
b. The economic opportunities gained by the e-health sector (European industry and extra working opportunities in the sectors of the e-health services).
c. The saving related to a reduced need of institutional care i.e. the opportunity of moving to a less expensive home-based care solution supported by the technology and the early detection and prevention of degenerative trends.

The following table reports the results of past studies related to the effectiveness of remote monitoring with specific focus on cardiac diseases:

[10] It is possible to take a more narrow view and make a calculation - for instance – for the patients and their families disregarding the costs and benefits to others who may be affected or – on the contrary - to focus on public sector alone and disregard the older users. However it should be noted that only a societal perspective represents an appropriate basis for priority setting if suboptimal decision making is to be avoided.

Study	Outcomes	Notes
European Commission (2005)	The report estimated in 11.7% the potential cost saving of the Healthcare System in 2016: • 2.0 % linked to the introduction of extended EHR systems; • 1.9 % thanks to e-Prescribing; • 0.9% related to saving in administrative processes; • 6.9% in the area of Telemedicine.	
WSD study (Whole System Demonstrator) conducted in UK	It estimated as a result of the use of tele-monitoring: ▪ 15% reduction of ambulatory and emergency visits, ▪ 14% reduction of hospitalization, ▪ 15% reduction in "bed days" with a total saving of 1.2 billion Euro in 5 years.	The WSD study is the largest pilot executed in the world with 3,000 patients (COPD, diabetes, heart failure)
Study in Germany	the benefits of telehealth were quantified in a cost reduction in the range of 1.5 B Euro.	
Analysis of 14 randomised controlled trials (4264 patients with chronic heart failure)	Comparison between remote monitoring and simple telephone support showed the advantages of tele monitoring: - 21% reduction in the rate of admission to hospital, - 20% reduction in all cause mortality - Better quality of life - Reduced costs.	See R. A. Clark, S.C. Inglis, F.A. McAlister, J.G.F. Cleland, S. Stewart: "Telemonitoring or structured telephone support programmes for patients wiyh chronic heart failure: systematic review and meta-analysis" BMJ – 3 May 2007
Italy 2008 Randomized Controlled Study on 230 heart failure patients	Comparison of 230 patient treated with home-based telemanagement (HBT) with 230 patients treated with usual care: HBT group evidenced: - Lower readmission to hospital, - Lower mean health care cost.	See A. Giordano, S. Scalvini, E. Zanelli, U. Cirrà, GL Longobardi, VA Ricci, P. Baiardi, F. Glisenti: "Multicenter randomised trial on home-based telemanagement to prevent hopsital readmission of patients with chronic heart failure" – Int. J. Cardiol. 2009 Jan 9.
Trans-European Network – Home care Management Study (TEN-HMS) – 426 patients with chronic heart failure	Comparison between: a. home telemonitoring (HTM), Nurse telephone support (NTS) and Usual Care (UC): - Number of readmission to hospital and mortality: similar in HTM and NTS groups but the mean duration of admissions was reduced by 6 days with HTM; - Mortality was higher in the UC group.	See paper of J. Cleland, A. Louis, A. Rigby, U. Janssens, A. Balk published in Science Direct (www.sciencedirect.com(science/article/pii/S0735109705004845)

Unfortunately some of these studies refer to pilot projects and short term outcomes which limit the ability to generalize most assessment findings. Most of these studies are not guided by a systematic framework for evaluating the socio-economic benefits of new healthcare policies.

There is still a great need for high quality evaluation studies giving the evidence required by decision makers in healthcare.

A working group of the Continua Health Alliance has been devoted to conduct a comprehensive study of all of the remote patient monitoring (RPM) trials that have been conducted over the last 5 years in Europe and the United States. This study represents the corner stone in a broader strategy to understand what additional proof may be necessary to ultimately achieve universal reimbursement by private or public payers for personal telehealth technologies worldwide.

3.2.1 THE COST ANALYSIS

A cost analysis for CHIRON is reported in the following table

Type of cost	Value (Euro)	Note
Equipment (H/W)	500 (amortization quota)	Sensors set per patient: average 1000 Euro; Personal device: 500 Euro; Amortization over 3 years; yearly amortization quota: 500 Euro
Service (yearly fee) + Internet access (traffic)	250	Approx. 12 Euro/month for traffic + 100 Euro/year for service fee
Cost for follow up	1,440	Cost of professional personnel (medical doctor, emergency service operator) – Average 2 hours/month per subscriber equivalent to 120 Euro (average gross cost of 60 Euro per hour)
Time spent for training	70	5 hours (3h at the start up and 2h during the lifetime of the equipment/services); hourly cost: 40 Euro. Amortization over 3 years; amortization quota per year = 70 Euro
Maintenance costs	240	Labour and other costs; average: 9 hours over the 3 years of the service/devices lifetime. Hourly cost: 60 Euro. Amortization over 3 years; amortization quota per year = 180 Euro
TOTAL YEARLY COSTS	2,500	

3.2.2 THE BENEFITS MATRIX

Stakeholder → / Benefit ↓		Patient (primary user)	Family members – Informal carers	Medical pro-fessional and other formal carers	Institutions and National / Local Health/ Social Care Services	The Business Community	The OVERALL COMMUNITY
ECO-NO-MY	Reduction of the time spent by nurses (domiciliary care)		52 hours/year = 2,200 Euro (see note 1)				2,200 Euro at yearly level
	Additional productivity						
	Reduced loss of working hours for the family members (informal carers)		52 hours/year = 450 Euro (2)				450 Euro at yearly level
	Reduced loss of working hours for the patient	200 hours/year = 1800 Euro (3)					1800 Euro at yearly level
	New opportunities for the industry					1575 Euro per year per person (6)	1575 Euro per year per person
HEALTH	Prevention or mitigation of degenerative trends and reduced needs of consultation with GPs and specialists (ambulatory and at home visits)				160 Euro as average per year (5)		160 Euro at yearly level
	Reduced costs for hospitalization due to acute episodes (reduced need of ambulance services, Reduced number of hospitalization, Reduced total and average length of stay in hospital)				3,000 Euro (4)		3,000 Euro

Stakeholder ⇨ / Benefit ⇩		Patient (primary user)	Family members – Informal carers	Medical pro-fessional and other formal carers	Institutions and National / Local Health/ Social Care Services	The Business Community	The OVERALL COMMUNITY
Intangible benefits	Reassurance						
	Peace of mind for the family members						
	Better quality-of-life and increased life satisfaction						
	T O T A L in Euro	1800	2650		3160	1575	9185

NOTE: Quantification of the benefits

Ref.	Type of benefit	Value in Euro at yearly level	Explanation
1	Reduction of the time spent by nurses (domiciliary care)	2,200 Euro	By using the data of a previous study done in Sweden we considered a reduction of 1 hour per week and we applied the hourly cost for domiciliary assistance applicable in Italy of 42 Euro (Ref. E. Petazzoni : Case history 1 – Experiences in the field of the domiciliary assistance – (in Italian).
2	Reduction of the lost working hours by the family members	450 Euro	By using the data of a previous study done in Sweden we consider a reduction of 1 hour per week and we applied the average monthly salary of 1300 Euro valid in 2010 for the Italian citizens (Source: ISTAT 2011).
3	Reduction of the lost working hours by the patient	1800 Euro	We assume a reduction of approx. 200 hours of lost working hours (a reduction of 2 days per month). By adopting the average yearly salary of 16,900 Euro applicable in Italy (1,300 Euro x 13 months – source: ISTAT 2011), the average yearly benefit is approx. 1800 Euro.
4	Reduced costs for hospitalization due to acute episodes	3000 Euro per person per year	According to a study executed in the United States ("K.D. Frick, L.C. Burton, R. Clark et al. – "Substitutive Hospital at Home for Older Persons: Effects on Costs", January 2009 – www.ajmc.com) and involving 455 older patients (286 observation patients and 169 intervention patients) suffering from acute COPD (chronic obstructive pulmonary disease) or CHF (Congestive Cardiac Disease), a unit cost saving of 1900 Euro (2400 US$) was found for the intervention group.

Ref.	Type of benefit	Value in Euro at yearly level	Explanation
			The "Hospital management" magazine in an article published on October 13, 2011 ("Top trends for healthcare to 2012" – www.hospitalmanagement.net) reports the result of a clinical trial executed in UK where a telehealth program involved 74 elderly patients: the comparison was between the costs of the 12 months before the starting of the program and the 12 months in the year after the technology was fitted; the spending per patient went down from 5640 Euro to 1170 Euro with a saving per patient of 4475 Euro at a yearly level. For our analysis we consider an average yearly saving of 3,000 Euro per patient.
5	Reduced needs of consultation with GPs and specialists (ambulatory and at home visits)	100 Euro / year due to less consultations and 60 Euro/year due to saving in time per visit	According to the outcomes of previous studies, the number of consultations with the *general practitioner* will decrease due to the implementation of e-health services. A report published in 2010 (J. Van Ooteghem, A. Ackaert, S. Verbrugge, D. Colle, M Pickavet, P. Demeester – " Economic viability of eCare solutions**")** estimated a 20% decrease in costs (of which 5.9% for in practice consultations and 14.1% for home consultations). The total amount of time savings per patient per year i.e. less consultations and savings in time per visit is estimated at 198 and 122 minutes, respectively. By considering an average monthly salary of GPs of 4336 Euro (value valid for Italy – source: ISTAT) for a total of 152 hours/month (38 h / week), we obtain a saving of approx. 100 Euro/year for less consultations and of 60 Euro/year for saving in time per visit.
6	New opportunities for the Assistive Technology industry	1,575 Euro per assisted user per year	The costs spent for the CHIRON services will generate new labour opportunities (e-health Industry, Medical Services) that can be estimated as below indicated (see section 3.2.3): Hardware : gross margin of 35% (price minus material costs) = 175 Euro; Other : average personnel cost equal to 70% of the price = 1,400 Euro

3.2.3 DISCOUNTING OF COSTS AND GENERATED BENEFITS

We assume a dynamics of the costs as below indicated:

a. For the first year of market uptake (in the table considered 2014 just for reference): 30% price reduction for the HW and for the services fee (compared to the base price calculated in the previous section) and 20% price reduction for the other parts of the solution which are highly linked to labour cost (here the 20% is mainly considered an increasing of productivity and efficiency in the workflow organization);
b. In the period 2015-2020: an average price reduction of 6% per year;

At the same time the additional benefit for the e-health sector that was calculated equivalent to 1575 Euro (35% of the hardware cost plus 70% of the other costs) will be adjusted accordingly as indicated in the following table:

COSTS	Base	2014	2020	BENEFITS	Base	2014	2020
				Benefit for the e-health sector			
Hardware cost	500	350	240	Contribution margin	175	122	84
service fee & Internet access	250	200	138	Labour content	175	140	97
Follow up costs	1440	1152	644	Labour content	1008	806	451
Training & Maintenance	**310**	250	170	Labour content	217	175	119
				TOTAL	**1575**	**1243**	**751**
				Other benefits (see note 1)	**7610**	**7610**	**7610**
TOTAL	**2500**	**1952**	**1192**	**Total Benefits**	**9185**	**8853**	**8361**

NOTE 1: For the other benefits we assume that their value will remain constant over time.
In fact they are labour-related or referring to hospitalization; they are costs that – on the contrary of the hardware and/or to the ICT services – are not affected by economy of scale.

As already mentioned we used a "societal perspective" where we included all the costs and benefits no matter who bears the costs and who receives the benefits.

Societal approach
(per person and per year)

	Base	2014	2020
Cost	2500	1952	1192
Benefit	9185	8853	8361
Benefit/ cost ratio	3.7	4.5	7.0

The effectiveness of the solution is clearly demonstrated.
The main contributors of the overall "societal" benefit are:

a. The saving in the time spent by the nurses (domiciliary assistance) (2,200 Euro as base value). The saved time can be used to provide assistance to more people i.e. to allow – at equal overall cost – the access to the healthcare services to a larger portion of citizens;
b. The reduced loss of working hours for the patient and his/her relatives (2,250 Euro);
c. The economic opportunities gained by the e-health industry (1,575 Euro as base value) (extra working opportunities);
d. The saving related to a reduced need of hospitalization and ambulatory visits (3,160 Euro).

From a "societal perspective" the amortization quota of the investments will be recovered in 3 months already starting from the 1st year.

3.3 BOOSTING THE UPTAKE OF THE E-HEALTH INDUSTRY / MARKET

According to a report issued by HINE (Health Information Network Europe) in 2006 ("European eHealth forecast"), the eHealth industry in the EU15 was estimated to be in the range of 21 billion Euro in 2006 and 50-60 billion Euro at a worldwide level.
"The health ICT industry has the potential to become the third largest industry in the health sector". An average growth rate of 11% is expected.
But currently 71% of this market is covered by "secondary usage non-clinical systems" i.e. by HW & SW solutions used for the back-up office management.

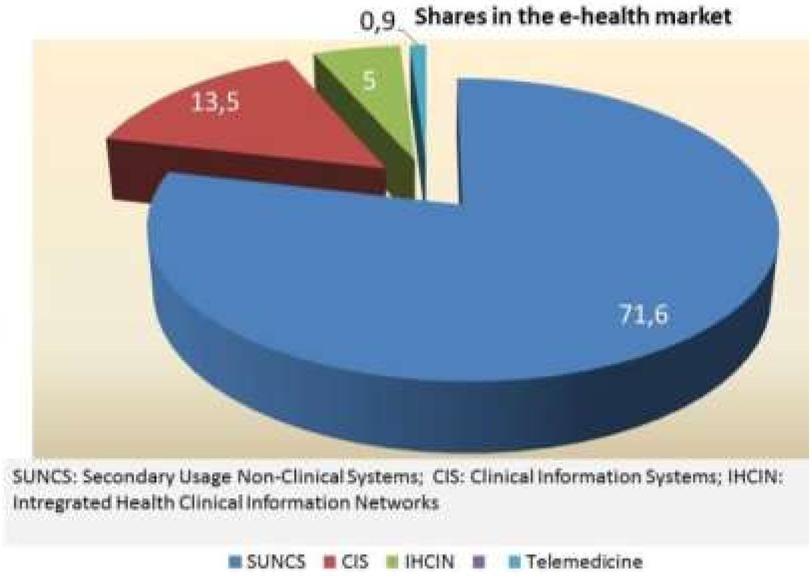


Fig. 12: Shares in the e-health market

3.3.1 PERSONAL HEALTHCARE

The personal healthcare solutions have less than 1% penetration (of which 70% related to Cardiovascular diseases); 10 to 15 years is the estimated time to mainstream adoption (Source: Gartner report, 2008) ; no proven solution for prevention and early diagnosis has still reached the market.

Fully mainstreamed products	Partially mainstreamed products	Localized instances	Only pilots and trial activity	Little or no activity
none	U.S.A.	Denmark, Spain, Finland, United Kingdom, Germany, Sweden	Italy, France, Hungary, The Netherlands, Poland, Japan	Other countries

CHIRON aims to open opportunities for the uptake of the e-health market which is considered by the European Commission a “lead market” i.e.

- *a “market for innovative products and services or technological solutions with high growth potential”,*
- *a market where EU industry can develop competitive advantage,*
- *a market that requires action by the public authorities to deal with regulatory obstacles.*

e-prescriptions, deployment of EHRs, tele-monitoring and homecare, Internet services for patients are expected to be among the segments with the largest potential.

The outcomes of the CHIRON project will provide new opportunities to the Industrial Partners of the Consortium (and not only) as described in the deliverable D8.2.2; some examples of exploitation plans are reported here below:

- MOBILI started the development of the Mobils framework, which is a tool for developers, enabling them to add sensoric connections to their mobile applications in the area of mHeath, telecarare, sport, wellness, research, automotive. The first version of Mobilis framework (*Mobilis SenseView*) is already available and won the "App of the Month December 2013" of Bluetooth.org.
- The University of Rome created a spinoff company (WSENSE S.r.l) devoted to the design of sensing systems and the security solutions developed within the project are in the process of being included in WSENSE products

- TECNALIA is studying the possibility to exploit CHIRON results by transferring the acquired knowledge to local e-health companies (Inviza, Clinica Asunción,…). They intend to develop a social health platform oriented to chronic diseases.

- CEIT established contacts with very interesting companies operating in the healthcare field; also in this case the discussion is related to a knowledge transfer. Furthermore CEIT is envisaging the possibility of exploiting the knowledge in sensors acquired in CHIRON also in new fields, as amateur and professional sport practice.

- WLAB used the abstraction layer designed in CHIRON in the area of structural monitoring and introduced the DISsense protocol that was employed to monitor the construction of a tunnel in a new metro line in Rome.
  Discussion with Telecom Italia is in progress for the use of the WLAB solution in the monitoring of indoor pollution in public spaces such as schools or offices. Similarly, the abstraction layer has been adapted to support the data acquisition from RFID. This solution is now proposed in partenership with TENEGA (www.tenenga.com).

- ATOS will use its sales force and the established channels to reach customers and present the products implemented during the CHIRON project.

- ICOM is enriching its Personal Healthcare Record (PHR) platform by adding location and environmental information monitored through the Bluetooth Low Energy (BLE4)-based solutions developed in CHIRON. It will give added value to the services Intracom plans to provide in the near future though mobile operators and IP-TV providers.

3.3.2 IMAGING

BARCO and FIMI will use the developed Direct Led Backlight and the simulation platform for medical displays in the new generation of high-end medical displays for the primary diagnosis market.
Furthermore newly developed QA methods are already included in a first product and have the potential to be implemented in future QA technologies.

Interesting opportunities are also those related to the iPad application for reviewing of medical images that is already available in the Apple stores.

3.3.3 MEDICAL SYSTEMS

For Philips the main business opportunity generated by CHIRON is represented by the advanced solution of X-ray / ultrasound images integration. This has already led to a commercial product, the EchoNavigator.

ZG has various contacts for the commercialization of its openEHR platform (see www.medrecord.nl) developed by using the outcomes of the CHIRON research work.
Mainly the UK based National Health Service (NHS) has great interest in the platform since it is 100% standardized, and now also open source.
Discussions are also in progress with Philips with regards to the definition of a business model for the developed solutions and with Barco[11] for the i-pad based solution.

[11] ZG, Barco and Philips are involved also in the ARTEMIS JU project HIGH PROFILE.

PART 4 – OVERALL ASSESSMENT

We report here below the outcomes of a self-assessment done by the CHIRON Partners. They analysed the level of achievement of the technological, medical, social and economic (business related) objectives of the Project by scoring them in a scale of 1 (very poor results) to 5 (excellent results).

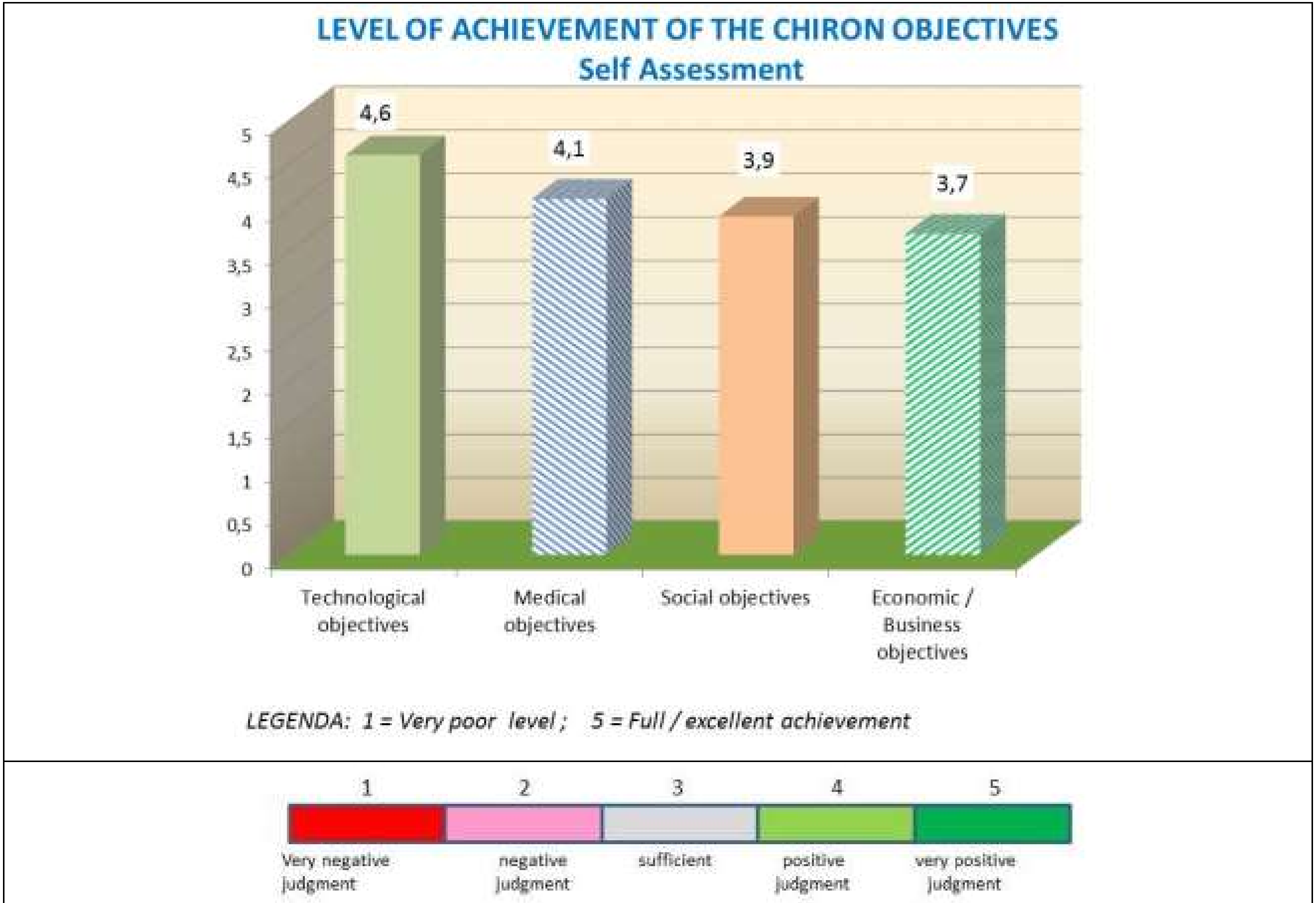


Fig. 13: Self assessment of the CHIRON Consortium

The self-assessment is very good with average scores above 4 (positive to very positive judgment) for the technological and the medical objectives.
An average score in the range of 3 to 4 (sufficient to positive judgment) was given to the social and the economic /business objectives.

Here below we report some comments given by the Partners; they are useful for a better understanding of the above mentioned judgments.

A. TECHNOLOGICAL OBJECTIVES

Both scientific objectives (e.g., new methods for automated analysis of medical images) and technological ones (e.g., granting the reliability of the patient-doctor communication chain) have been excellently reached (UNITS).

The technological objectives were fulfilled completely. The proposal of the CHIRON project was written in 2009 and almost 5 years after we see a significant increase in the number of similar projects also as a result of the improvement of mobile and sensor-related technologies. This interest is a clear indicator of the success of the basic concept inspiring the CHIRON project; CHIRON, in this regard, was the first of the ice-breakers (MOBILI).

The integration of a number of components of heterogeneous domains necessary to achieve CHIRON objectives is extremely challenging; in most cases it demands practical solutions rather than new or cutting edge-ones. CHIRON succeeded in it (WLAB). The CHIRON system represents the first attempt in integrating all necessary domains into a single system for monitoring and management of CVD patients (SOTON).

The full interoperability between heterogeneous sensors and devices and the compliance with the standards in the exchange of medical data achieved in both approaches indicated by CEN/ISO 13606 (CDA R2 and openEHR) represent outstanding achievements of the project (UOR, UNIGE). We could not have done better; there are not other examples of full integration and standard compliance (ZG).

The overall CHIRON platform has been demonstrated to work across the entire chain in all planes (user, medical, nomadic) (PHILIPS); with CHIRON the user can be continuously monitored in real-time at both locally and remotely (SELEX ES).

B. MEDICAL OBJECTIVES

The Observational Study clearly showed that telemedicine is accepted by the patients and it is feasible also for relatively long time spans.
It is essential to imagine a forthcoming randomized investigation to validate that what we saw about the "surrogate end-points"[12] and the relationship with the measured parameters may indeed impact on CHF patient outcome when the relationships are modified. A great potential should then open and it would have a high public health impact (UOR – Policlinico Umberto I).

More clear relationships have been determined between the patients' vital parameters and the severity of their disease. This is relevant to prevention issues. The effects on cost reduction will be apparent in a near future (UNITS).

CHIRON monitor the patients gathering information from many heterogeneous data covering 67 different parameters even if in some sub-modules only some of them are used. To completely achieve the original medical goal, observational study need to be extended (CIMNE).

The number of patients was not as expected at the beginning of the project. However, we succeeded to extract some important conclusions that prove the quality of the CHIRON system (CEIT).

We demonstrated that the CHIRON technology is capable of providing medically valuable data, but we have not been able to properly interpret these data yet (and the amount of data gathered may also be insufficient for this) (JSI). The limited scale observational study provided some initial medical outcomes but needs to be complimented for a firm conclusion to be reached (SOTON).

X-ray / ultrasound integration will increase efficiency of medical procedures; with regard to the remote monitoring the CHIRON observational study would need to be extended to completely achieve the original medical objectives (PHILIPS).

---

[12] In the Observational Study we considered as "surrogate events" the worsening of the health status as perceived by the patient himself.

C. SOCIAL OBJECTIVES (QoL)

Better CVD management through the CHIRON system can lead to an improvement in the quality of life of patients and their family but a clinical trial is required for this to be assessed (SOTON).
A larger scale clinical trial is required to establish users' acceptability (ISI).

Probably some work is still needed with regard to more user-friendly solution for patients (CIMNE). Some additional efforts must be made to reach the patients in a user-friendly and sure way (UNIGE).
The CHIRON technology has been accepted by the patients quite well and it shows promise of impact on the quality of life, but it is not yet mature enough to actually make this impact (JSI).
The social objectives are not yet visible and will be appreciated only in the future (UNITS).

The usability of the individual components of the CHIRON system is good and the solutions have the potential to provide significant benefits in terms of quality of life; there is still a "technological barrier" that makes difficult the full acceptance by the users (SELEX ES).

D. ECONOMIC / BUSINESS OBJECTIVES

Very good results were achieved
Some products with high success potential in the e-health market were released during the CHIRON project such as the SenseView framework of Mobili and the Barco tablet applications (CEIT, ATOS).
The "App of the month" award earned by one of the partners is a clear indicator of the potentialities of the Chiron industrial partners to attain an even stronger business position in their field (UNITS).

Some of the enabling conditions for an effective exploitation were realized:
The results obtained in the different demos and the acquired knowledge represent good starting points for building a business in the e-health market (TECNALIA, IBERMATICA).
CHIRON platform enables continuity of care and data flow between hospital and home care. This solution and service model open new market opportunities for the Telemedicine domain (I+).
Standard-based implementations and semantic interoperability realized in CHIRON will allow a spread adoption by the market (ATOS).
Use of existing medical and communication standards in CHIRON solutions represents the key towards commercialisation of CHIRON individual modules and sub-systems (ISI)
The CHIRON platform provides a good basis for further activities in the e-health domain, in particular because it is based on existing standards (PHILIPS).

Barriers and problems still exist
The deployment of healthcare solutions requires the development of a complex ecosystem in which many players have to interact. This is mostly a procedural and legislative issue in which CHIRON, by its nature, only partially can contribute (WLAB).

To get a full exploitation the telemonitoring solutions need to be integrated within the conventional approaches used by the National Healthcare Services in the treatment of CHF patients (CIMNE, UNIGE).

The CHIRON system established the foundation for new business opportunities in a rapidly growing market, but it needs to find the right vehicle, including new business models (SELEX ES).

Further work is still needed
CHIRON is a research project and the time-to-market still remains very long. It is our belief that the business opportunities of the project would be expanded greatly with the addition of a CHIRON2 project, limited to pilot and commercialization phases (MOBILI).

ANNEX 1: BUSINESS OBJECTIVES - EXPLOITATION PLANS OF THE CHIRON PARTNERS

See also deliverable D8.2.2

Partner	Product description	Link to CHIRON (WPs contributing to the product creation and development)	Estimated contribution of the CHIRON research (in %) in the realization of the product	Year of market intro-duction	Market segment	Expected cumulative revenue in the first 5 years of sales
BARCO	Direct Backlight	WP5	15%	2015	New high-end medical display platform for primary diagnosis applications	50MEuro
	Barco iPad calibration application	WP5	50%	2011		
	Barco QA Check Software	WP5	50%	2013		
MOBILI	Mobilis Framework Mobilis SenseView framework helps clients connect mobile sensors for a variety of uses, and in a fraction of the time.	WP2 WP3	25	2013	Developers, research projects	1.000.000
	SmartPhone for seniors with: -simplified UI - location services - SOS - connection to informal/formal carers - bio-sensors Made with Mobilis Framework	WP3	25	2013	SeniorCare	300.000
	SenseView Description: https://play.google.com/store/apps/details?id=si.mobili.senseview Made with Mobilis Framework	WP2 WP3	25	2013	Medicine, Sport, Wellness, Research	500.000
UOR	Secure communication stacks for wireless sensor networks	WP3/WP4	20% (indeed the research performed in	A couple of years from now	Embedded systems	NA

Partner	Product description	Link to CHIRON (WPs contributing to the product creation and development)	Estimated contribution of the CHIRON research (in %) in the realization of the product	Year of market intro-duction	Market segment	Expected cumulative revenue in the first 5 years of sales
			CHIRON will not immediately translate into a product but will be the technological background and knowhow for product development)			
TECNALIA	Tecnalia plans to introduce a mobile telecare system that monitors in real time the evolution of the patient health parameters, generating alarms and notifications to the patients themselves since health parameters collected by their own Smartphone based in the mobile app created to CHIRON	WP6	70%	2	Clinical health applications	
SELEX ES	Secure Access Gateway	WP4	25%	2015	Secure Communications/ Smartcities	2M€
WLAB	DISSense – energy efficient collection protocol	WP4, WP7	60%	2011	Energy efficent monitoring	It is open source (http://code.google.com/p/dissense/). We hope to make money from the customization.
	Abstraction Layer	WP4, WP7	100%	2012	Integration of heterogeneous sensors	It is open source (http://sourceforge.net/projects/wsnfuse/). We hope to make money

Partner	Product description	Link to CHIRON (WPs contributing to the product creation and development)	Estimated contribution of the CHIRON research (in %) in the realization of the product	Year of market intro-duction	Market segment	Expected cumulative revenue in the first 5 years of sales
						from the customization. Already adptaed to RFDI domain.
ATOS	EHR Gateway, The Vdr Bridge library, openEHR configurator and openEHR visualisator, are the set of tools called the EHR Gateway to access the openEHR REST API facilitating the access to the rest of components (DSS, MEST, etc) using health standards. The software allows storing and retrieving the data from the EHR (openEHR based), but instead of using the xpaths (sometimes unmanageable), the inputs and outputs are translated into meaningful configurable concepts. hl7 CDA and IHE profiles can also be covered by the EHR Gateway. The EHR Gateway is planned to be included in the ATOS solution to provide EHR management.	WP6	60%	2	Telemedicine	
	Slim Mest, A robust system which allows the medical professional to analyze the data of the patient collected in the observational study	WP6	100%	2	Telemedicine, clinical health applications	
		WP6	25%	5	Clinical health applications; EHR management	
Philips	Echonavigator	WP5	20%	2013	Interventional cardiology	15 - 30 M€ (including leverage of sales of ultrasound equipment and cathlabs)
ZG	MEDrecord, a 100% standardised open source	WP1, WP7	50%	2013	eHealth	5 million Euro's

Partner	Product description	Link to CHIRON (WPs contributing to the product creation and development)	Estimated contribution of the CHIRON research (in %) in the realization of the product	Year of market intro-duction	Market segment	Expected cumulative revenue in the first 5 years of sales
	EHR platform					
ICOM	intLIFE PHR Platform/Services	WP2, WP4	10%	2014/2015	e-Health services	TBC
	BLE4-based communication/sensing	WP2	25%	2014/2015	Environment Security e-Health	TBC
IBERMATICA	Literature Search Module The Product allows literature searching of original and relevant biomedical literature.	WP6	70%	2	Clinical health applications	