1 Public Summary

March 2008 – August *2013*

1.1 Introduction Public Summary

Dear Reader,

Thanks for your interest in HeartCycle

This is the last public report by the HeartCycle consortium. This publishable summary comprises a description of the HeartCycle project objectives, the progress of work, achieved results in the period March 2012 to August 2013, and their potential impact and use within the Integrated Project FP7-216695 HeartCycle Compliance and effectiveness in HF and CAD closed-loop management.

For more information, questions, or remarks please visit our website or contact me directly.

Harald Reiter
HeartCycle Project Manager

1.2 Objectives

HeartCycle is aiming at researching, developing and clinically validating innovations for the next generation of telehealth systems for disease management. Therefore, HeartCycle starts from an application point of view. We have investigated and analysed the needs of patients and medical professionals for specific disease management solutions. Based on the identified needs, we investigated and developed specific HeartCycle concepts. These concepts are applications that are tailored to a specific patient group.

In order to achieve the HeartCycle intentions we have defined a so called HeartCycle process that has resulted in meaningful technical solutions that achieved a maturity level for clinical validation.

The process is depicted in the picture below:

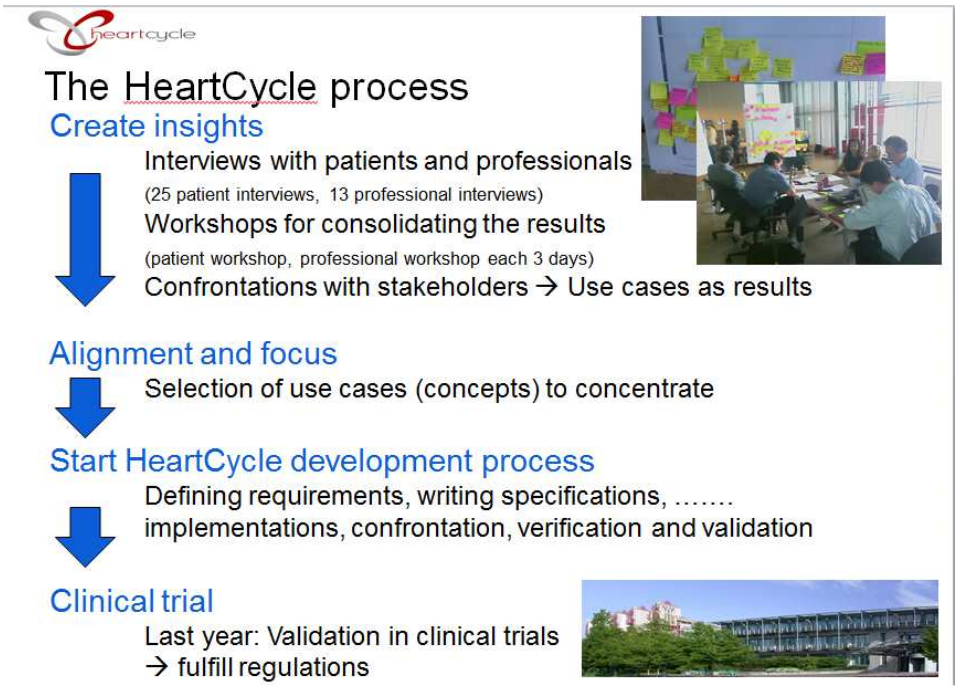

Figure 1: *The HeartCycle Process: Starting from insights into existing needs of patients and professionals in telehealth, innovations have been developed and tested in clinical studies to finally allow acceptance and endorsement of the medical community for the new telehealth services*

1.3 Performed Work

Insight creation:

To manage the insight creation in a propoer way a number of workshops have been planned at the beginning or the project work.:

Workshop on patient characteristics

In this workshop typical but different patients per application (CAD and HF) – socalled personas– were developed. These personas were the basis for further discussions and also for the specifications as they were representative with regard to their disease status, their handicaps, their concerns and worries etc. Interviews with patients and their informal caregivers –in several countries – were carried out in preparation of this workshop.

During the workshop, input from medical experts was used to refine the characteristics of the respective personas.

Concept enrichment workshop (workshop on patient loop)

The concept enrichment workshop was build on the results of the workshop on patient characteristics: Together with the medical experts we analysed in detail the patient's interaction with the HeartCycle system in order to derive the appropriate set of specifications for the different modules.

Workshop on the professional loop (professional backend)

The workshop on the professional loop involved all medical professionals who will later work with the HeartCycle system, i.e. not only cardiologists but also primary care physicians and nurses. Topics of the workshop were data representation, alarms, careplan adaptations, appropriate means of communication between the different professionals and also between the professionals and the

patients. These discussions helped to set up the specifications for the professional backend of the HeartCycle system.

Workshop on business scenarios

The workshop on business scenarios focused on stakeholder analysis and the development of an initial value proposition. WP9 compiled information on the legal framework and the re-imbursement schemes in the different countries involved (e.g. UK, Spain, Germany).

Finally HeartCycle focused medical and technical innovations on three concepts:

	**Heart failure Management (HFM)** including – Medication Management via TeleHealth – Decision Support (Patient & Professional) for TeleHealth – Education & Automated Coaching for Patient Self-Management via TeleHealth – Health Maintenance
	**Guided Exercise (GEx)** including – Independence & Compliance for cardiac rehabilitation training – Safety & Confidence for patients – Improved Treatment Delivery & Closer Follow-up – New sensor and vest / whole system developed from scratch
	**Assessment Use Case (AUC)** including – Novel Sensors to Enhance Patient Assessment in the Home Environment – New Information Processing for Integration & Interpretation of Sensor & Patient Data – Improved Decision Support

HeartCycle has developed, implemented and validated these concepts to a maturity level that allowed operation in clinical test beds. Important aspects have been testing the technical feasibility, the user acceptance in these groups and that concepts present new ways to deliver improved healthcare to patients and reduce workflow for professionals.

The goal of the first year has been to establish a process allowing creating and further developing the concepts (use cases) in a way that the insights gained by the concept development are accepted by the stakeholders from both, medical community and business. The second year has been the time to focus on the final use cases, to develop requirements and specifications for the innovations used in the clinical validations and do further research on innovative sensors, advanced algorithms, decision support and user interaction including education, coaching and motivation. This research has been continued in year three. In addition the major focus in year three and four has been on the final development, implementation and testing of the HeartCycle systems to be used in the clinical studies running in year 5, the definition of the clinical study designs and preparation of all documents needed to pass ethics and competent authorities for getting the approval for the studies. The approval procedure in all three countries took more time than expected as this is an interactive process and competent authorities and ethics separately are asking for more and more information to be provided. In addition new legislation (Medical device directive due March 2011) has to be taken into account and reacted to.

Clinical trials started in January 2012 in Hull first therefore the HeartCycle consortium has asked the Commission for a project prolongation to be able to finalize clinical studies and respective analysis and reporting. Finally HeartCycle has been extended until 31. August 2013.

In the validation period from January 2012 till August 2013 the main concentration of the HeartCycle consortium has been on executing the clinical studies. This period is part of "Phase 2 – Clinical Validation. As recommended by the reviewers on the HeartCycle review 2012, HeartCycle has been extended to 66 months duration to enable clinical study operations as there have been delays with achieving approvals from ethics and competent authorities. This should safeguard that innovative technologies and concepts developed in HeartCycle can be sufficiently validated to be able to get endorsement by medical community for future exploitation of HeartCycle technologies:

- Clinical study execution period was successful.
- The additional 18 months have been used extensively by the consortium to complete the work plan and get the best out of the clinical studies
- The consortium worked hard to achieve the goals of HeartCycle
    - Clinical study management
    - Technical developments/mitigations/support
    - Final business assessments and exploitation
    - Major workload on clinical HeartCycle partners and study management

Clinical HeartCycle studies

The three studies carried out within HeartCycle have been structured to accomplish different scientific, medical and technical objectives. These objectives have also shaped the needs for each of the studies and the strategy to be followed for the posterior analysis of the data in each of them.

HFM:

An Observational Trial with Randomised Components Investigating the Ability of a Third Generation Home Telemonitoring System (HTM) to Enhance The Management of Patients with New-Onset, Recurrent or Persistent Severe Heart Failure):

The purpose of this study was to investigate how HTM can be used to optimise therapy safely and efficiently. It also attempted to 'calibrate' changes in HTM vital signs in response to daily life challenges. The study developed the concept of health maintenance, rather than crisis-detection as the basis for HTM, providing information on the proportion of time that a patient could be kept in their ideal range of vital sign measurements.

a) Objectives:

- *"Primary*:
    - Phase A: The ability of the system to support titration of life-saving medication safely and effectively to target doses [observational].
    - Phase B: The ability of the system to reduce diuretic doses safely in patients whose symptoms were well controlled and to increase them appropriately in patients in whom symptoms were not well controlled [randomized].
    - Phase C: How aspects of everyday life alter vital signs [observational but observer blinded].
    - Phase D: The proportion of time that the system could keep patients in the ideal range for weight, blood pressure and heart rate [observational].
- *Secondary*:
    - Quality-adjusted life-years in program [observational]
        - An assessment of the potential socio-economic impact of the telehealth system [observational].
        - Patients' educational attainment on the Dutch Heart Failure Knowledge Scale, and self-care activities with the European Heart Failure Self-care Behaviour scale [observational].

- An assessment of patients and health professionals views of ease of use and utility of a telehealth system for the different phases and interventions of the trial" [observational].

b) Study design:

The study consists of different protocols: A, B (phase 1), B (phase 2), C and D.

GEx:

The GEx system was a closed-loop disease management system that was intended for the prescription and administration of cardiac rehabilitation therapies based on physical exercise in patients with coronary artery disease (CAD), and the provision of educational contents that improve patients' awareness on their condition and adherence to the rehabilitation program.

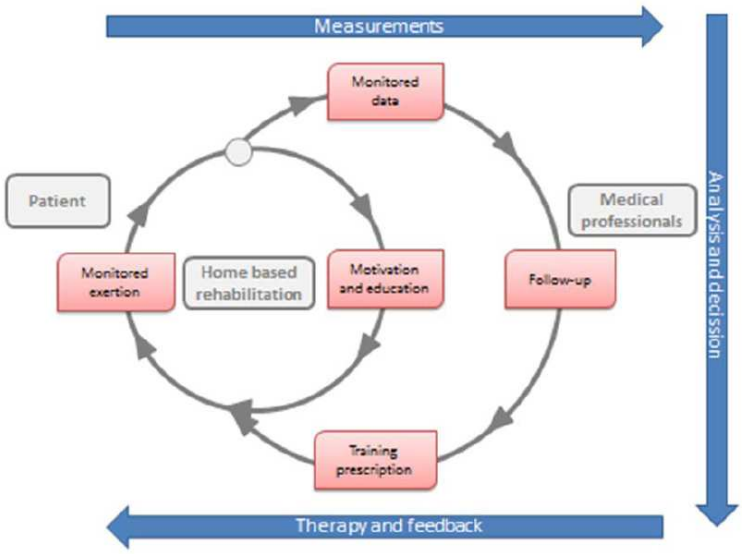

Figure 2 Closed-loop approach for GEx system

In this open, prospective, randomized, parallel group, German, British and Spanish, three-centre, Phase I study, the standard national approach to cardiac rehabilitation were compared to an approach adding the new training steering and feed-back GEx-System, which enables training at home supervised with heart monitoring and multimedia feedback.

a) Study object:

The object of this study was to determinate the improvement obtained in long-term adherence to home-based rehabilitation programs (cardiac rehabilitation – CR- phase III) when following a guided exercise training prescription supervised by an innovative system specifically designed compared to the standard usual care given in each country for this kind of patients. The innovative system consisted of a sensor that monitors the vital parameters during exercise training sessions, used in combination with a software that provided feedback of the patient based on the training prescription provided by the doctor and the level of exertion monitored.

b) Primary objective:

The main objective of this study was to evaluate, whether GEx system could improve physical capacities ($VO2_{peak}$) at 6 moths follow up after CR long term (phase III) home based compared to national standard of CR.

c) Treatments groups:

Patients were randomised to:

- Treatment according to national CR recommendation or
- Treatment according to national CR recommendation + GEx system.

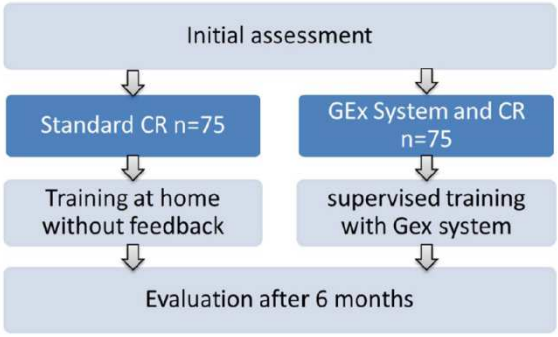

Figure 3 GEx study design

AUC:

The Assessment Use Case is shaping the various concepts and bringing together innovations from the various work packages to form an advanced decision support system via the combination of innovative sensors, computational algorithms and clinical knowledge. Expert knowledge was gathered and compiled into knowledge bases and supported clinical applications have been further consolidated and finalised. This allows to demonstrate how customized therapies and careplans might look in the future. This represents an opportunity to set up the bases to obtain new clinical and technical evidence that can be applied later on to the previous and other use cases and lead the path for the next generation of PHS closed-loop systems". The integrated Assessment Use Case Concepts (Haemodynamic Tailoring, Arrhythmias and Sleep Disorders) were tested in 2 clinical trials in the UK and Spain.

The validation plan for the Assessment Use case was based on a set of different activities to evaluate and test the elements that compose the assessment use case system:

- Hemodynamic tailoring system
- Sleep disorders and arrhythmia detection system
- Professional Decision Support System (entirely developed within HC).

The validation strategy designed for this case was structured in three main phases that would provide, in combination, a holistic assessment of the performance, utility and potential clinical impact of the three systems.

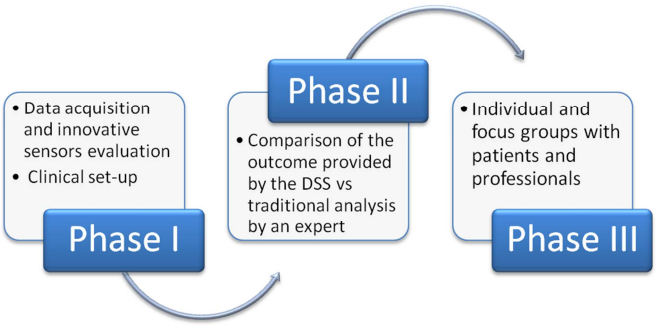

Figure 4 AUC validation phases

Goal was to take a series of measurements with the innovative sensors from two groups of patients in a controlled environment, assuring the medical supervision of the measurements and the reliability of the data collected.

Objective

To assess the capability to detect changes in patient status, in more detail to investigate whether the easily acquired parameters reflecting cardiovascular function can be used to evaluate the haemodynamic status of a heart failure patient during decompensation or get insights into sleep disorders or arrhythmias. These parameters have been evaluated by comparing them with standard assessment of cardiovascular and sleep function by professional experts.

Patients

Patients on stable, guideline-indicated therapy for heart failure, including a loop diuretic, who either have left ventricular dilatation and reduced ejection fraction or an NT-proBNP >400ng/L.

Study Execution

The three studies have been conducted in the last year of HeartCycle in different European countries.

	HFM (Hull UK, Heidelberg Germany, Bardelona Spain) 126 patients enrolled followed for 1 year
	GEx (Hull UK, Aachen Germany, Madrid Spain) 132 patients enrolled followed for 6 months
	AUC (Hull UK, Madrid Spain) 35 patients enrolled inside hospitals

Having clinical studies executed in a successful way requires a lot of interaction and team work between the participating partners. From the medical site these are the nurses doing recruitment, enrollment and the daily interaction with patients using HeartCycle technologies, the responsible principle investigators at each site and other medical staff experienced in performing and monitoring clinical studies. From the technical site these are concept champions, the sponsors, the HeartCycle partner providing technology or supporting daily management of the clinical studies. Intensive training for nurses how to use the HeartCycle systems is important for the engagement of nurses in recruiting enrolling and managing patents participating in the studies. The team work of all participants was successful and helped to find solutions in case technical problems occur and other upcoming issues.

Many onsite visits, meetings and telephone calls are needed to ensure that the trials are executed in a proper way. Additional measures have been applied e.g. observing monthly incoming data from patients (after anonymisation) to make sure the systems are used in the right way by patients as well as by nurses.

Most parts of the HeartCycle trials program were running better than expected, few problems due to technology obstacles occurred but overall the validation phase of HeartCycle can be seen as great success. The results obtained from the studies are very promising, confirming our hypotheses about what innovations are meaningful and can be applied via personal health systems.

Conclusions

Each of the clinical trials in the HeartCycle programme has produced important new information that will contribute importantly to the science of medicine.

1.4 Final results

Each of the clinical trials in the HeartCycle programme has produced important new information that will contribute importantly to the science of medicine. In general the innovations for the next generation of telehealth systems are working and are feasible. Detailed information will be provided on scientific publications soon.

The HeartCycle programme has made several giant conceptual steps forward in the arena of remote patient support and made some first practical steps. Uniquely, this has brought under one umbrella, novel sensor technologies, software development, the design of the patient- professional communication interface, clinicians and patients together to address the common and growing problems of coronary artery disease and heart failure. It is hoped that this consortium ('family') will continue to collaborate to investigate the rich data-set created, to increase knowledge and to provide new means of managing patients.

Another unique contribution of the HeartCycle programme has been the development of randomised interventions (medication withdrawal, changes in diet) designed to assess the reproducibility and sensitivity to change of a range of sensors. These have thrown up some surprises in terms of received wisdom. Overall, there is significant space to extend the analysis of the data presented in this document to extract meaningful conclusions that can drive the adoption of the more mature systems, this is, HFM and GEx, and direct the focus of research of the most innovative lines of work of the project constituting the AUC.

1.5 Impact and use

The consortium will pursue the publication of these results in different scientific journals and will continue to use the feedback received through the validation activities as input for the improvement of the prototypes developed within the project.

The completion of the three clinical studies of HeartCycle represents the closing of the final chapter of the highly successful HeartCycle project. The project, running since 2008, has seen several phases and generated much valuable research work in the cardiovascular domain. Starting with an exploratory phase, 3 concepts for improving the cardiovascular health of Europe were developed, analysing not only their technical aspects, but also their business value, and their potential to generate a clear clinical impact in the medium term.

A long list of partners were involved in the execution and analysis of these studies, and their hard work has resulted in the successful completion of the validation activities, providing valuable telemonitoring data which will the source of analysis for many years to come.

Activities have started by HeartCycle partners to prepare exploitation of the clinically validated HeartCycle innovations into markets.

The following table shows the contact details of the Project Coordinator. Project Coordinator – Project Manager.

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1.5.1 Public Project Website

The Public Project Website can be found on:

http://www.HeartCycle.eu

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Figure 5: *Project logo*