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D. 7.4 Use case deployment & evaluation

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Executive Summary

This deliverable is present the pilot deployment of CARRE service in two different sites for the initial assessment of system usability and its impact for the empowerment of patients. The service was deployed for evaluation in Alexandroupoli, Greece (School of Medicine, Democritus University of Thrace and the General University Hospital of Alexandroupoli) and the Vilnius University Hospital, Lithuania. The impact of CARRE was assessed via a randomized, single-blind controlled pilot study. Preliminary results revealed that CARRE service positively influenced participants increasing health literacy and empowerment. Also, participants reported an above average assessment of the usability corresponding to an acceptable system.

About CARRE

CARRE is an EU FP7-ICT funded project with the goal to provide innovative means for the management of comorbidities (multiple co-occurring medical conditions), especially in the case of chronic cardiac and renal disease patients or persons with increased risk of such conditions.

Sources of medical and other knowledge will be semantically linked with sensor outputs to provide clinical information personalised to the individual patient, so as to be able to track the progression and interactions of comorbid conditions. Visual analytics will be employed so that patients and clinicians will be able to visualise, understand and interact with this linked knowledge and also take advantage of personalised empowerment services supported by a dedicated decision support system.

The ultimate goal is to provide the means for patients with comorbidities to take an active role in care processes, including self-care and shared decision-making, and also to support medical professionals in understanding and treating comorbidities via an integrative approach.

Terms and Definitions

The following are definitions of terms, abbreviations and acronyms used in this document.

Term	Definition
AIDS	Acquired immunodeficiency syndrome
API	Application program interface
BP	Blood pressure
CSS	Cascading style sheets
CHF	Chronic heart failure
CKD	Chronic kidney disease
D3.js	a JavaScript library for producing dynamic, interactive data visualizations in web browsers
DBP	Diastolic blood pressure
DSS	Decision support system
eGFR	Estimated glomerular filtration rate
EMP	Empowerment
FG	Fasting glucose
HLT	Health literacy
HDL	High-density lipoprotein
HDL-C	High-density lipoprotein cholesterol
HIV	Human immunodeficiency virus
HTML5	Markup language used for structuring and presenting content on the World Wide Web
IDF	International Diabetes Federation
jQuery	A cross-platform JavaScript library designed to simplify the client-side scripting of HTML
LDL	Low-density lipoprotein
MCS	Mental Component Summary
MetS	Metabolic syndrome
NYHA	New York Heart Association
PHR	Patient Health Record
PCS	Physical Component Summary
RDF	Resource Description Framework
SBP	Systolic blood pressure
SF-36	36-Item Short Form Health Survey, as a part of the Medical Outcomes Study (MSO)
SPARQL	a semantic query language for databases, able to retrieve and manipulate data stored in Resource Description Framework (RDF) format
TGC	Triglycerides
URL	an address to a resource on the Internet
WC	Waist circumference

1. Introduction

The goal of CARRE service is to provide the means for the patients with comorbidities to take an active role in care processes, including self-care and shared decision making, and to support medical professionals in understanding and treating comorbidities via an integrative approach.

The deployment and evaluation of CARRE service addresses both CARRE sub-systems or interfaces, one for the patients and one for the experts. Following the evaluation methodology presented in D.7.1, we have concluded phase 1 on component lab testing (D.7.2) and phase 2 on system lab testing and understanding (D.7.3). This deliverable presents phase 3 of the service evaluation on a real setting.

This third phase of evaluation involves the following different parts:

(1) informative user satisfaction of system components, conducted in a controlled setting;

(2) an evaluation of the user satisfaction for the expert and the patient CARRE sub-systems (process); and

(3) an assessment of the effectiveness of CARRE service on the empowerment of patients (outcome).

User satisfaction for the risk factor management system was assessed via controlled experiments which involved medical experts performing preselected scenarios of use and then responding to structured questionnaires and forum semi-structured discussions.

User satisfaction of the patient empowerment system was assessed via

- controlled experiments which involved medical experts performing preselected scenarios of use and then responding to structured questionnaires and forum semi-structured discussions; and
- extended use of the system by patients in real deployment for a period of up 3 months and then responding to structured questionnaires.

The assessment of the effectiveness of CARRE service for the empowerment of patients involved a two-center clinical investigational study with two different groups of CARRE patients.

Section 2 summarizes the current state of development of CARRE service, including both subsystems (for the patient and for the expert) and gives technical details for the two working deployments of the system in Greece and Lithuania. Section 3 presents the informative assessment for the CARRE subsystem for the medical expert, i.e. the risk factor management system and the informative assessment for the CARRE subsystem for the patient, based on results from controlled experiments involving medical experts. Section 4 presents the clinical investigational evaluation study of the CARRE deployment in a real set-up involving two different sites. Section 5 brings the presumptive discussion and conclusions CARRE service evaluation and the implications thereof. Finally, Annex 1 presents various forms used for the clinical investigational study, and Annex 2 presents the instruments used for assessing CARRE impact.

2. CARRE service

CARRE innovation lies in semantic interlinking of 3 types of data (a) medical ground knowledge; (b) up-to date medical evidence; and (c) personal patient data, in order to create a personalized model of the disease and comorbidities progression pathways and to empower patient. Personalized model of comorbidities is used for shared decision support services targeting personalized education, complex risk calculation for disease progression and comorbidity trajectories, creates alerts for personalized monitoring. Visual presentations forms the basis for patient empowerment services.

2.1. CARRE for the patient

CARRE system has been implemented as a web-based tool for integrated visualisation and analysis of personalised measurements and risks. The risk model and measurement data is stored as RDF triples on the

server and accessed by the client sides via SPARQL queries. The data analysis and visualisation are implemented in JavaScript with the use of HTML5, CSS, jQuery and the visualization library D3.js.

The role of visualisation is to visualise health data, risk factor data and provide integrated visual analysis of health data and risk factor data. In CARRE the data can be generally categorised as fitness measurement data collected from sensors, medical biomarker measurements from personal electronic health records (PHR) and risk model data extracted from medical literature. To gain intuitive knowledge of the health status data and the risk data, visualisation is employed in CARRE to provide patients and clinicians with the ability to view, understand and interact with this linked knowledge and take advantage of personalised empowerment services. The aim is to help patients to understand their own health status and risks, which in turn empower them to take more active control of their health self-management and disease treatment.

Based on the risk model and the personal health data, the visualization design requirements of CARRE include:

- visualisation of individual's measurement data, including fitness data and PHR data, to help users to understand the data; and
- visualisation of individual risks and allowing for analytical analysis of the impact of behaviour changes to the risks to help the patient to understand the relations between the outcomes and their behaviours.

CARRE provides web-based components for interactive health data visualization and risk analysis, including dashboard for health information summary, Healthlines for fitness and biomarker data, and interactive risk evaluation diagram for risk monitoring and analysis.

2.1.1. Dashboard

There are many components and data that can be accessed by the user from the CARRE visual interface. However, as there is a variety of data sources and visualisations, it is very difficult for a user to grasp an overview with important notifications from the scattered health status information. To present the user a quick overview of their health status, CARRE provides a dashboard as the front page. The dashboard is the entry point of the CARRE visual interface which provides a summary of the user's latest health status with important notifications, including latest measurement, the current risk status and the latest risk alerts (Figure 1).

2.1.2. Visualization of measurements

Fitness and medical measurement data are inherently time dependent. To visualise time-varying data, a linear form timeline is a natural choice and has been used by many of the previous works. To visualise multiple variables, the CARRE Healthlines, a special form of timeline group, is used to visualise multiple variables of fitness sensors and biomedical markers. Data trends can be observed and data correlations may be discovered by comparison of the data curves of the multiple variables. As the data records may cover a long period, interactive techniques such as zooming and overview of detailsare employed. The users can also select the interested variables from the variable list by drag-and-drop. Figure 2 shows multiple measurements visualised in the interactive healthline in CARRE.

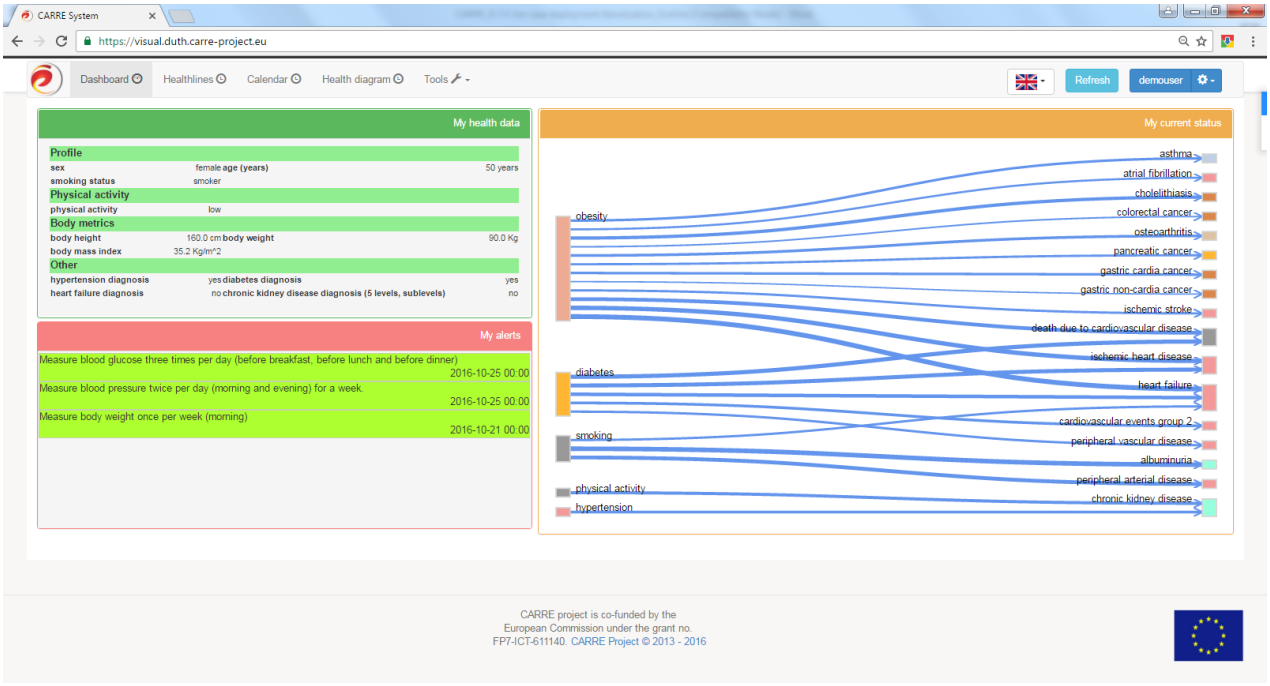


Figure 1. CARRE Visual Interface Dashboard

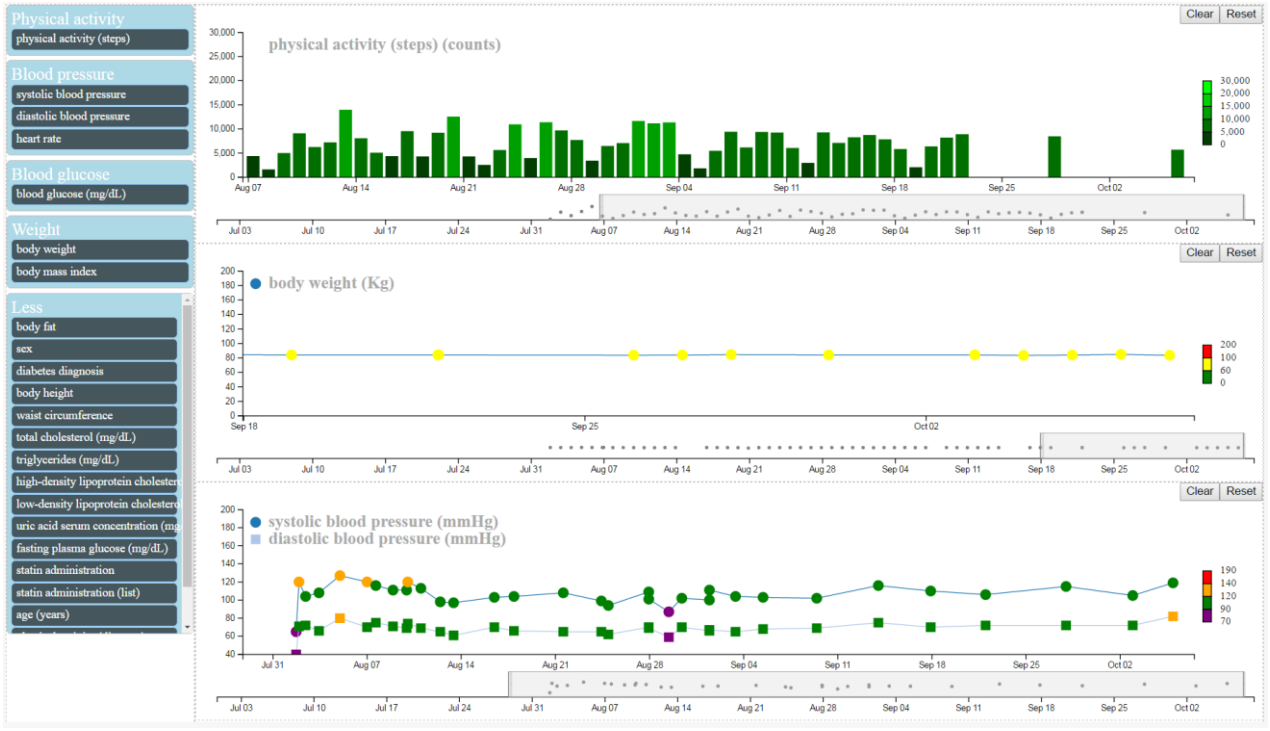


Figure 2. The healthline visualises personal fitness and biomarker measurement

2.1.3. Interactive visual risk assessment of an individual patient

CARRE aims to integrate the measurement data and the risk factor database to promote patient empowerment and individualised risk assessment and management. To achieve this goal an interactive risk evaluation diagrams designed and implemented based on the risk model and measurements, both real and simulated of the user. The visual interface is composed of a risk node-link diagram and a measurement slider panel. The risk assessment is performed by the risk condition per se which takes the risk evidence condition equations and the measurement values as input and evaluate them if the conditions hold true. For example, if the blood pressure drops to the normal range, the hypertension risk element may disappear. In another example if the user walks more, the obesity risk element and all risk factors related to obesity may disappear.

To empower the patients to perform interactive risk analysis, a node-link risk diagram and an interactive measurement slider panel are introduced as the user interface to enable the user to understand potential risks, and the ways to reduce existing risks. By interactively adjusting the measurement values in the slider panel, the risks highlighted in the node-link diagram may emerge, grow, shrink or disappear to reflect the risk changes with the patient's predicted conditions.

2.1.3.1. The risk diagram

The risk diagram is an interactive force-directed node-link diagram visualization where the nodes represent the risk entities and the links represent proven risk progressions (associations) extracted from medical literature. Though all the risk associations in the CARRE system are included in the diagram, only those risks that are considered highly possible by the risk condition parser based on the risk model and the patient's measurements are highlighted in the diagram, as shown in Figure 3, thus reducing the visual complexity.

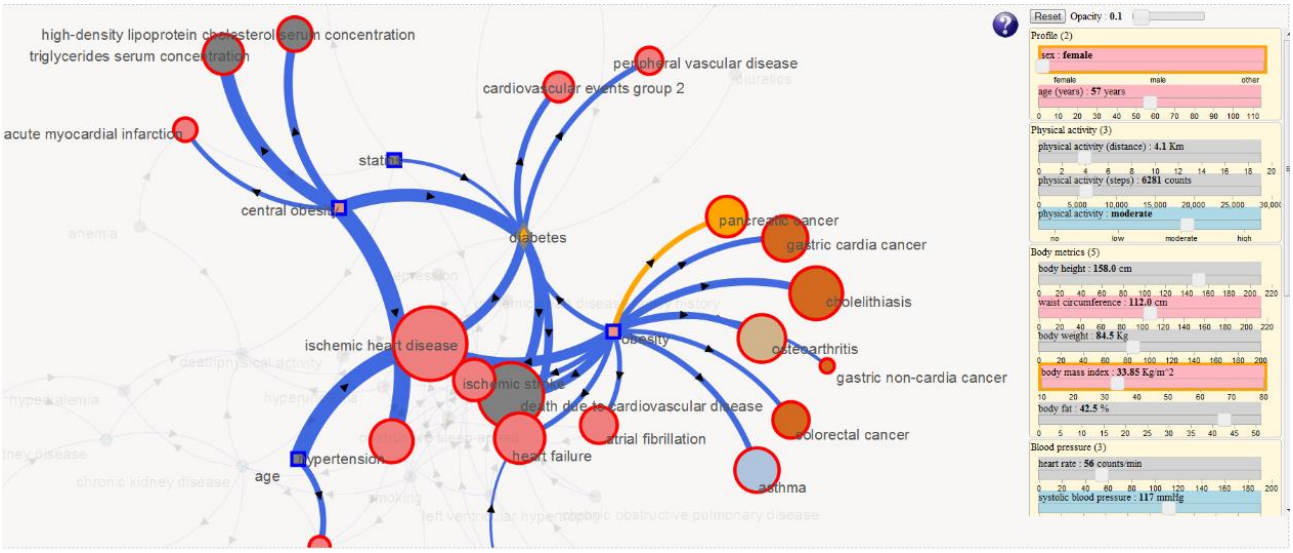


Figure 3. Interactive risk analysis: risks highlighted and changed according to individualised measurements

The node fill colour represents the general disease type based on disease ontology, while the border colour and the shape of a node represent the risk element types: risk source, risk target or both.

The size of a node indicates the estimated scale of risks: the higher the risks, or the number of the incoming risk sources, the larger is the node size. However, this size is only used in an indicative sense for patients and does not reflect the real risk probability.

The direction of the link represents the direction of the risk association and the thickness of the links represent the relative risk ratio of the risk association.

The risk elements and associations that do not apply to the user are visualised with a transparency as the background in the diagram. The opacity can be adjusted by the opacity slider in the right panel.

2.1.3.2. The measurement slider list panel

The measurement slider panel is introduced to enable the user to understand potential risks and the potential ways to reduce existing risks. Risk predictions can be made by interactively adjusting the measurement values in the slider panel to reflect the risk changes with the patient's predicted conditions dynamically. The slider list shows and allows adjustment of all the numeric, enumerate and boolean measurements of the user.

The background colour of the sliders represents if the measurement relates to the risk model and user risks. A grey slider background implies the measurement is not directly associated with any risks in the risk model while light blue and pink indicate the potential risk measurements and the acting risk measurements respectively.

When the user clicks on a risk link, the link is highlighted. Meanwhile the borders of related acting measurement sliders will also be highlighted to remind the user the corresponding measurements of the selected risk association (disease development), as shown in Figure 3.

2.1.4. Personal medical data entry

PHR manual data entry system is a system, where the patient is able to enter her/his medical data. PHR manual data entry system is being used by patient primarily to enter observable measurements that cannot be entered via devices. These are measurements such as disease diagnosis.

PHR manual data entry system is based on observables that are defined on public RDF. PHR allows entering of those observable measurements into private RDF. PHR works as a website system, thus it can be accessed by navigating to PHR' URL in the internet browser.

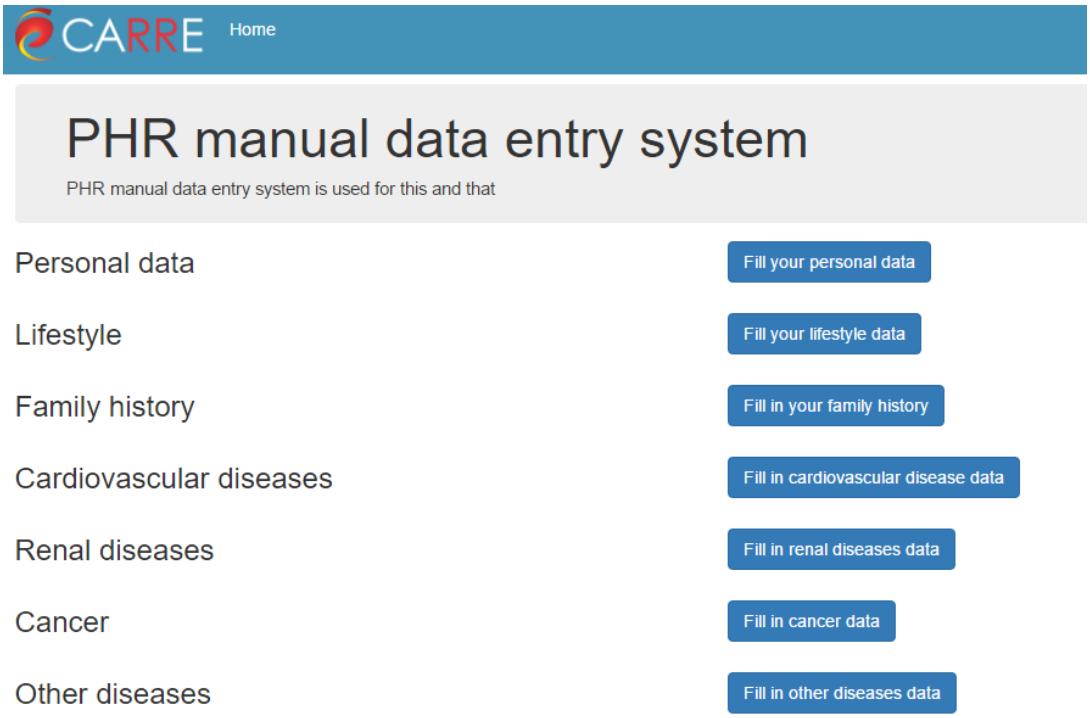


Figure 4. PHR manual data entry system

PHR manual data entry is realised by grouping observable measurement inputs into related categories – forms. Following categories were established: personal data, lifestyle, family history, cardiovascular diseases, renal diseases, cancer, other diseases, biometric measurements, laboratory tests, drugs (Figure 4).

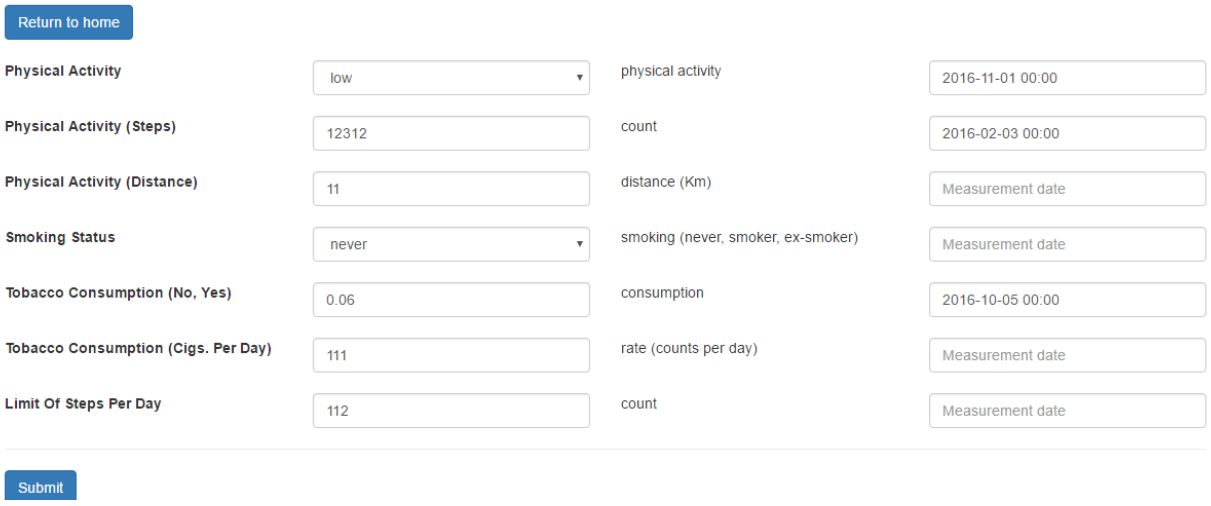


Figure 5. PHR manual entry form.

Every form has a list of observables that are assigned to that form. If observable type is scalar - simple text input field is generated for it, for boolean type observables - a checkbox, for enum - dropdown. Every measurement has an optional attribute of date (for an instance when the disease was diagnosed), if the date field is left empty it is defaulted to current day (Figure 5).

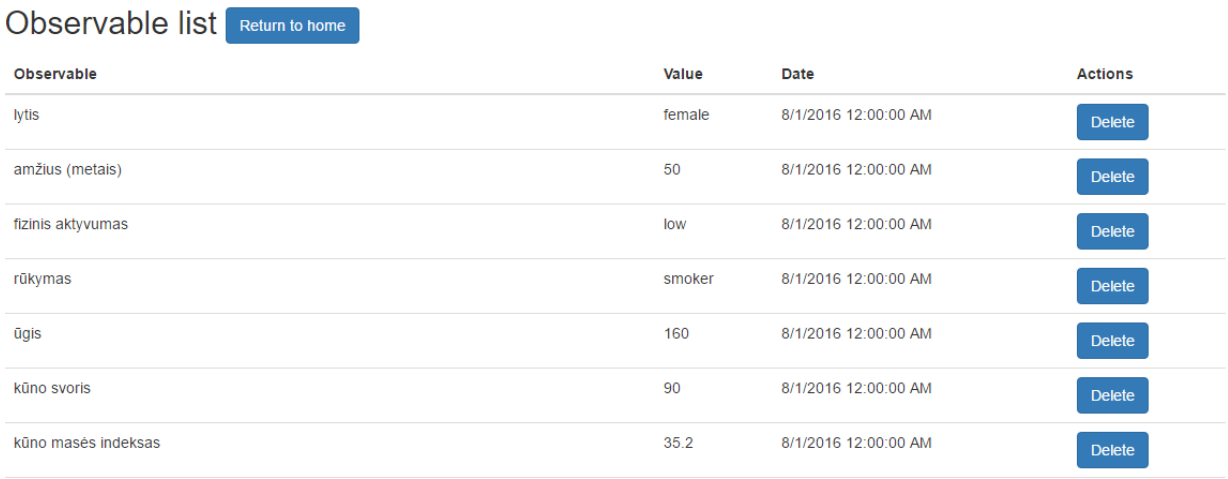


Figure 6. PHR's saved observable list.

Saved observable measurements can be viewed in the aggregated list, where they are sorted by their measurement date. From the same list, measurements can also be deleted (Figure 6).

PHR manual data entry systems' entry forms are realised by dynamically generating their inputs based on data that is retrieved from public RDF, this allows easy addition of new observable measurement input fields to the system.

2.1.5. Decision support

In CARRE system decision support service will determine the optimal solution, predict future trends and patterns based on information data analytics and formal reasoning formed on ontologies, which are the main techniques supported by RDF Linked Data, which then will be the main source of decision recommendations for CARRE. Together with Interactive Visual Interface, DSS will support patient application, by providing user-friendly visualisation of the current disease status with appropriate personal recommendation and advices to his lifestyle.

It should be mentioned that this tool's API for supporting alerts entry system was implemented as a separate part of CARRE RESTful API described in D.4.1. This application is a RESTful API developed using Flask, which is a Python-based web Framework.

Decision support service retrieves the data over RESTful web service APIs, provided both by the public and private CARRE data repositories. After receiving the appropriate data the DSS analyses the data to determine optimal recommendations and solutions for the patient to fulfil following users queries and interactions with this system component. Based on assessment of inputs from semantic data entry system the Personal Patient DSS should select educational materials based on current disease state and risks, suggest personal diet adherence and physical activities plan as well as provide alerting mechanisms and appropriate advises for changes.

All the above pieces of information are sent to private RDF Repository to be an input data to Interactive Visual Interface, by means of text recommendation to intuitive and user-friendly visualisation in patient application.

The risk alerts calculated by the DSS module are stored in the private repository and can be accessed for risk alert visualisation by components in the visual interface. Figure 7 and Figure 8 bellow show the risk alert visualisation after risk alert calculation.

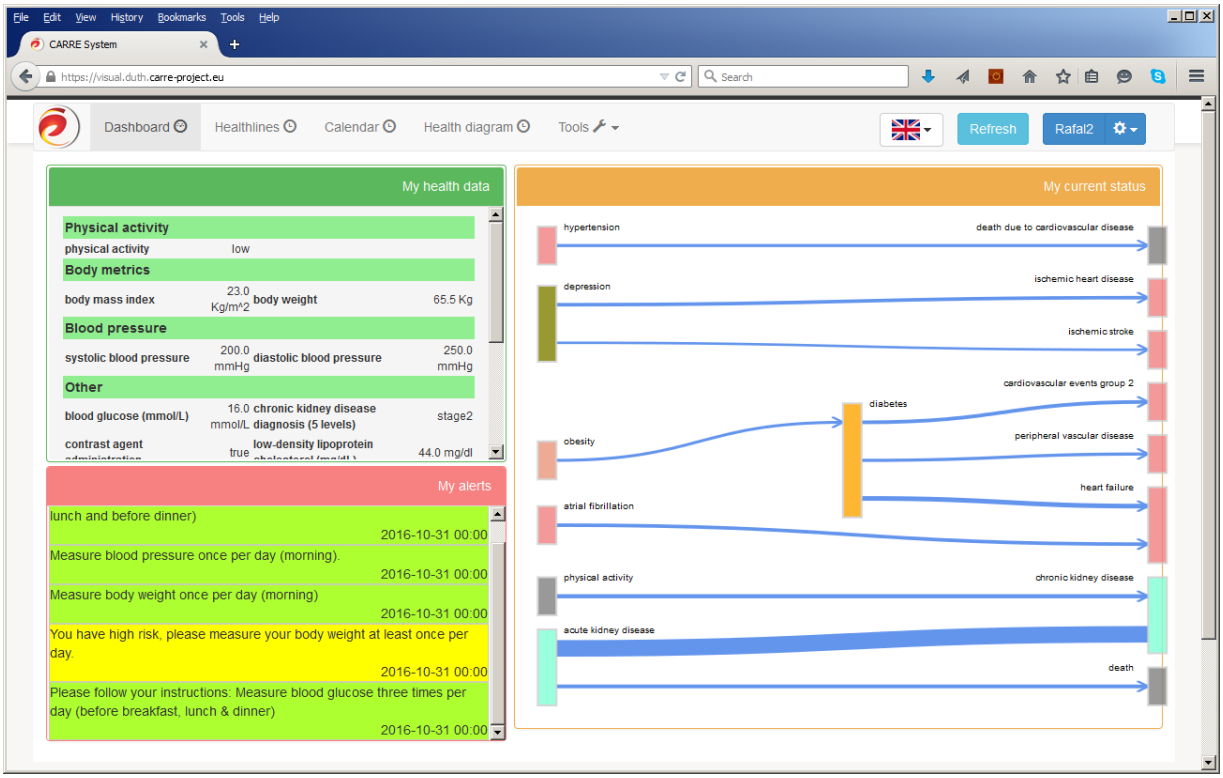


Figure 7. DSS Alerts visualization (as a part of main user interface)

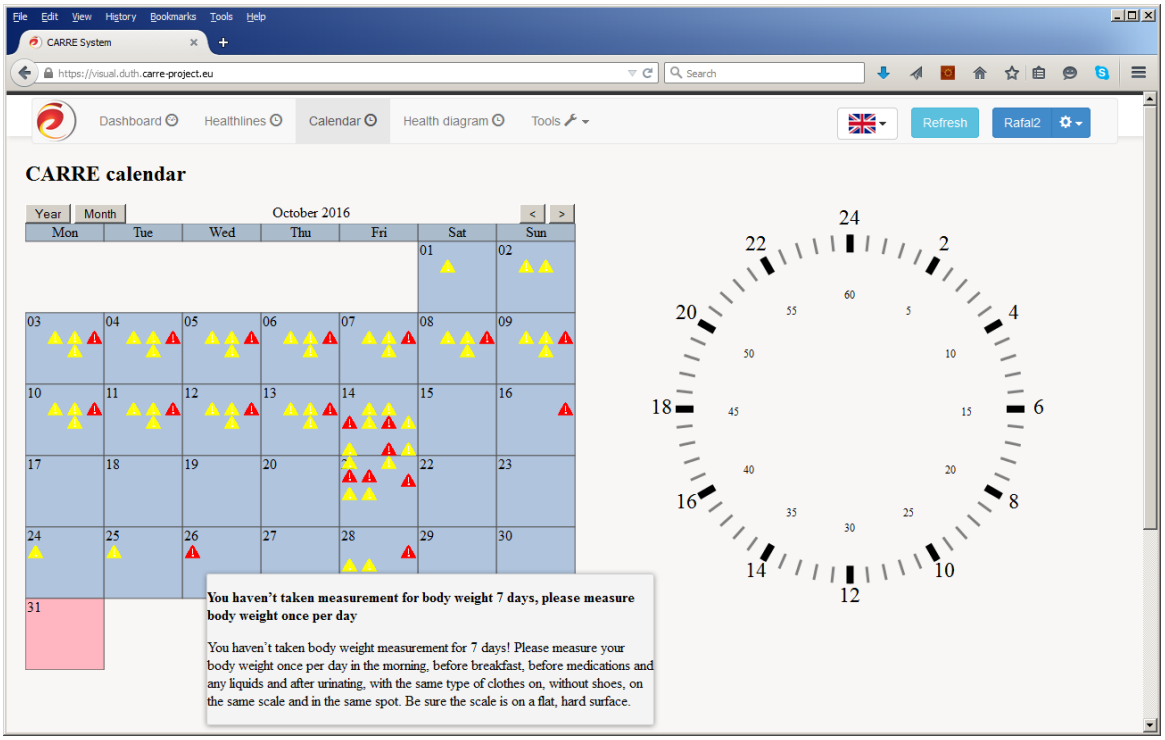


Figure 8. Historical DSS Alerts visualization

2.1.6. Personal sensor data aggregators and CARRE Devices site

The sensor data aggregators and the CARRE Devices site (as described in D.3.2) are responsible for handling user authentication with CARRE, and with the third-party sensor manufacturer cloud sites, as well as the aggregation of sensor data and its enrichment with RDF according to the CARRE ontology for storing in the semantic repositories. The aggregators were deployed on the relevant servers and configured for the appropriate networks.

The major change in deploying the aggregators outside of the original OU server was the necessity to configure new application keys with each third-party manufacturer cloud. To communicate with, for example, Fitbit[1], each application requires a set of authentication credentials provided by the manufacturer which are used for communication with, e.g., the Fitbit API. These credentials, for security, will only work on a single server at a time – the manufacturer must have the ability to send a confirming message back to an application server in order to avoid attacks via client spoofing. We thus needed to configure separate sets of credentials for each of the deployments. Doing so introduced some difficulties –in particular, we uncovered an issue internal to the Fitbit API in which neither of the CARRE use case servers receives notifications when registered users have synchronised new data from their devices. This issue is still unresolved. The workaround involves configuring the use case servers to make periodic (daily) requests to Fitbit to check for new data. It required a certain amount of experimentation to ensure that data synchronisation ended up working as smoothly on the use case servers as on the original OU-hosted server. We are monitoring and adjusting this process throughout the trials to make sure it continues to perform.

The aggregators collect measurement data from the third-party cloud APIs and store the data as RDF in the private RDF repository, as required.

[1] http://www.fitbit.com

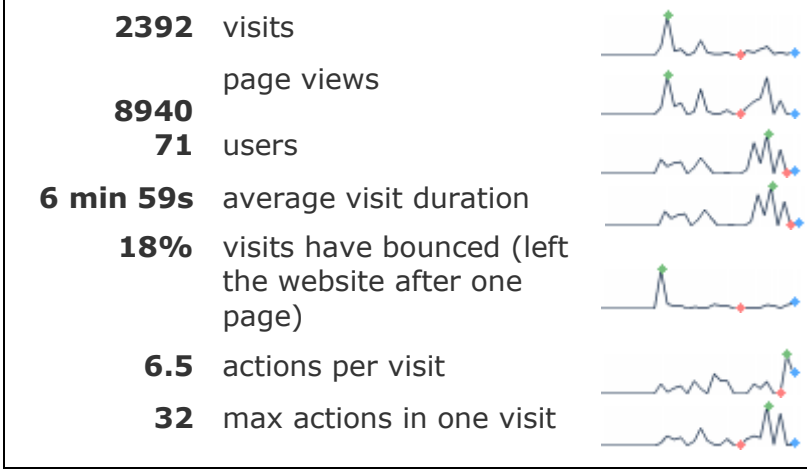
2.1.7. Analytics of visitors

An analytics service has been deployed for the monitoring of the system use by patients. The software used is a customized version of Piwik[2], an open-source analytics platform. CARRE analytics is deployed at https://analytics.carre-project.eu and is currently serving as privacy enhanced analytics system for sensitive-private data and restricted areas. CARRE analytics is also integrated with proprietary analytics software like Google Analytics for public websites and data. Such tools are essential for real time analysis and research as they provide immediate user feedback by sending daily reports and thoughtful insights regarding user's actions and intentions.

An example of analytics report is shown in Table 1 and Figure 9, which summarizes a snapshot of CARRE service usage for a period of one month by patients in the two deployed pilots in DUTH and VULSK (for a detailed pilot description see Section 2.3 and Section 4).

Table 1. Summary report of system usage by patients in the pilot deployment during October 2016.

2392	visits
8940	page views
71	users
6 min 59s	average visit duration
18%	visits have bounced (left the website after one page)
6.5	actions per visit
32	max actions in one visit



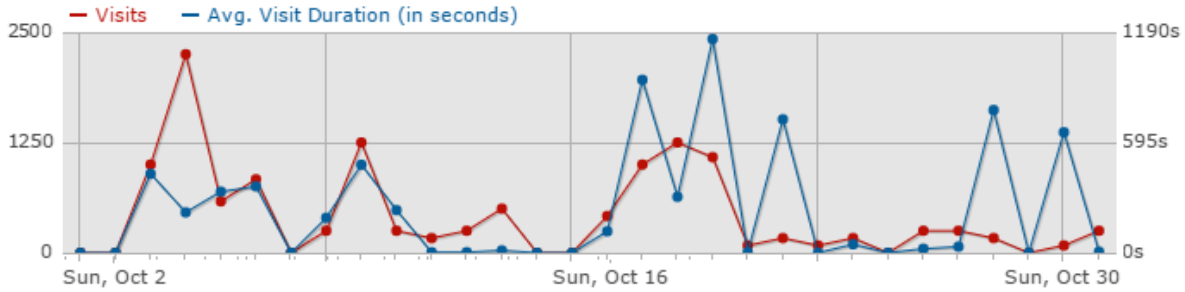


Figure 9. Number of visits and average of visit duration for both sites deployments (Oct. 2016).

2.2. CARRE for the medical expert

The core of CARRE functionality revolves around the concept of comorbidity, and in particular comorbidities in the case of cardiorenal syndrome. To enable the open and seamless use and reuse of these described medical risk factors, we have developed an on-line web based system for their description. Also, the resulting risk factor descriptions are available as Linked Data, in the Resource Description Framework (RDF) format [**Error! Reference source not found.**], via an open access RDF repository. The system has been designed

[2] https://piwik.org/

based on the concept of microservices architecture[3] and is implemented in HTML5 and JavaScript using the AngularJS framework[4]. The application follows a graph data model and the data scheme is described by the CARRE risk factor ontology.

2.2.1. Risk factor system dashboard

The risk factor management system is available publicly at https://entry.duth.carre-project.eu/ and also via the project web site. The landing page is the system dashboard which exhibits a summary of the system functionality and repository content. As shown in Figure 10, the landing page explains graphically the concept of risk factor and how this is treated in CARRE and also gives dynamic statistics of the repository contents; the menu on the left allows access to the system functionalities; more information on the risk factor concept and the functionality of the system can be accessed via the help menu (at the top of the menu bar) as seen in Figure 11. A registered medical expert can also login into the system (right upper corner) and thus gain access and authority to edit the risk factor information and add new risk factor data.

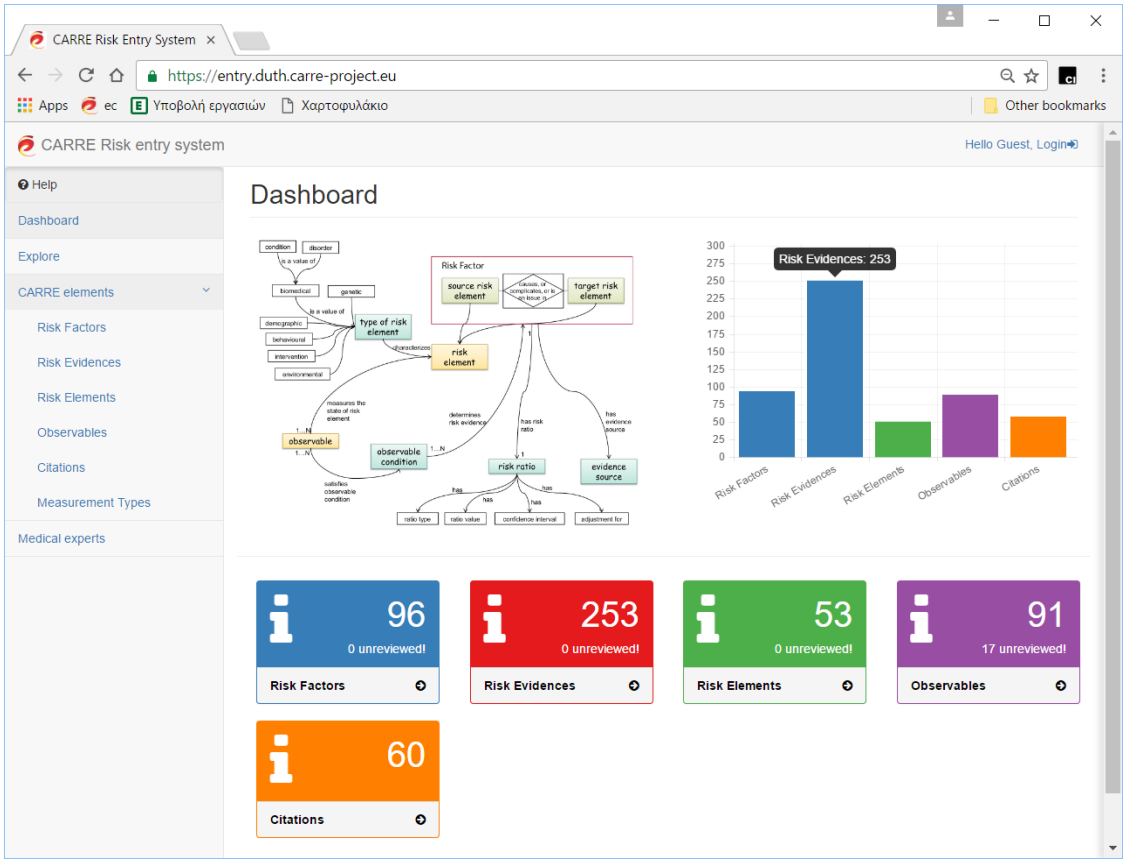


Figure 10. Rik factor management system: landing page.

[3] Namiot, D., Manfred, S.-S.: On Micro-services Architecture. Int. J. Open Inf. Techn. 2 (2014) 24–27

[4] Google; AngularJS framework https://angularjs.org/

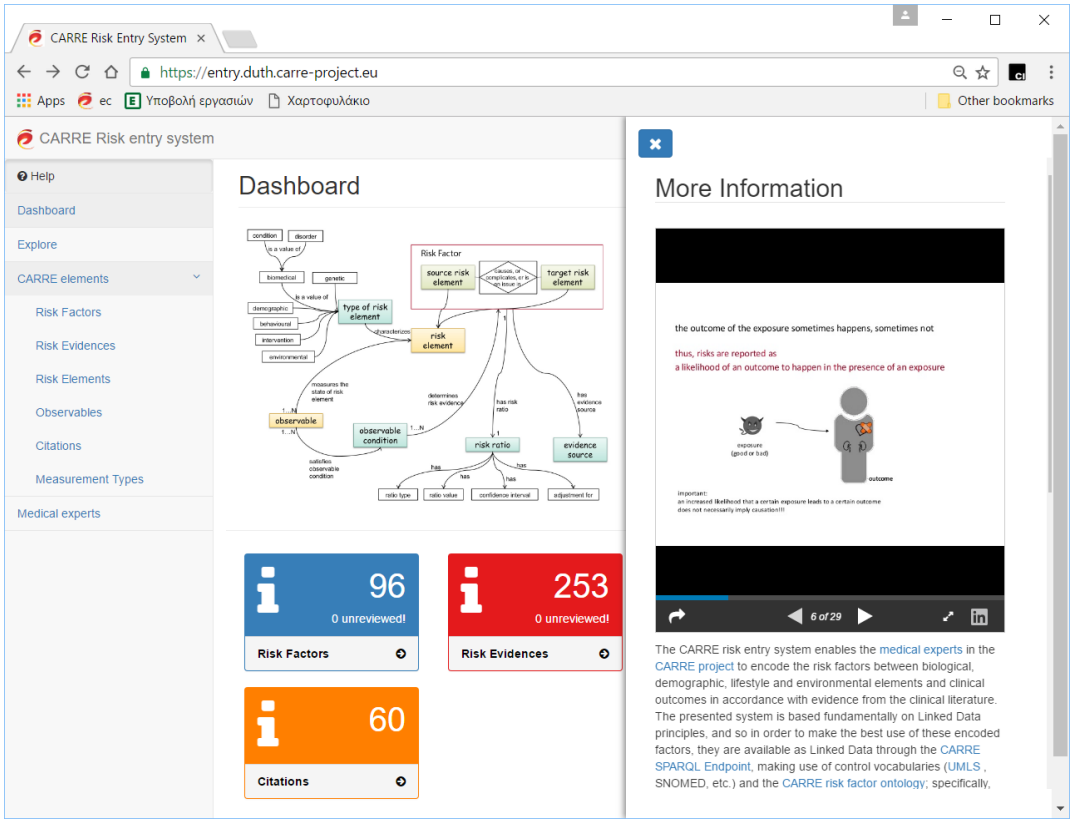


Figure 11. Rik factor management system: system help and information on risk factors.

2.2.2. Risk factor system: CARRE elements

The CARRE elements menu directs the medical expert to a flexible and customizable browser of the risk factor database. The Risk Factors tab displays a searchable list of the risk factors. The columns displayed can be customized in terms of their order or appearance and amended by the user to show more or less risk factor attributes by the icon on the upper right corner of the list (Figure 12). Search filters can be applied and data can be exported as a cvs[5] file.

By clicking on the icon on the left of each risk factor the user is directed to the detailed risk factor description page (Figure 13). This page displays detailed information on the risk factor including editors (i.e. the medical experts who inserted and reviewed this risk factor). The bottom half of the page is reserved for a customizable list of the individual risk evidences on this particular risk factor. These are also displayed graphically on the upper right part of the screen. The user can explore this rich graphical window to filter evidences by ratio value and display a quick view of the risk evidence data.

By clicking on the icon on the left of each risk evidence the user is directed to the detailed risk evidence description page (Figure 14). This displays all the detailed information on the risk evidence. Also, the abstract of the particular journal publication of this risk evidence is displayed on the right half of the page, with a link to direct the user to the PubMed citation. The risk elements (source and outcome) of this risk evidence and the observables used in the condition are active links that can bring the user to the description of the element or observable (Figure 15). These descriptions also display the respective terms from controlled medical vocabularies (e.g. where available the UMLS identifier or other related standardized terminology, e.g. ICD-10). The risk element description page also displays a cord diagram with the various risk connections for this element with other elements in the database. All description pages give the ability for the user to export data in cvs and also view and export data in RDF format.

[5] CVS, Comma Separated Values, is a simple file format used to represent tabular data and commonly recognized by software that handles such data, e.g. Microsoft excel or OpenOffice calc, etc.

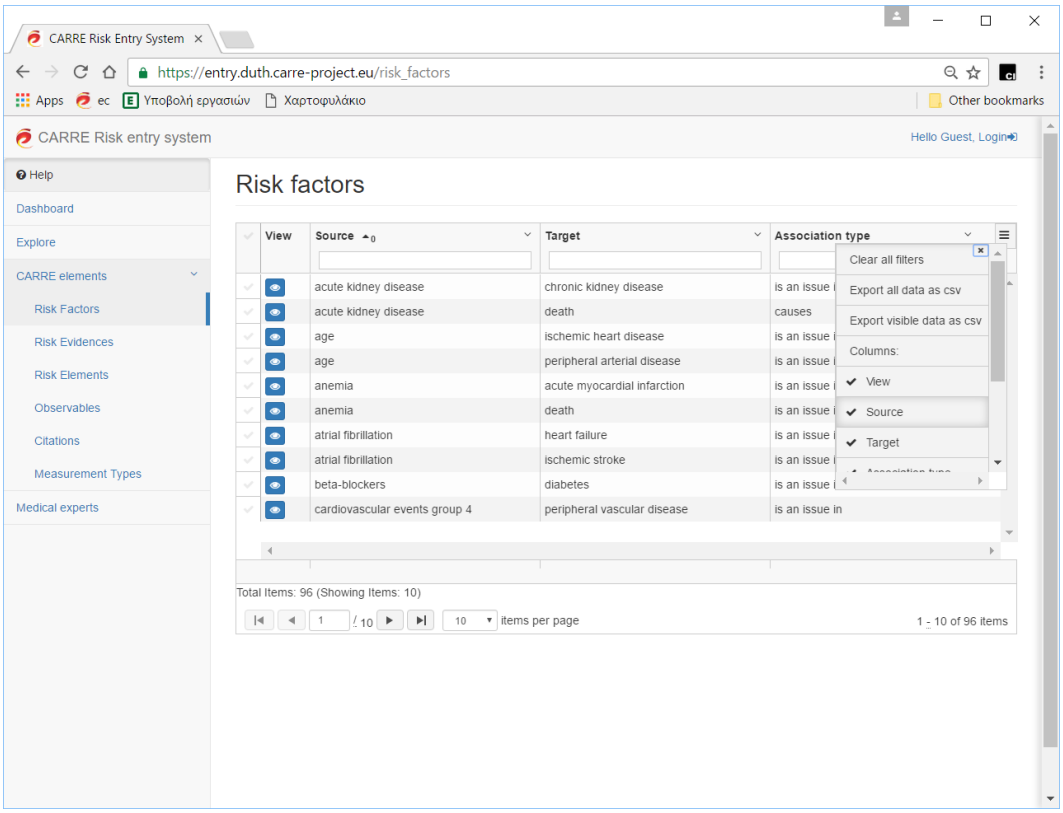


Figure 12. Risk factor list.

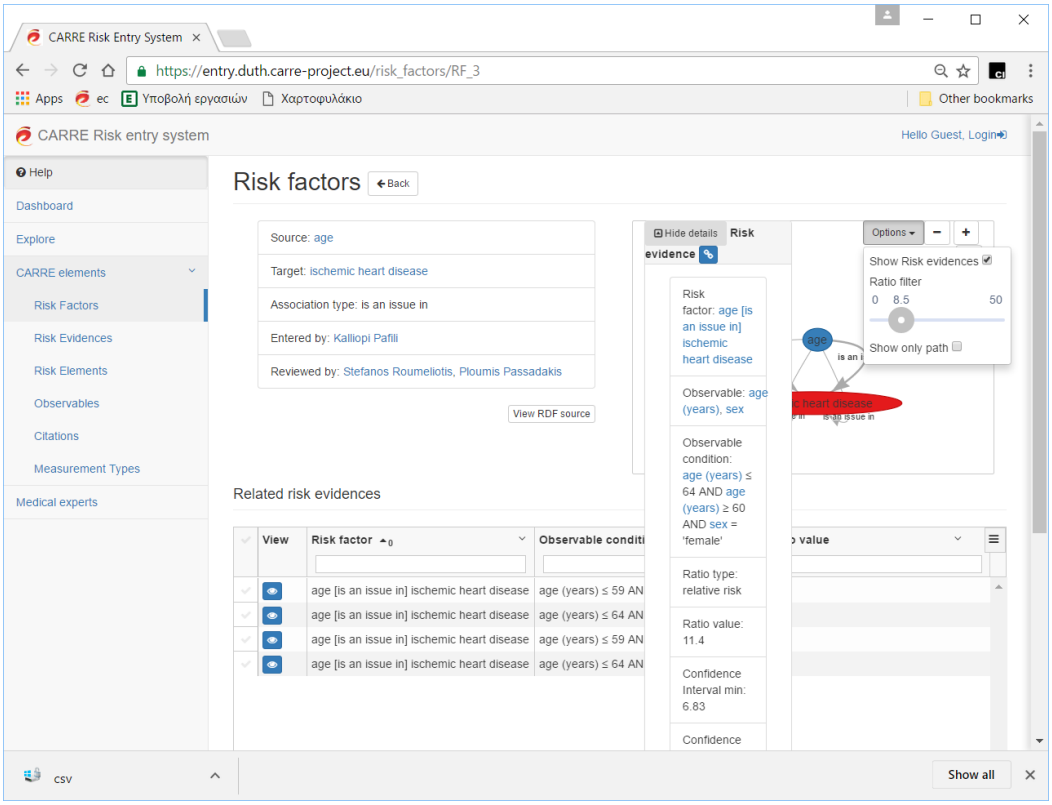


Figure 13. Individual risk factor description page.

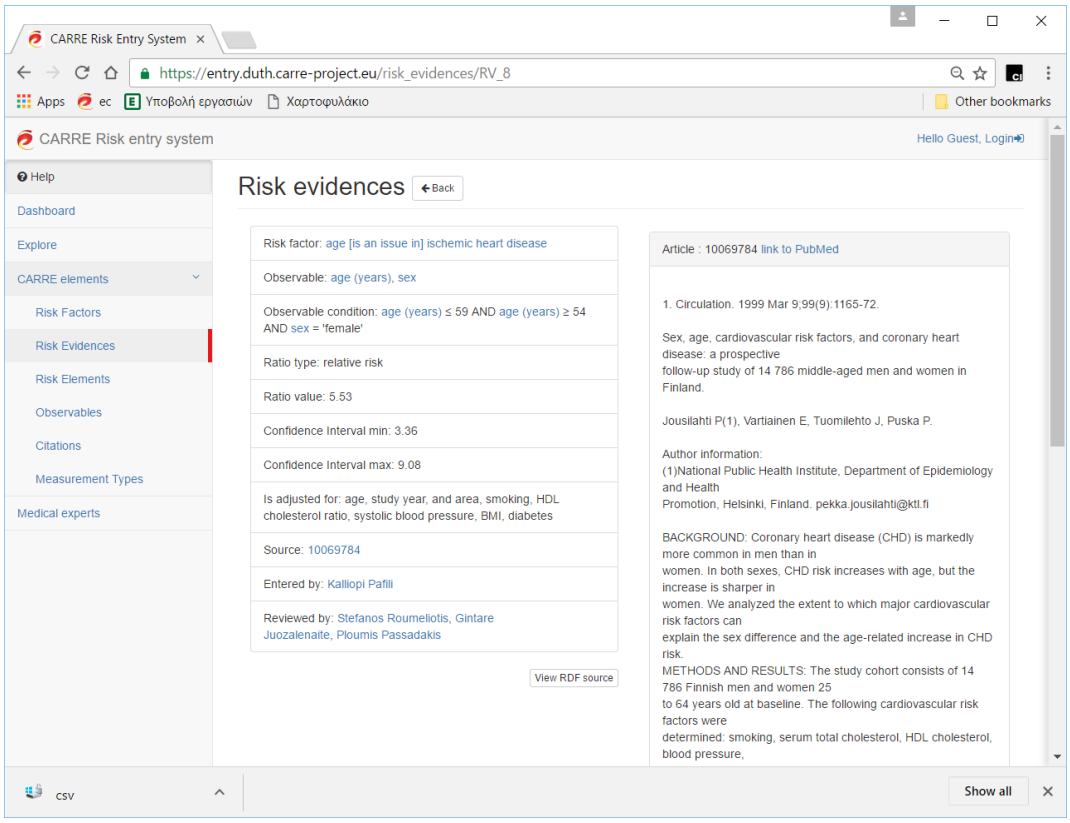


Figure 14. Risk evidence description page.

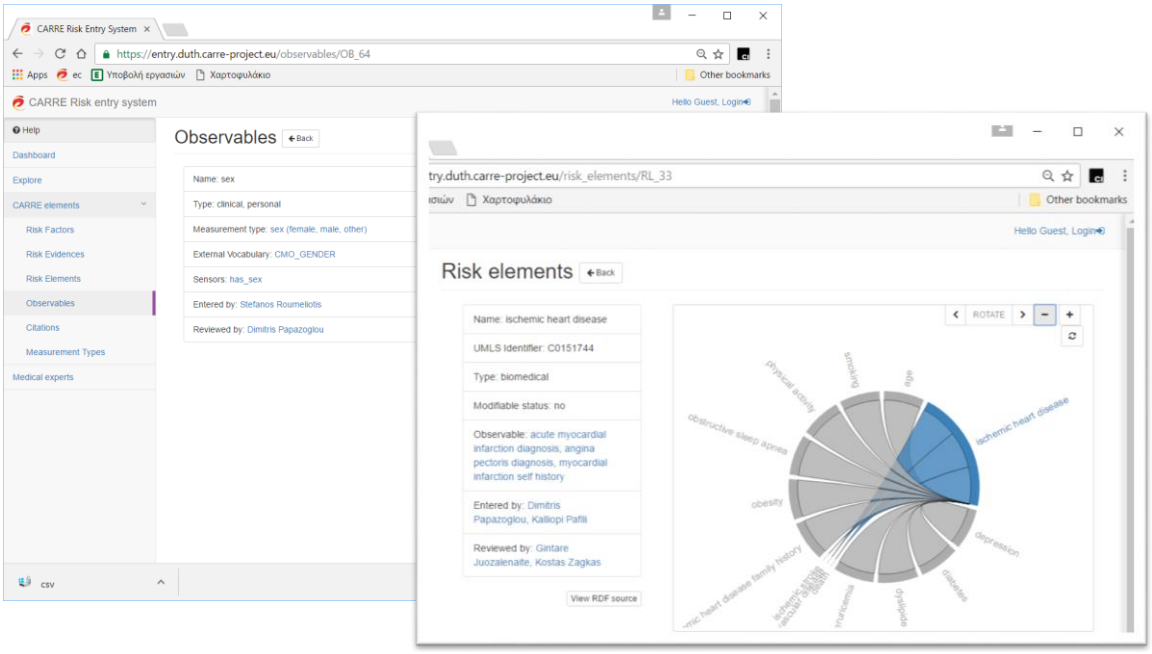


Figure 15. Observable and risk element description pages.

2.2.3. Visual exploration of risk factor data

The risk factor data can also be graphically explored via the *Explore* tab on the menu bar. The user can insert search terms, based on which the graph display is constructed. Display options include the conventional network graph, the Sankey and the cord representation (Figure 16). Clicking on each element brings up more risk connections of this element and expands the graph. Other options include showing risk evidences and filtering them based on ratio value (Figure 17).

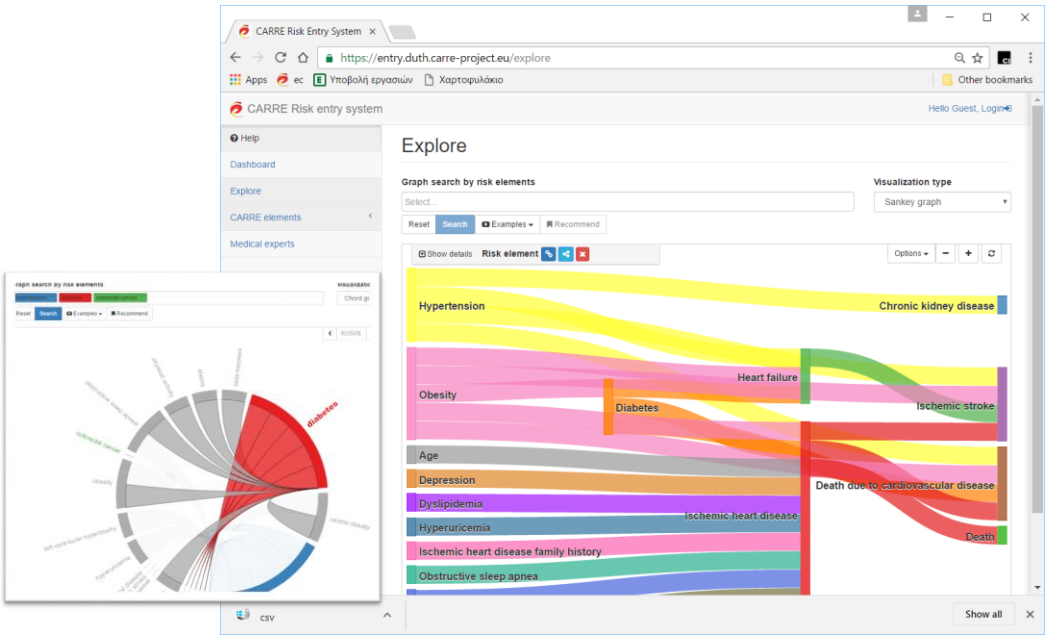


Figure 16. Graphical exploration of the risk factor data using the sankey and cord diagrams.

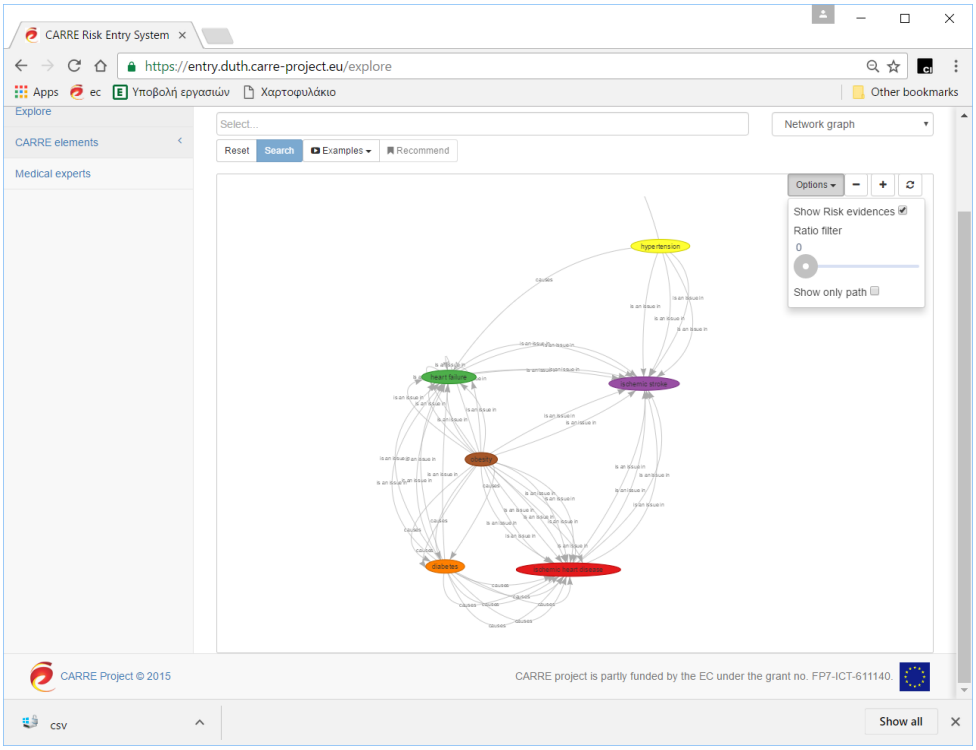


Figure 17. Network graph representation of risk factor data showing the filtering option.

2.2.4. Editing risk factor data

Registered (certified) medical experts can login and thus gain authentication to edit risk factor data. Once a user is logged in, the interface displays the *edit* option as an additional icon to left of the name of each element (risk factor, or risk evidence or observable or element) the and *add new* option as button on each element page. Figure 18 shows an example of how risk evidence browser is modified for the logged in user.

When edit option is selected, the detailed information of an element's description turns into a dynamic editable form and the user can change data. For convenience, the respective PubMed abstract and link to citation is also displayed (Figure 19).

To support user friendly editing of the observable logical condition a special component has been developed (Figure 20). This allows the user to create graphically new blocks of observable conditions visually grouped between logical operators (OR, AND) and where needed nested.

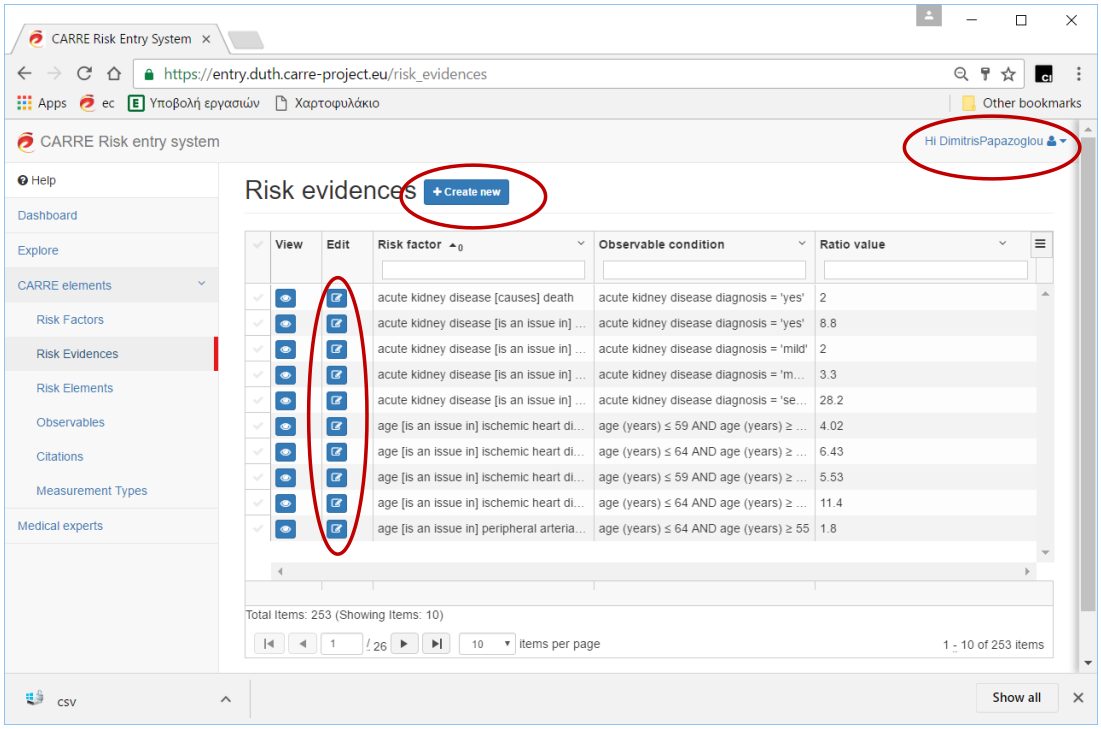


Figure 18. Risk evidence browser view for the logged in user.

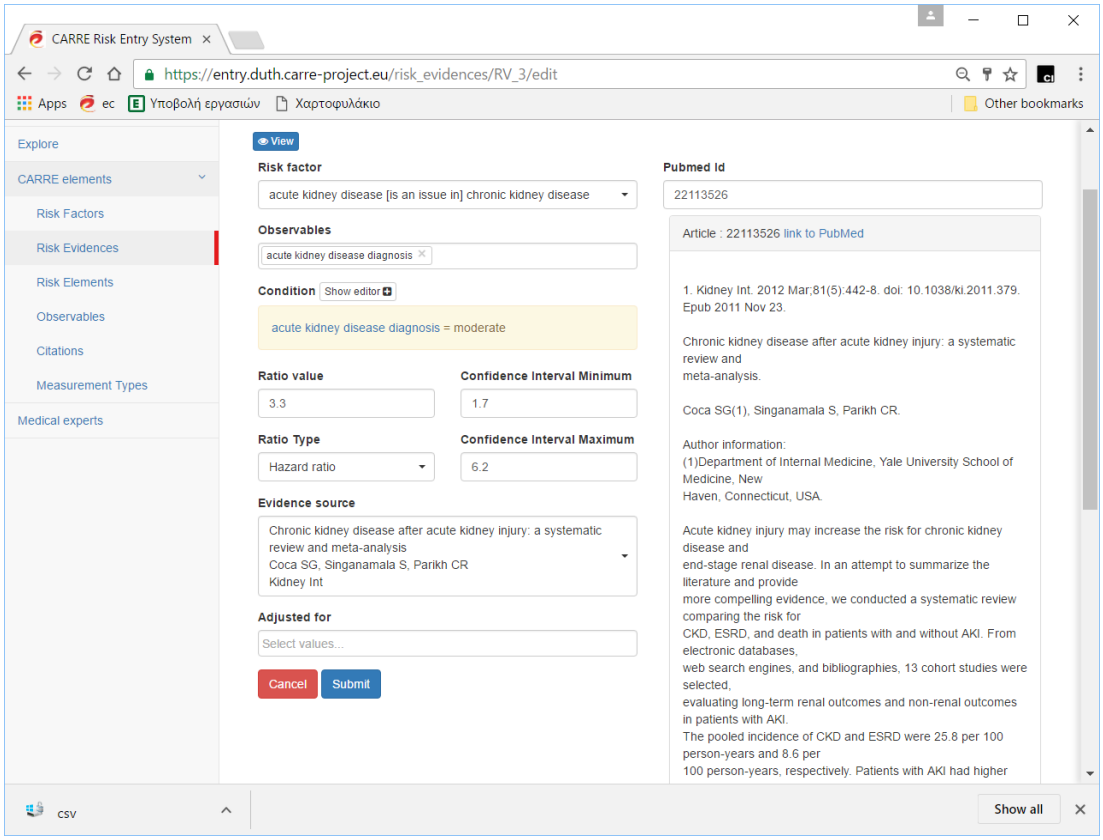


Figure 19. Editing a risk evidence.

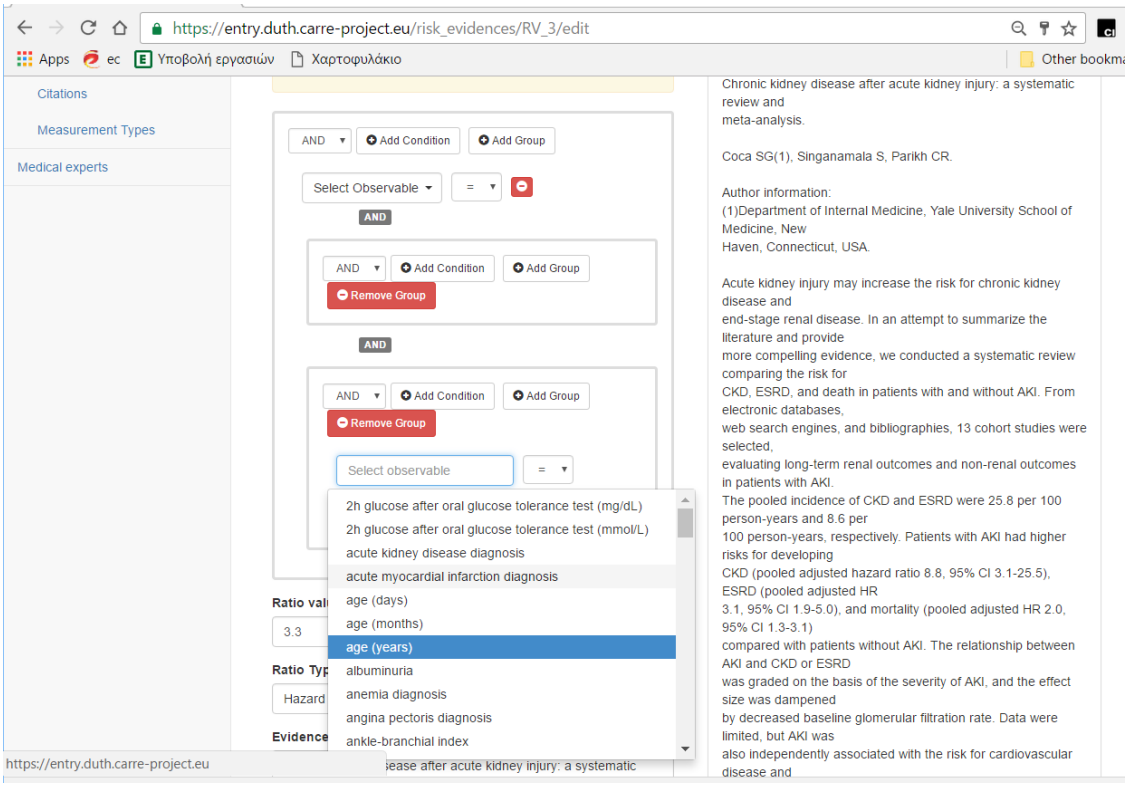


Figure 20. Graphical condition editor.

2.3. Pilot deployments of CARRE service

Based on the DoW, the evaluation of CARRE service requires to the service to be deployed in two different healthcare settings and nationalities, i.e. in the University Hospitals of VULSK (Lithuania) and DUTH (Greece). To account for legal, privacy and administration issues we deployed the CARRE service into two different exact copies, each copy installed in the facilities of each of the pilot hospitals. Additionally, we continue to support another working deployment which serves as the working development prototype for testing all bug fixes and new improvements before these are deployed (when stable) on the pilot implementations:

- Working development deployment: https://visual.carre-project.eu
- DUTH deployment: https://visual.duth.carre-project.eu
- VULSK deployment: https://visual.vulsk.carre-project.eu

Each pilot deployment (DUTH and VULSK) only constitutes of two virtual machines (VMs) that includes all CARRE subservices. The need of two VMs was necessary because some subservices are developed for Windows-based and some other for Linux-based platforms. The technical details of these VMs are shown in Table 2 and Table 3.

Table 2. Server details of Linux-based platform.

CARRE subservices	
– Visual interface – Data aggregators (sensor, PHR and management of them) – Access control component (including RESTFul API) – Decision support service – RDF repositories (public and private) – Educational resources aggregator – Risk factor entry system – Medical evidence aggregator – DSS alerts entry system	
Hardware details	
CPU	4 Cores, 2.39 GHz
Memory	10GB
Hard Drive	250GB storage
Software details	
Operating System	Linux, Ubuntu server 14.04.4 LTS (GNU/Linux 3.13.0-96-generic x86_64)
Environment	Apache v2.4.7 Tomcat 7 server NodeJS 4.x application server Java 8 Spring framework 4.1 Gate 8 and plugins ClearNLP 2.0 Python 2.7 Visrtuoso 7 Redis database

Table 3. Server details of Windows-based platform.	
CARRE subservices	
– PHR manual entry system	
Hardware details	
CPU	2 Cores, 2.39 GHz
Memory	4GB
Hard Drive	250 GB
Software details	
Operating System	Windows Server 2012 R2
Environment	IIS 7.0 Microsoft SQL server 2012 NET framework v4.5.1 NuGet package manager Visual Studio 2013

The CARRE semantic repositories (as described in D.4.1) serve as the central data store for the CARRE integrated system, providing both public and private RDF stores for risk factor and patient measurement data, respectively, as well as the RESTful APIs for interaction with the stored data.

The repositories were deployed on the servers provided for each use case setting, and configured appropriately under the *.duth.carre-project.eu and *.vulsk.carre-project.eu domains. In general, the deployments went smoothly. The major issues encountered related to differences in the software environments provided by the use case settings. In particular, where the (OU-hosted) original semantic repository used version 6 of the Virtuoso quad-store database management system[6], the use case settings used version 7, in which there had been some changes to the handling of SPARQL queries (in particular with regard to date/time datatypes). It took some experimentation to identify where these changes were affecting CARRE and to update them. Having made these updates, the deployed repositories provide the users on the relevant servers with the public and private RDF stores, and the RESTful API, as required.

3. Informative system assessment

During the final phase of deployment, both parts of the CARRE system (for the patient and the expert) were evaluated with groups of medical experts to assess user satisfaction and extract insights for improvements. For this informative evaluation we used proprietary questionnaires, specifically designed to address individual system characteristics and functionalities.

[6] http://virtuoso.openlinksw.com

3.1. Risk factor management system informative assessment by medical experts

3.1.1. Evaluation methodology

The informative assessment of the CARRE risk factor management system was performed by users in the two medical partners, DUTH and VULSK. In DUTH, the evaluation was performed by 20 medical undergraduates in their final year of their studies (6th year). The students were asked to participate on a voluntary basis via an announcement in DUTH School of Medicine. Final year (6th) undergraduate students were called for the evaluation to ensure that they are formally informed about the concept of health risk factor during their curriculum (Note: 6th year students are expected to have successfully completed all taught medical courses and are attending full time clinical practice). In VULSK, the evaluation was performed by 5 medical graduates, residents or certified medical experts.

The evaluation in DUTH was conducted via 3 focus groups (~6 participants per group) coordinated by one CARRE investigator. The evaluation took place at the computer lab (seminar room 5.03 of the Educational Department of the University Hospital in Alexandroupoli, Greece). Evaluation in VULSK was performed in one focus group (5 participants).

Participants were seated in front of personal computers and were introduced to the evaluation questionnaire, implemented in Google forms. Initially, participants were asked to complete the first part of the questionnaire with questions pertaining to user profile. Then the investigator presented briefly the CARRE risk factor management system via a short slide presentation based on the description as in Section 2.2. The investigator asked the participants to visit the system on the web and familiarize themselves with the landing page and the system for about 10 minutes. The participant were asked to respond to the part of the questionnaire related to the dashboard. The same procedure was followed consecutively with the participants engaging with the visual exploration of the database and answering the respective part of the questionnaire, and then engaging with browsing the list of risk evidences and answering the respective part of the questionnaire, and a final part of the questionnaires with questions on the overall system performance. The assessment was concluded with a semi-structured discussion where the investigator coordinated questions from the participants and directed the discussion on the strong and weak aspect of the systems and on suggestions for system improvement. General comments where summarized by each participant on the survey form.

3.1.2. Results and discussion

The profile of the participants in the evaluation, including their background computer literacy, is shown on Table 4. The participants were primarily senior undergraduate medical students (age 20-29) and sex balanced (52% female). Their self-reported computer/smart phone literacy is around 3.5 in a scale from 1 (novice) to 5 (expert); they are quite frequent users of smart phones, with a self-reported 3.92 in a scale from 1 (not at all) to 5 (all the time). However, they seem to have been moderately exposed to infographics, with a self-reported value of 3.00 in a scale from 1 (not at all familiar) to 5 (very familiar). Computer literacy of the participant group is also shown graphically in Figure 21.

User assessment of the dashboard is summarized in Figure 22. Users are satisfied (above average) by the information of the landing page and can understand the concepts presented; the lowest score (thought above average) is for the page design.

Assessment of visual exploration is presented in Figure 23 and of conventional list-based browsing and editing in Figure 24. Searching and conventional list-based browsing were well accepted. However, visual exploration scored on average less than conventional list-based browsing. Editing the risk factor data was found rather difficult and the editing the observable condition scored close to the lowest of the 1-5 easiness scale.

Overall the system was found moderately user friendly and enjoyable, however it scored highly useful (Figure 25).

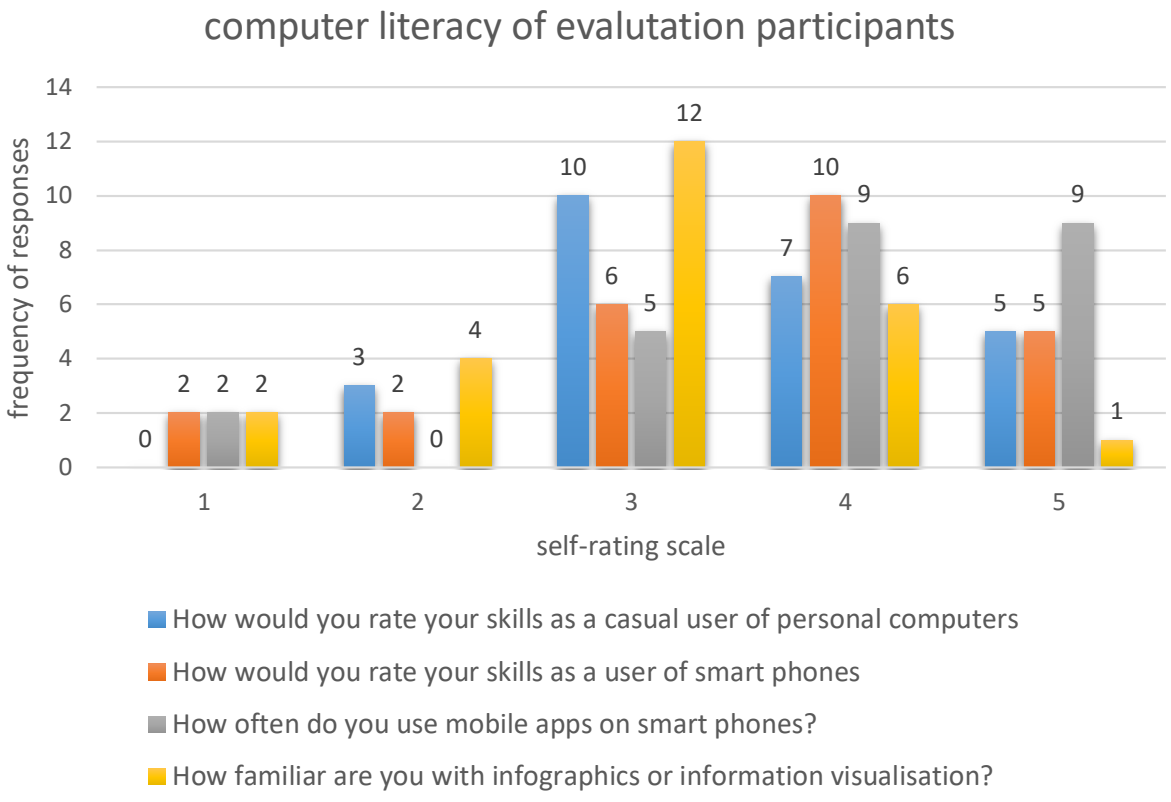
The free text comments and the focus group semi-structured discussion raised the following:

- the system is useful for medical education and medical practice;
- a more thorough introduction and explanation of the system functionality and the database contents is desirable – allow more time for the expert to get familiar with the system;

- direct link to PubMed abstract is a big plus;
- more information on risk factor should be retrieved and displayed on the visualization graphs;
- lettering on graphs should be more clear/large and visible;
- editing should be followed by review process before the changes are recorded in the public database;
- preset examples should be included to help with navigation and search;
- Sankey and cord diagrams were difficult to comprehend at first, but were a bit easier after some practice – the conventional network graph seemed more easy to understand and should be the default diagram.

Table 4. Descriptive characteristics of the risk factor system evaluation participants, mean±SD or N(%). Computer literacy is based on self-rating using a 1-5 scale.

characteristic	value
N	25
Female	13 (52%)
Age (yrs)	
20 – 29	22 (88%)
30 – 39	2 (8%)
50 – 59	1 (4%)
Senior medical students	20 (80%)
Graduates	5 (20%)
Rate your skills as a casual user of personal computers	3.56 ± 0.89
Rate your skills as a user of smart phones	3.56 ± 1.29
Frequency of use of mobile apps on smart phones?	3.92 ± 1.27
Familiarity with infographics or information visualisation?	3.00 ± 0.88



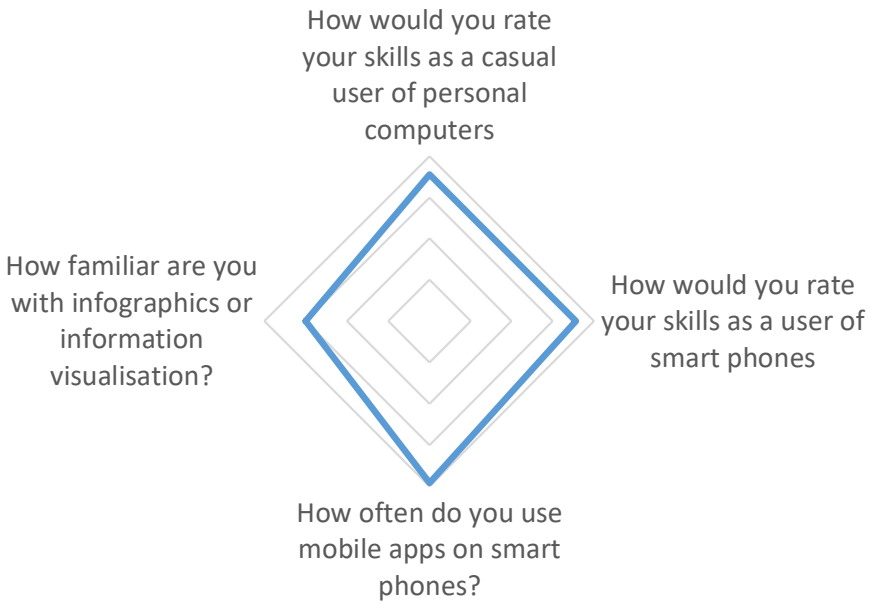


Figure 21. Frequency diagram and radar plot of means for computer literacy self-rating.

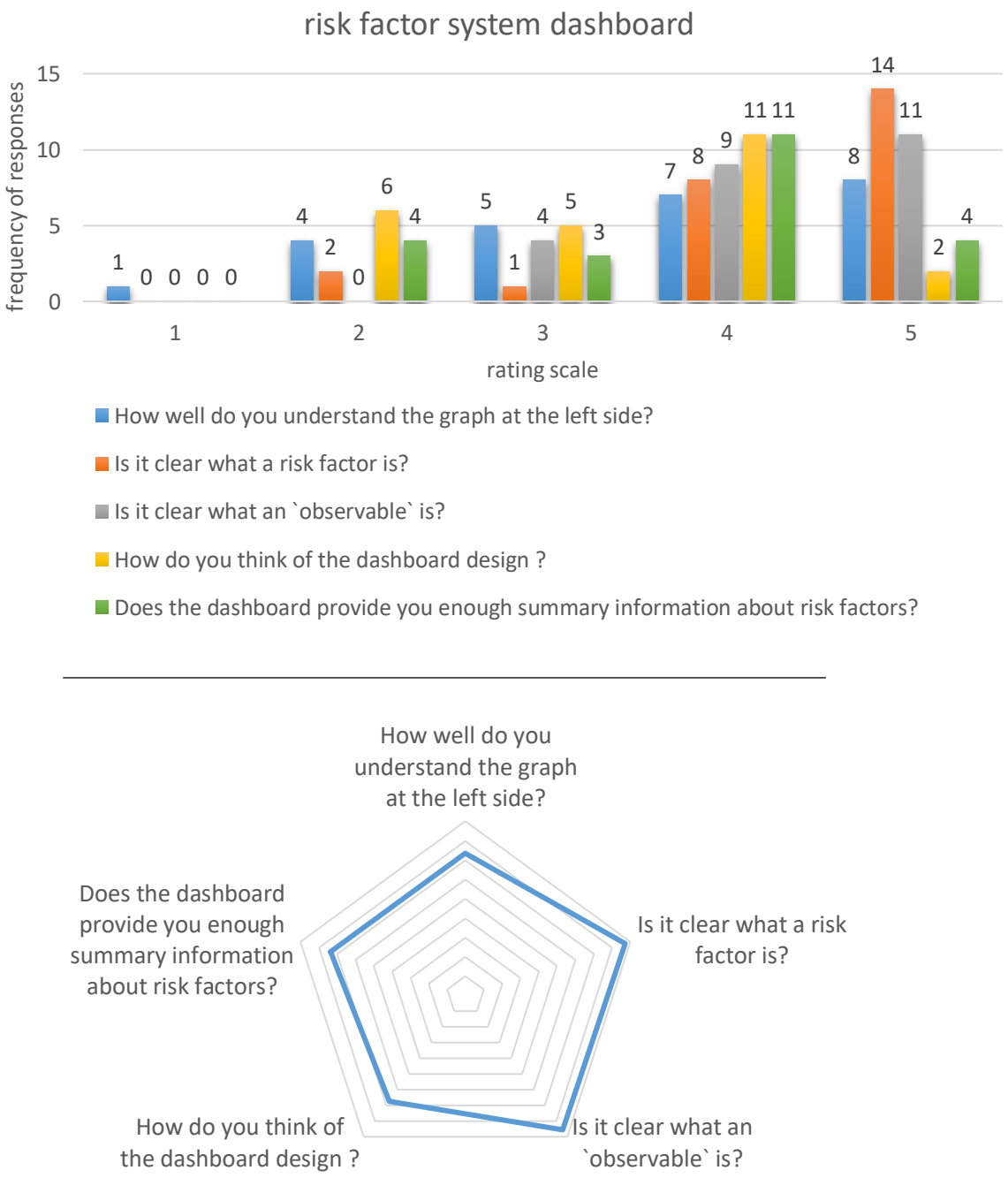
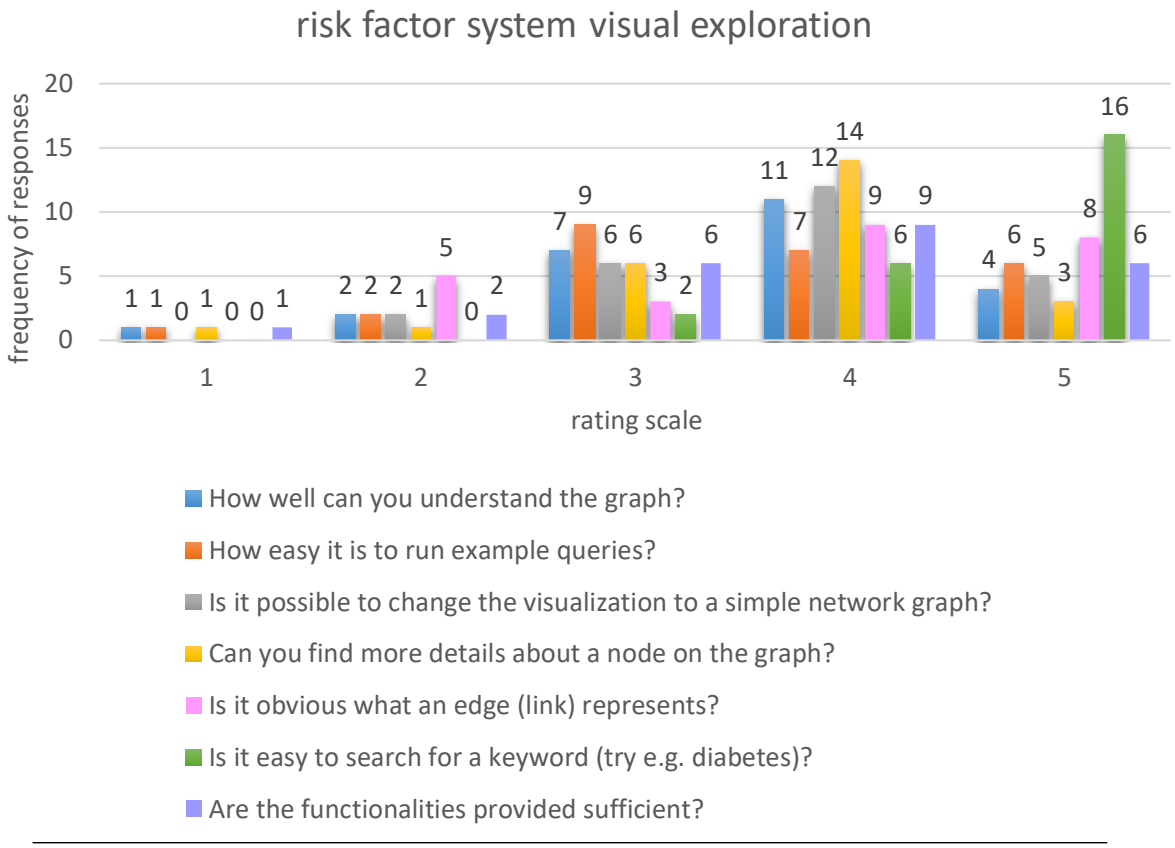


Figure 22. Frequency diagram and radar plot of means for the assessment of risk factor system dashboard.



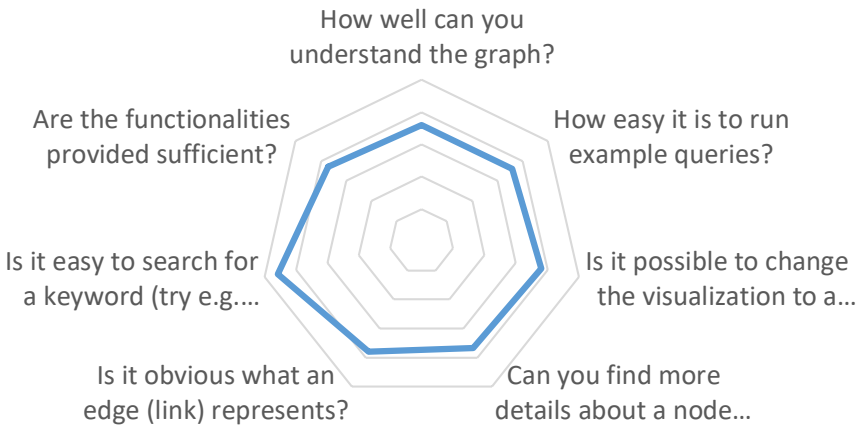
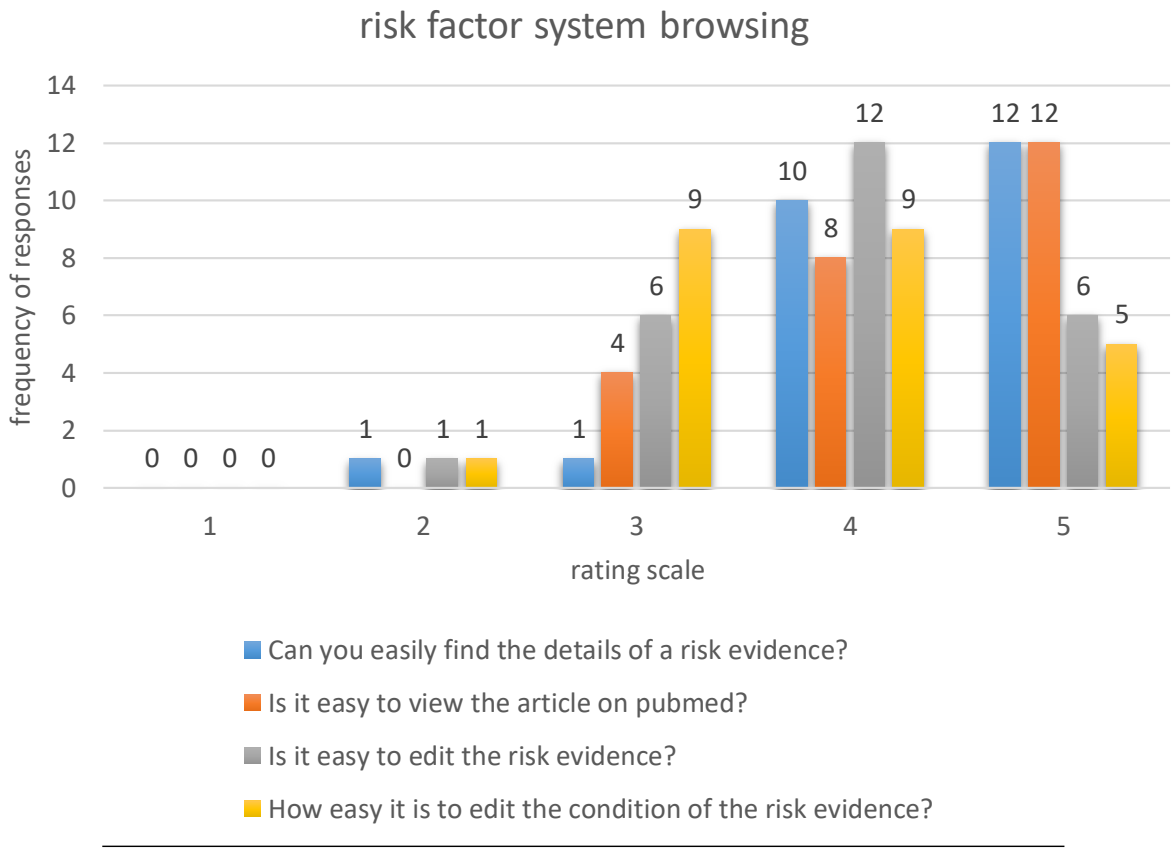


Figure 23. Frequency diagram and radar plot of means for the assessment of risk factor system visual exploration.



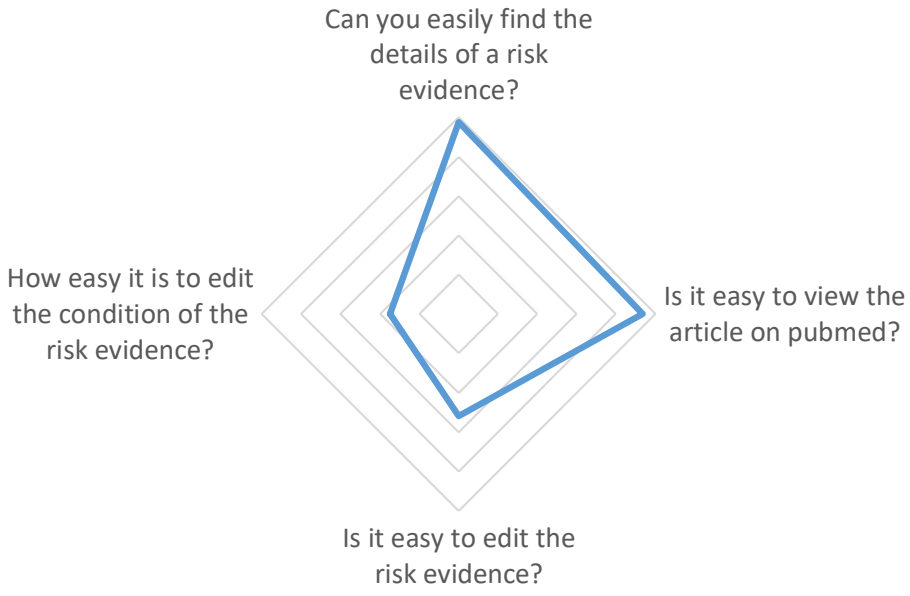
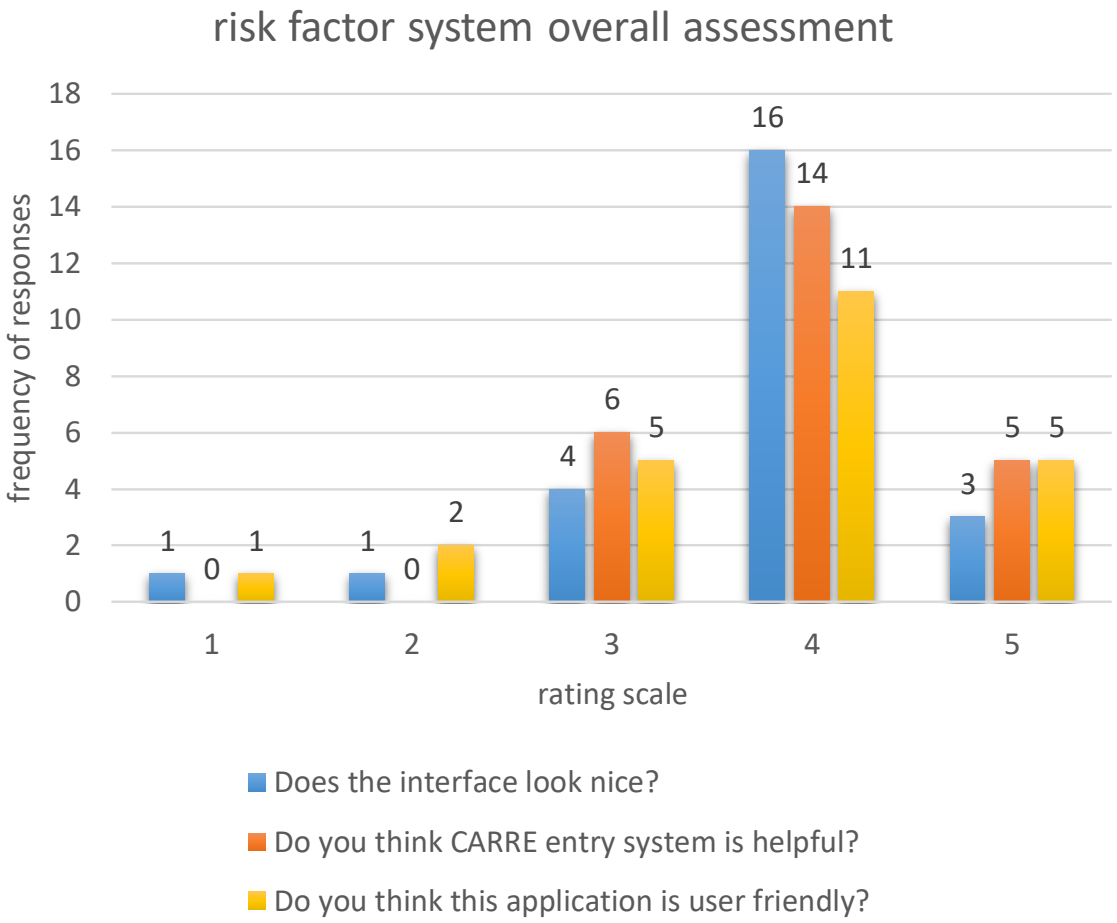


Figure 24. Frequency diagram and radar plot of means for the assessment of risk factor system list browsing.



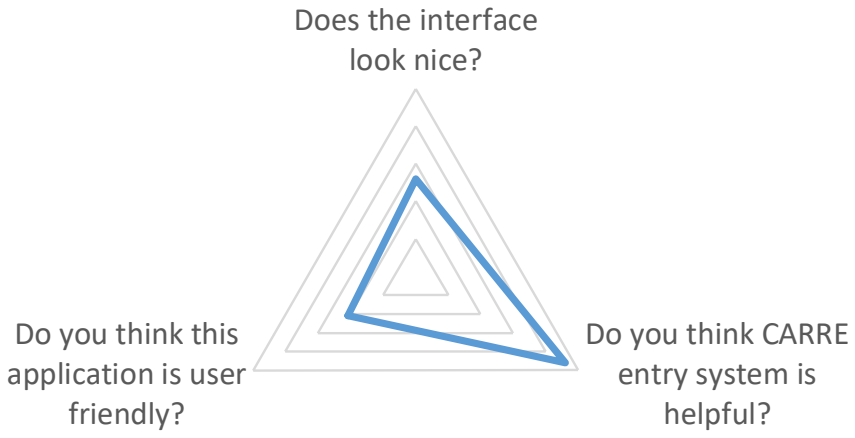


Figure 25. Frequency diagram and radar plot of means for the overall assessment of risk factor system.

3.2. Patient empowerment system informative assessment by medical experts

3.2.1. Evaluation methodology

The informative assessment of the CARRE patient empowerment system was performed by users in the two medical partners, DUTH and VULSK. In DUTH, the evaluation was performed by 13 medical undergraduates in their final year of their studies (6th year). The students were asked to participate on a voluntary basis via an announcement in DUTH School of Medicine. Final year (6th) undergraduate students were called for the evaluation to ensure that they are formally informed about the concept of health risk factor during their curriculum (Note: 6th year students are expected to have successfully completed all taught medical courses and are attending full time clinical practice). In VULSK, the evaluation was performed by 13 medical graduates, residents or certified medical experts.

The evaluation in DUTH was conducted via 2 focus groups (~6 participants per group) coordinated by one CARRE investigator. The evaluation took place at the computer lab (seminar room 5.03 of the Educational Department of the University Hospital in Alexandroupoli, Greece). Evaluation in VULSK was performed in 2 focus group (~6 participants per group).

Participants were seated in front of personal computers and were introduced to the evaluation questionnaire, implemented in Google forms. Initially, participants were asked to complete the first part of the questionnaire with questions pertaining to user profile. Then the investigator presented briefly the CARRE patient empowerment system via a short slide presentation based on the description as in Section 2.1 The investigator asked the participants to visit the system and log in as one of the preset demo patient users and familiarize themselves with the landing page and the system for about 10 minutes. The participant were asked to respond to the part of the questionnaire related to the dashboard. The same procedure was followed consecutively with the participants engaging with the healthlines visualization page and answering the respective part of the questionnaire, and then engaging with personal risk graph and answering the respective part of the questionnaire, and a final part of the questionnaires with questions on the overall system performance. The assessment was concluded with a semi-structured discussion where the investigator coordinated questions from the participants and directed the discussion on the strong and weak aspect of the systems and on suggestions for system improvement. General comments where summarized by each participant on the survey form.

3.2.2. Results and discussion

The profile of the participants in the evaluation, including their background computer literacy, is shown on Table 5. The participants were senior undergraduate medical students (38%) and medical graduates (62%), with ages primarily in the range 20-29, and almost balanced sex (58% female). Their self-reported computer/smart phone literacy is around 4.4 in a scale from 1 (novice) to 5 (expert); they are quite frequent users of smart phones, with a self-reported 4.3 in a scale from 1 (not at all) to 5 (all the time). However, they seem to have been moderately exposed to infographics, with a self-reported value of 3.2 in a scale from 1 (not at all familiar) to 5 (very familiar). Computer literacy of the participant group is also shown graphically in Figure 26.

The questionnaire for evaluating the visual interface dashboard was designed to provide a score for each functionality included in the dashboard. Therefore, each functionality was rated on a 5 point scale (5: high to 1: low). Figure 27 shows a graph of the means for each assessment axis.

With a mean score of 4.3 (min = 3; max = 5) and standard deviation of 0.6, the question “Does the dashboard provide you enough summary information about your health?” scored the highest value, followed by question “Can you clearly identify your current health risks from the risk panel visualisation in the dashboard?” with a mean scored of 4.0. Questions “What do you think of the dashboard design?” and “Can you clearly identify your current health risks from the risk panel visualisation in the dashboard?” both received the same mean score of 3.9. Question “How well do you see your health data in the health measurement panel?” received the lowest score (3.8 and standard deviation of 0.9).

Figure 28 shows a graph of the means for each assessment axis of the healthlines visualization page. With mean score of 4.1 (min = 3; max = 5), 96% of the participants scored 4 or 5 to indicate how easy is to learn to use the health lines functionality. The same score of 4.1 was obtained to rate the questions “Can you read the measurement values by hovering the mouse on the data points?” and “Are the functionalities sufficient?” both

questions “How well the Health lines show your health data at present and in the past?” and “Is the interaction of the health lines convenient?” received the same score of 3.9, which was the lowest score.

Figure 29 shows a graph of the means for each assessment axis of the personal risk graph page. A mean score of 4.3 with a standard deviation of 0.8 indicates that 91% of the participants scored 4 or 5 to specify that they can clearly see the health risks from the health diagram. Question “Can you make the difference between the nodes and the links in the health diagram” received the lowest score (3.6) with 91% of participants scoring 3 to 5.

Figure 30 shows a graph of the means for each assessment for the overall system assessment. The question “Do you think CARRE system is helpful?” scored the highest mean value (4.2, standard deviation 0.9) with 86% of participants scoring 4 or 5 followed by questions “Does the interface look nice?” and “Do you think this application is user friendly?” with a mean value of 4.1.

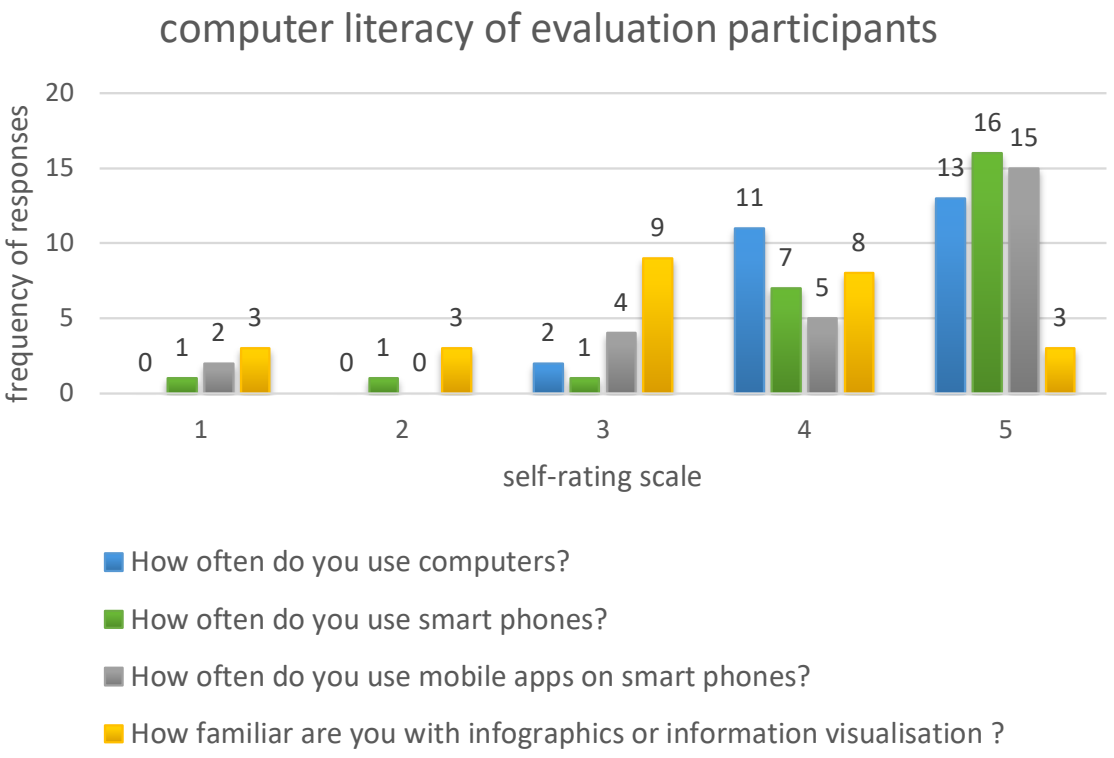
The results from our study reveal that the CARRE visual functionalities are encouraging in addressing visual needs of CARRE platform.

The free text comments and the focus groups semi-structured discussion raised the following:

- the risk factor graph should improve colours;
- the risk factor graph should display with caution risk elements that may increase anxiety (e.g. death);
- the risk factor graph should display;
- the display of alerts should be more obvious to find;
- a more detailed demonstration of how to use the sliding bar in healthline visualization is required;
- medical terms used should be improved to become more informal.

Table 5. Descriptive characteristics of the patient empowerment system evaluation participants, mean±SD or N(%). Computer literacy is based on self-rating using a 1-5 scale.

characteristic	value
N	26
Female	15 (58%)
Age (yrs)	
20 – 29	18 (69%)
30 – 39	6 (23%)
50 – 59	2 (8%)
Senior medical students	10 (38%)
Graduates	16 (62%)
Rate your skills as a casual user of personal computers	4.42 ± 1.02
Rate your skills as a user of smart phones	4.38 ± 1.02
Frequency of use of mobile apps on smart phones?	4.19 ± 1.20
Familiarity with infographics or information visualisation?	3.19 ± 1.17



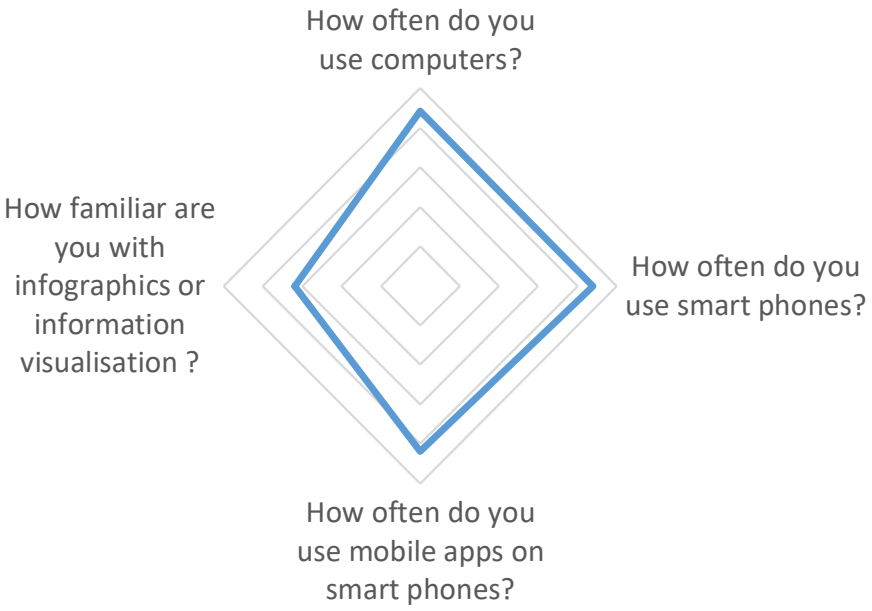
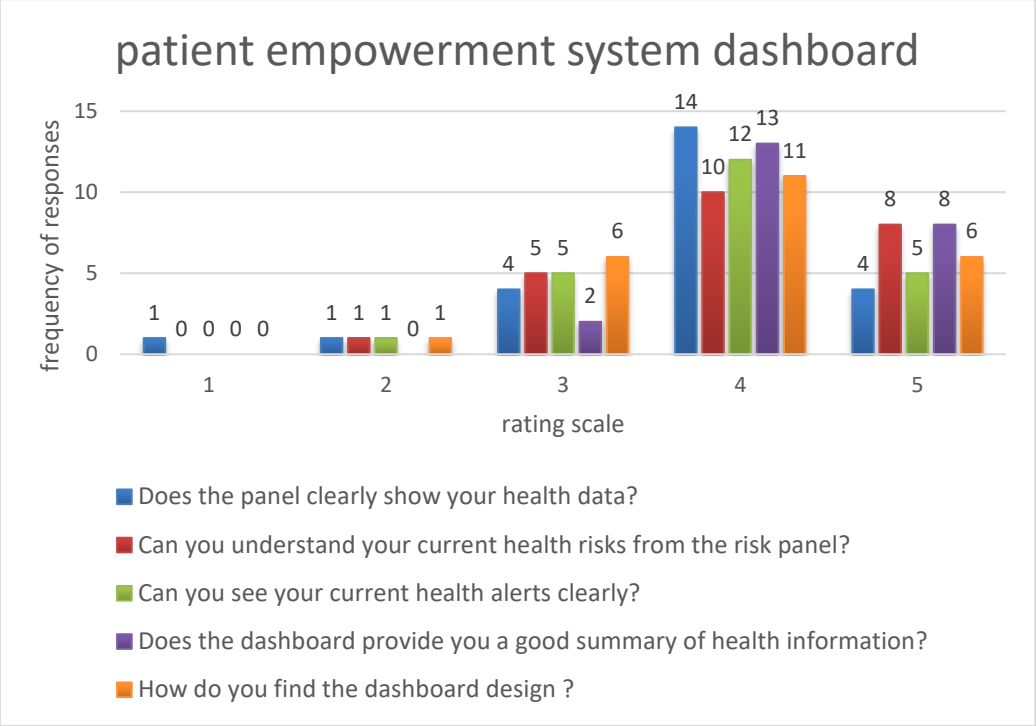


Figure 26. Frequency diagram and radar plot of means for computer literacy self-rating.



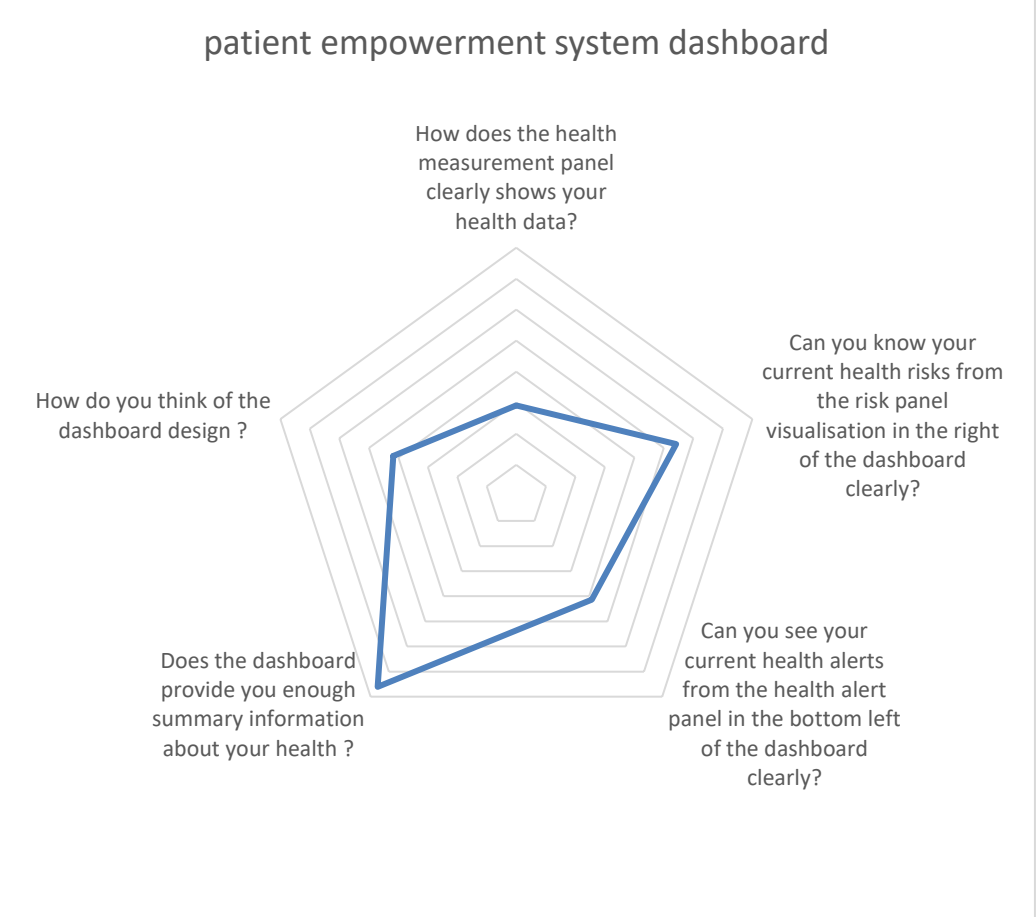
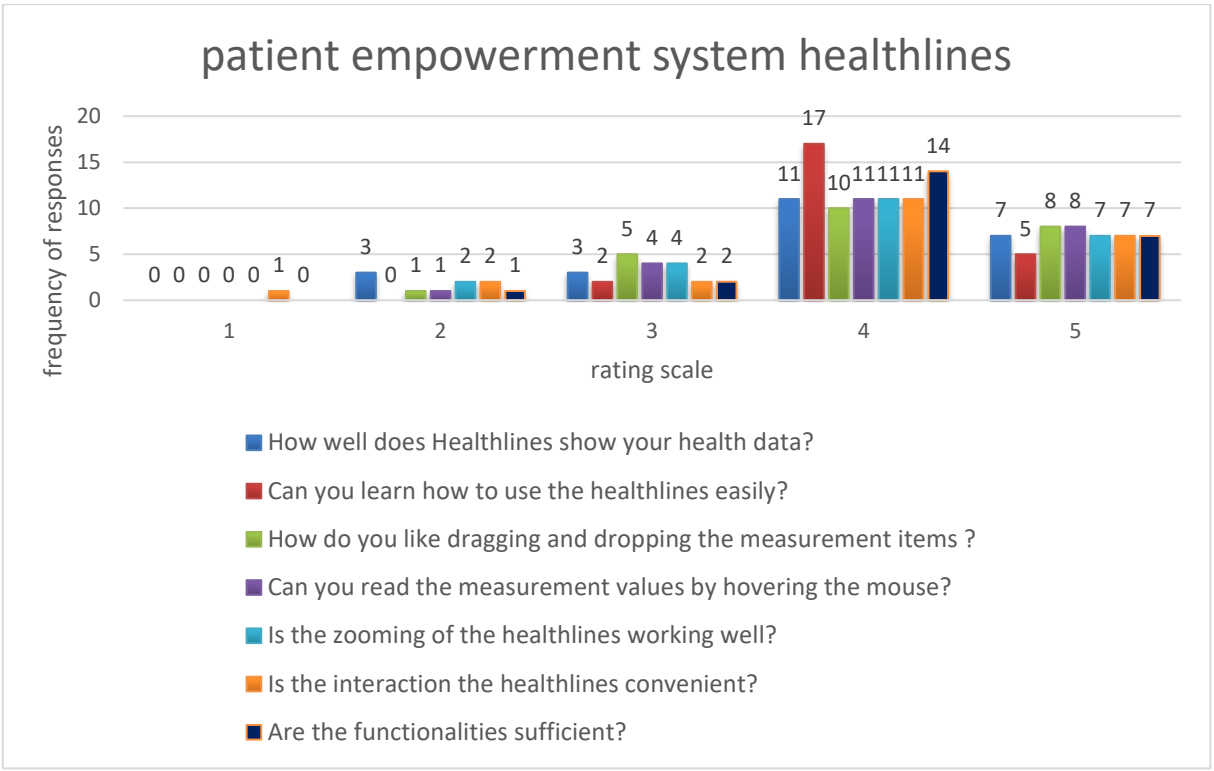


Figure 27. Radar plot of means for the assessment of patient empowerment system dashboard.



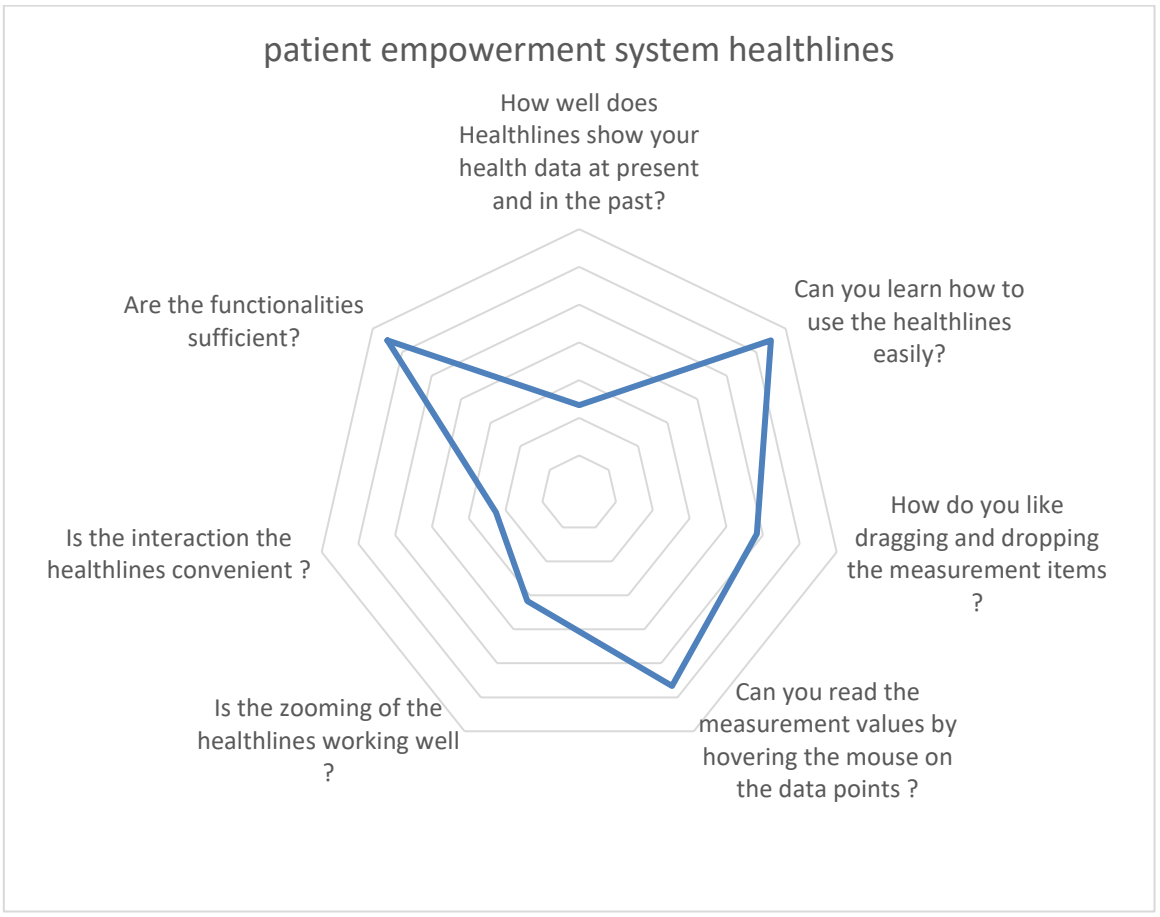
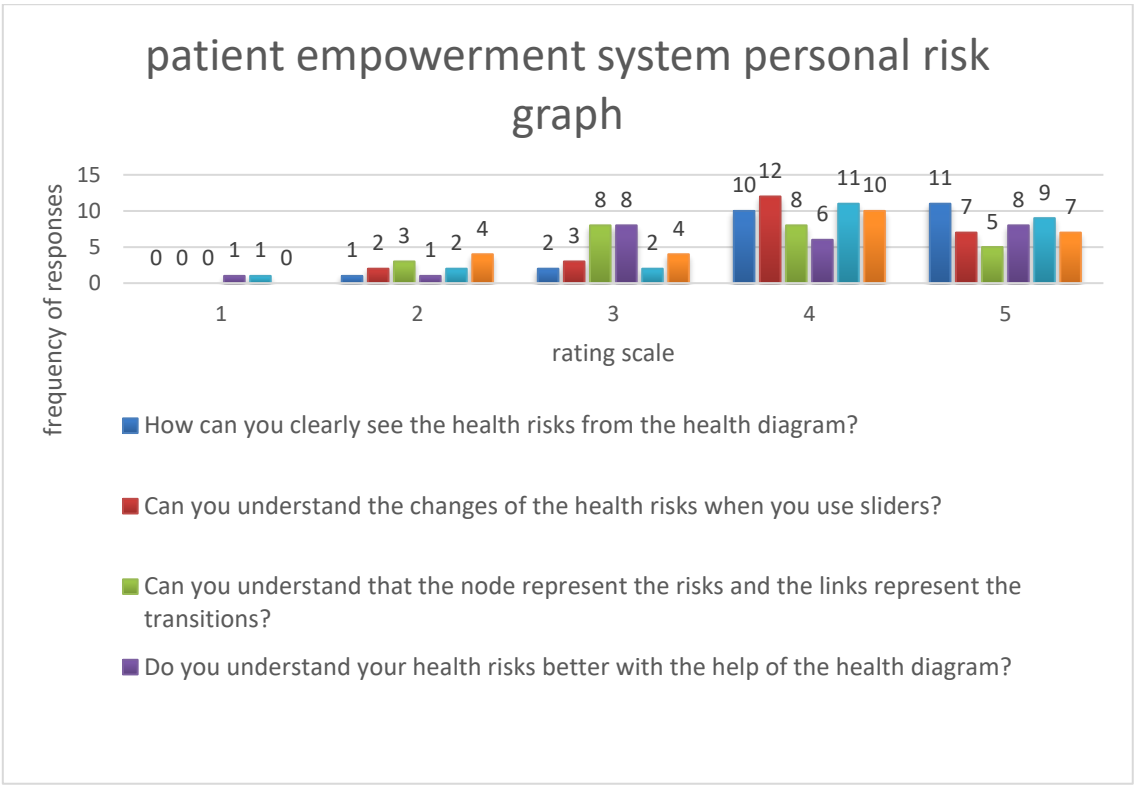


Figure 28. Radar plot of means for the assessment of patient empowerment system healthlines.



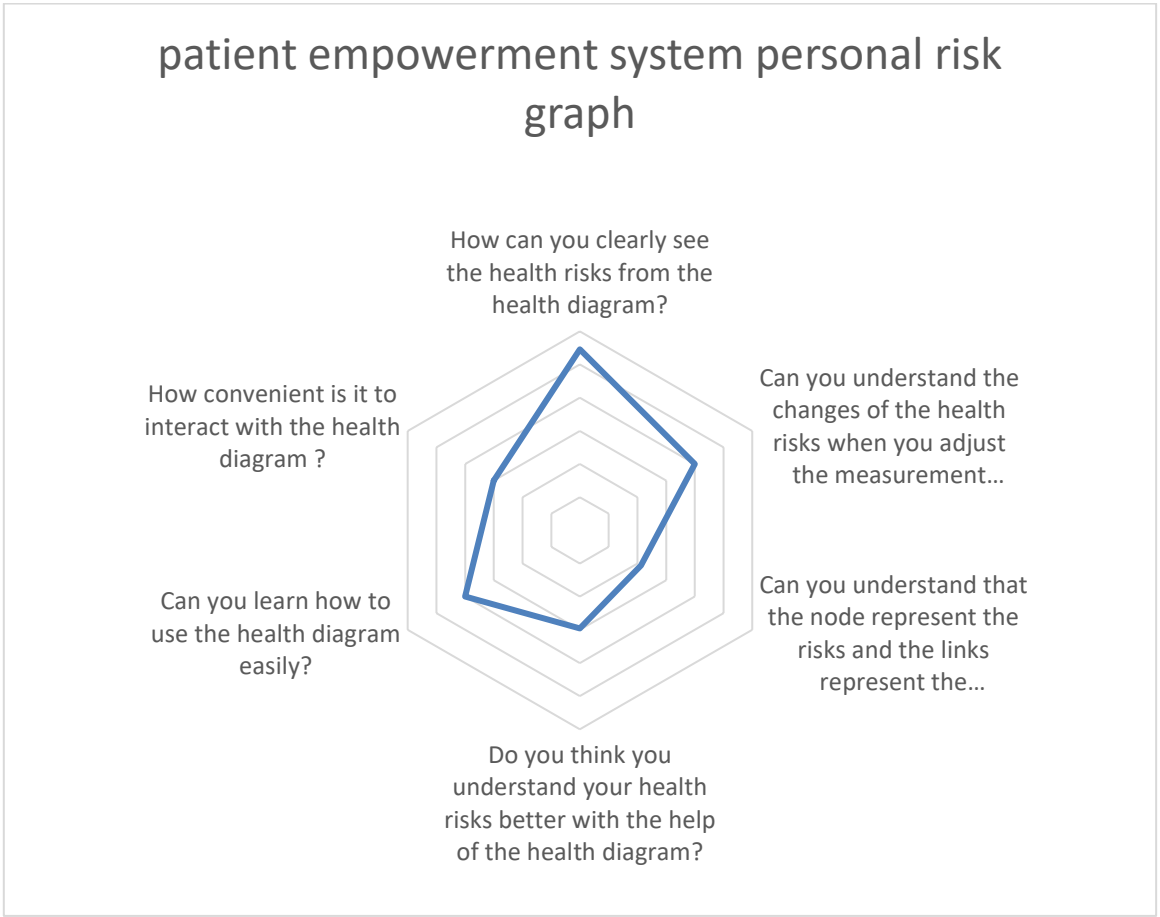
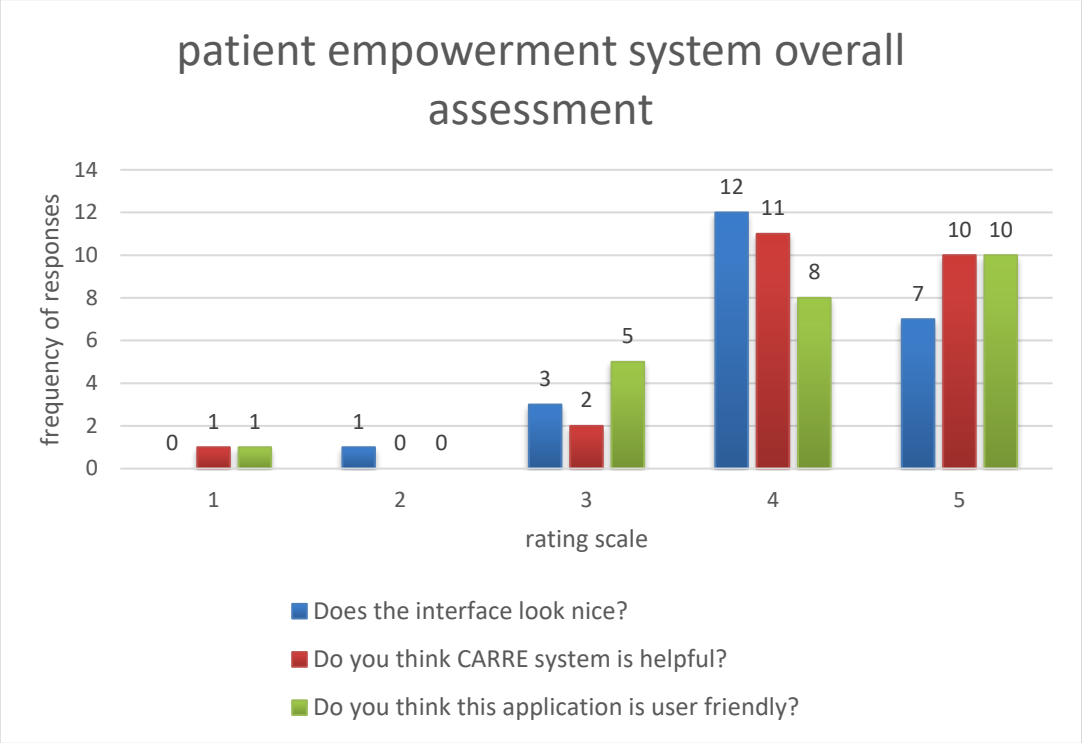


Figure 29. Radar plot of means for the assessment of patient empowerment system personal risk graph page.



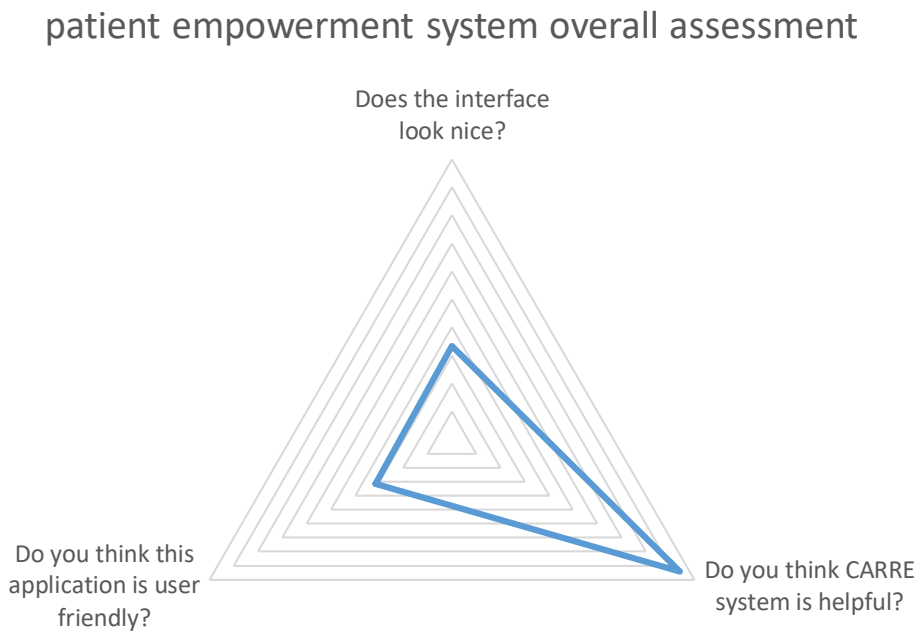


Figure 30. Radar plot of means for the overall assessment of patient empowerment system.

4. Clinical investigational study

4.1. Study protocol

4.1.1. Design overview

CARRE aims at researching and innovating towards a service environment for providing personalized empowerment and shared decision support services for cardiorenal disease comorbidities.

The core of CARRE effort lies in semantic interlinking of three types of data (a) medical ground knowledge (b) up-to-date medical evidence and (c) personal patient data in order to create a personalized model of the disease and comorbidities progression pathways and trajectories. Visual presentations of this personalized model (against ground knowledge and against statistical views of 'similar' patient groups) will form the basis for patient empowerment services that will target understanding of comorbidities in the personal setting. Finally, the personalized model of comorbidities will be used for shared decision support services targeting personalized education, complex risk calculation for disease progression and comorbidity trajectories, alerts for adverse events of multiple co-existing treatments and personalized planning for monitoring.

The protocol of the study was developed by medical professionals from DUTH an VULSK. The protocol is described in the following sections; the various protocol forms are included in Annex 1 and the instruments used to assess impact in Annex 2.

In brief, this Pilot Study aims to assess the CARRE service along four different axes:

a) the efficacy of CARRE service in increasing health literacy;

b) the ability of the CARRE service to empower patients;

c) the impact of the service on quality of life; and

d) improvement of the medical condition of the patient.

4.1.2. Rationale for benefits assessment

The paragraphs below provide a short discussion and justification on the various instruments used for the assessment CARRE service. The complete instruments are presented in Annex 1.

4.1.2.1. Health literacy

The phrase *health literacy*[7] is used to describe persons' capacity to obtain, process, and understand health information. There are multiple definitions of health literacy[8] because involves both the context in which health literacy demands are made and the skills that people bring to that situation. Studies[9] reveal that only 12% of the adults in the U.S. have proficient health literacy. This means 77 million adults have basic or below basic health literacy. These individuals have difficulty with common health tasks. Accordingly, the European Commission and the European Office of the World Health Organization[10] are highlight health literacy as a strategic priority area to promote patient empowerment and population health. Low health literacy has been

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7 Sørensen K1, Van den Broucke S, Pelikan JM, Fullam J, Doyle G, Slonska Z, Kondilis B, Stoffels V, Osborne RH, BrandH; HLSEUConsortium(2013)."Measuring health literacy in populations: illuminating the design and development process of the European Health Literacy Survey Questionnaire (HLS-EU-Q). BMC Public Health. Oct 10;13:948.

8 A. Pleasant & J. McKinney (2011). "Coming to consensus on health literacy measurement: An online discussion and consensus-gauging process". Nursing Outlook 59 (2): 95–106.e1

9 America's Health Literacy: Why We Need Accessible Health Information". health.gov. Retrieved 2015-11-20

10 Regional Committee for Europe. (2012, September). Health 2020: A European policy framework supporting action across government and society for health and well-being. Geneva, Switzerland: World Health Organization Regional Office For Europe.

associated with non adherence to treatment plans and medical regimens, poor patient self-care, high healthcare costs, and increased risk of hospitalization and mortality[11].

Accurate measurement of health literacy is a critical component to identify topics and populations most in need of support[12]. Haun et al.[13] summarize and compare 51 instruments for Health literacy measurement. They identified 26 questionnaires which measure general health literacy, 15 which are disease specific and 10 which are related with specific population. Take to account the strengths and the limitations of the questionnaires, we concluded that a questionnaire which will be consisted of general questions about health literacy, using the European Health Literacy Questionnaire enriched with questions from Lipkus Expanded Health Numeracy Scale which is a questionnaire which indicate if patient perceive his/her health risk, is the most appropriate questionnaires combination for our study.

4.1.2.2. Empowerment

In health science, patient empowerment is understood as an enabling process or outcome[14,15] by which patients are encouraged to construct self-regulation, self-management and self-efficacy in order to achieve maximum health and wellness[16]. Empowerment can therefore be described as a process where the purpose of an educational intervention is to increase patients' ability to think critically and act autonomously; while it can also be viewed as an outcome when an enhanced sense of self-efficacy occurs as a result of the process[17]. According to the European Network for Patient Empowerment [18] an empowered activated patient:

- understands her/his health condition and its effect on her/his body;
- feels able to participate in decision-making with her/his healthcare professionals;
- feels able to make informed choices about treatment;
- understands the need to make necessary changes to her/his lifestyle in order to stay healthy and/or effectively manage disease;
- is able to ask questions and challenge her/his healthcare professionals;
- takes responsibility for her/his health and actively seeks care when necessary.

The assessment of patient empowerment in CARRE will be based on the instrument developed in the EU funded SUSTAINS project questionnaire[19]. The background to the SUSTAINS project has three drivers that SUSTAINS contributes to: a) enabling and strengthening empowerment of patients; b) enabling better medical results; c) enabling a more efficient use of healthcare resources and containing costs. The instrument developed in the project is available in many European languages, amongst them Greek and English.

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[11] King A (2010)."Poor health literacy: a 'hidden' risk factor". Editorial . Nat Rev Cardiol. 2010. PMID: 20725102

[12] McCormack L, Haun J, Sørensen K, Valerio M (2013).Recommendations for advancing health literacy measurement. J Health Commun. 2013;18 Suppl 1:9-14. doi: 10.1080/10810730.2013.829892.

[13] JN. Haunab, MA. Valerioc, LA. McCormackd, KSørensene & MK. Paasche-Orlowf, Health Literacy Measurement: An Inventory and Descriptive Summary of 51 Instruments, Journal of Health Communication: International Perspectives, Volume 19, Supplement 2, 2014

[14] Freire P., 1993. Pedagogy of the oppressed, New York: Continuum.

[15] McAllister M, Dunn G, Payne K, Davies L, Todd C., 2012. Patient empowerment: the need to consider it as a measurable patient-reported outcome for chronic conditions. BMC Health Serv Res. 13;12:157.

[16] Lau D.H., 2002. Patient empowerment – a patient-centred approach to improve care. Hong Kong Med J. 8 (5): 372-374.

[17] Anderson R.M., Funnell M.M., 2010. Patient empowerment: myths and misconceptions. Patient Educ Couns. 79(3):277-82.

[18] ENOPE, Patient Empowerment, 2014. Available at: http://enope.eu/patient-empowerment.aspx

[19] O. Unver, W. Atzori, Document D3.2 – Questionnaire for Patient Empowerment Measurement Version 1.0, SUSTAINS: Support USers To Access INformation and Services, January 2013, EU CT PSP Grant Agreement No 29720

4.1.2.3. Quality of Life

In the field of healthcare, quality of life is often regarded in terms of how a certain ailment affects a patient on an individual level. This may be a debilitating weakness that is not life-threatening; life-threatening illness that is not terminal; terminal illness; the predictable, natural decline in the health of an elder; an unforeseen mental/physical decline of a loved one; or chronic, end-stage disease processes. Researchers at the University of Toronto's Quality of Life Research Unit define quality of life as "The degree to which a person enjoys the important possibilities of his or her life". Their Quality of Life Model is based on the categories "being", "belonging", and "becoming"; respectively who one is, how one is not connected to one's environment, and whether one achieves one's personal goals, hopes, and aspirations[20].

Research shows that quality of life ratings are associated with clinical outcomes in nursing homes. Some, but not all dimensions of quality of life among nursing home residents were shown to be prospectively associated with clinical outcomes[21]. In another study, scholars showed that caretakers' proxy ratings were associated with residents' own ratings though not perfectly so[22].

The most common used questionnaires for Quality of life measurement are:

- **The Short Form (36) Health Survey** is a 36-item, patient-reported survey of patient health. The SF-36 is a measure of health status and an abbreviated variant of it, the SF-6D, is commonly used in health economics as a variable in the quality-adjusted life year calculation to determine the cost-effectiveness of a health treatment. The original SF-36 came out from the Medical Outcome Study, MOS, done by the RAND Corporation. Since then a group of researchers from the original study released a commercial version of SF-36 while the original SF-36 is available in public domain license free from RAND. A shorter version is the **SF-12**[23]. If having only adequate physical and mental health summary scores is of interest, "then the SF12 may be the instrument of choice" [24].
- **The Euroqol EQ-5D**, which is a widely-used survey instrument for describing health-related quality of life states. It is one of several such instruments that can be used to determine the quality-adjusted life years associated with a health state. The name is derived from the survey methodology, which measures quality of life in five dimensions and was developed by the EuroQol Research foundation[25].

The consortium decided to use SF-36, as it appears to be the most comprehensive and the most commonly used, while it is validated for both pilot languages (Greek[26] and Lithuanian[27]).

Note: to assess the popularity of the questionnaires, we conducted a series of systematic queries in PubMed (a synopsis is shown in Table 6). This search indicated that the SF-36 is most commonly used of all; this makes it the assessment instrument of choice, as its popularity allows comparison of CARRE results with the highest number of other interventions.

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[20] Quality of Life: How Good is Life for You?". University of Toronto Quality of Life Research Unit. Retrieved October 14, 2009.

[21] Degenholtz, Howard B., et al. "The association between changes in health status and nursing home resident quality of life." The Gerontologist 48.5 (2008): 584-592.

[22] Mittal, Vikas, et al. "Perception gap in quality-of-life ratings: an empirical investigation of nursing home residents and caregivers." The Gerontologist 47.2 (2007): 159-168.

[23] SF 12- http://www.sf-36.org/tools/sf12.shtml

[24] Jenkinson, Crispin (1996-11-03). "A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies?". Journal of Public Health Medicine. 19(2) (1997): 179–186. PMID 9243433.

[25] EuroQol Group (1990-12-01). "EuroQol--a new facility for the measurement of health-related quality of life". Health Policy (Amsterdam, Netherlands) 16 (3): 199–208. ISSN 0168-8510.

[26] Pappa E, Kontodimopoulos N, Niakas D.Validating and norming of the Greek SF-36 Health Survey. Qual Life Res. 2005 Jun;14(5):1433-8.

[27] Rugiene R, Dadoniene J, Venalis A. Adaptation of health-related quality of life ("SF-36") questionnaire, its validation and assessment of performance for control group and patients with rheumatoid arthritis]. Medicina (Kaunas). 2005;41(3):232-9. Lithuanian.

Table 6. Synopsis of PubMed queries about common QoL instruments.

PubMed Query	Number of papers
Results for all years until today (2016/02/04)	
"**SF-36**"[All Fields] AND ("1900/01/01"[PDat] : "2016/02/04"[PDat])	15,087
"**EQ-5D**"[All Fields] AND ("1900/01/01"[PDat] : "2016/02/04"[PDat])	4,071
"**SF-12**"[All Fields] AND ("1900/01/01"[PDat] : "2016/02/04"[PDat])	2,757
Results for last 10 years (2005 - 2015)	
"**SF-36**"[All Fields] AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	11,382
"**EQ-5D**"[All Fields] AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	3,730
"**SF-12**"[All Fields] AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	2,337
Results for last 10 years (2005 - 2015) in the health domain related to CARRE **Keywords: cardiorenal, heart, renal, kidney, obesity, hypertension, diabetes**	
("cardiorenal"[All Fields] OR "heart"[All Fields] OR "renal"[All Fields] OR "kidney"[All Fields] OR "obesity"[All Fields] OR "hypertension"[All Fields] OR "diabetes"[All Fields]) AND ("**SF-36**"[All Fields] NOT ("EQ-5D"[All Fields] OR "SF-12"[All Fields])) AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	1,941
("cardiorenal"[All Fields] OR "heart"[All Fields] OR "renal"[All Fields] OR "kidney"[All Fields] OR "obesity"[All Fields] OR "hypertension"[All Fields] OR "diabetes"[All Fields]) AND ("**EQ-5D**"[All Fields] NOT ("SF-36"[All Fields] OR "SF-12"[All Fields])) AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	475
("cardiorenal"[All Fields] OR "heart"[All Fields] OR "renal"[All Fields] OR "kidney"[All Fields] OR "obesity"[All Fields] OR "hypertension"[All Fields] OR "diabetes"[All Fields]) AND ("**SF-12**"[All Fields] NOT ("EQ-5D"[All Fields] OR "SF-36"[All Fields])) AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	307
Results for last 10 years (2005 - 2015) in the area of ehealth, excluding concurrent questionnaires ***Keywords: telemedicine, mHealth, e-Health, eHealth***	
("telemedicine"[All Fields] OR "mHealth"[All Fields] OR "e-Health"[All Fields] OR "eHealth"[All Fields]) AND ("**SF-36**"[All Fields] NOT ("EQ-5D"[All Fields] OR "SF-12"[All Fields])) AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	23
("telemedicine"[All Fields] OR "mHealth"[All Fields] OR "e-Health"[All Fields] OR "eHealth"[All Fields]) AND ("**EQ-5D**"[All Fields] NOT ("SF-36"[All Fields] OR "SF-12"[All Fields])) AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	16
("telemedicine"[All Fields] OR "mHealth"[All Fields] OR "e-Health"[All Fields] OR "eHealth"[All Fields]) AND ("**SF-12**"[All Fields] NOT ("EQ-5D"[All Fields] OR "SF-36"[All Fields])) AND ("2005/01/01"[PDat] : "2015/12/31"[PDat])	14

4.1.2.4. System Usability

The usability of a system, as defined by the ISO standard ISO 9241 Part 11, can be measured only by taking into account the context of use of the system — i.e., who is using the system, what they are using it for, and the environment in which they are using it. Furthermore, measurements of usability have several different aspects: effectiveness (can users successfully achieve their objectives); efficiency (how much effort and resource is expended in achieving those objectives); and satisfaction (was the experience satisfactory)

There are many survey instruments available for the usability assessment of a product or service. System Usability Score (or SUS) is an easy and effective tool for assessing the usability of diverse products including

hardware, software, mobile devices, websites and applications. SUS, initially developed by Brooke[28] has become an industry standard, with references in numerous publications. SUS is a reliable, low-cost usability scale that can be used for global assessments of systems usability[29, 30].

When SUS is used, participants are asked to score the following 10 items with one of five responses that range from *Strongly Agree* to *Strongly disagree*, and assess:

- the ability of users to complete tasks using the system, and
- the quality of the output of those tasks
- the efficiency, i.e. the level of resource consumed in performing tasks
- and the satisfaction, i.e. users' subjective reactions.

4.1.3. Study objectives

Primary objectives of the study are the following:

1. to increase health literacy;
2. to increase level of patient empowerment;
3. to improve patient's quality of life;
4. to reduce the personal risk of cardiorenal disease related morbidities (as these are described in the CARRE risk factor database).

Secondary objectives of the study are the following:

1. to ameliorate or prevent the progression of clinical and laboratory parameters related to cardiorenal disease and comorbidities;
2. to improve lifestyle habits (smoking, physical activity, adherence to self-monitoring and therapy);
3. to limit the number or dose of essential drugs;
4. to test for intervention acceptability and/or user satisfaction.

4.1.4. Subject selection

In CARRE D.2.1 deliverable, five user groups were described.

- This first group mainly includes subjects with a positive family history of metabolic or cardiovascular disease and/or unhealthy lifestyle habits. The person is not considered actually a patient but rather a healthy individual with a statistically increased risk of developing medical conditions which have the potential to progress into a chronic heart or renal disease.
- The second group includes patients with diabetes, hypertension and/or hyperlipidemia. These metabolic disorders are considered as risk factors for heart or renal disease.
- The third group includes patients who have already been diagnosed with chronic heart or renal disease. These patients usually have one or more comorbidities and are regularly treated and monitored
- The forth group includes a patient with diagnosed renal and heart comorbidity, regularly treated and monitored.
- The fifth group include patient at end stage renal disease (ESRD) or end stage heart failure (NYHA-IV).

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[28] Brooke, J. (1996). SUS: a „quick and dirty" usability scale. In P.W.Jordan, B. Thomas, B.A. Weerdmeester, and I.L. McClelland (Eds.) Usability Evaluation in Industry (189-194). London: Taylor and Francis.

[29] Bevan, N, Kirakowski, J and Maissel, J, 1991, What is Usability?, in H.-J. Bullinger, (Ed.). Human Aspects in Computing: Design and use of interactive systems and work with terminals, Amsterdam: Elsevier.

[30] Kirakowski, J and Corbett, M, 1988, Measuring User Satisfaction, in D M Jones and R Winder (Eds.) People and Computers IV. Cambridge: Cambridge University Press.

From the groups description above, two different study populations arise:

- Group 1: Subjects with a diagnosis of metabolic syndrome who meet the inclusion and exclusion criteria will be eligible for participation in the study group 1. These patients are at increased risk for developing cardiovascular disease[31], type 2 diabetes mellitus[32,33], chronic kidney disease (CKD)[34,35], even incident heart failure[36].
- Group 2: Subjects with a diagnosis of either renal or heart disease, which already caused chronic heart failure (CHF) or chronic kidney failure. Those who meet the inclusion and exclusion criteria will be eligible for participation in the study group 2.

4.1.4.1. Study population Group 1

Subjects with a diagnosis of metabolic syndrome who meet the inclusion and exclusion criteria will be eligible for participation in the study group 1.

Inclusion criteria for Group 1

- Written informed consent (and assent when applicable) obtained from subject or subject's legal representative.
- Ability for subject to comply with the requirements of the study, including basic ability to handle personal sensors and computer equipment required for the CARRE service.
- Male or female between 18-65 years old.
- Patients who satisfy the criteria for metabolic syndrome based on the Joint Interim Statement[37] on harmonizing the metabolic syndrome, which defines that at least three abnormal findings out of 5 (as shown in Table 7) would qualify a person for the metabolic syndrome.

Exclusion criteria for Group 2

- CHF or CKD (eligible for inclusion in Group 2)
- Type 1 diabetes or gestational diabetes
- Advanced liver disease and/or cirrhosis
- Cancer
- Uncontrolled thyroid disorders
- Concomitant use of drugs known to affect metabolism (e.g. corticosteroids)
- Pregnancy
- Exacerbated chronic inflammatory disorders (e.g. rheumatoid arthritis)
- Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)
- Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis)

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31 Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. Am J Med. 2006;119(10):812.

32 Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care. 2005;28(7):1769.

33 Meigs JB, Wilson PW, Fox CS, Vasan RS, Nathan DM, Sullivan LM, D'Agostino RB. Body mass index, metabolic syndrome, and risk of type 2 diabetes or cardiovascular disease. J Clin Endocrinol Metab. 2006;91(8):2906.

34 Chen J, Muntner P, Hamm LL, Jones DW, Batuman V, Fonseca V, Whelton PK, He J. The metabolic syndrome and chronic kidney disease in U.S. adults.Ann Intern Med. 2004;140(3):167

35 Kurella M, Lo JC, Chertow GM. Metabolic syndrome and the risk for chronic kidney disease among nondiabetic adults.J Am Soc Nephrol. 2005;16(7):2134.

36 Wang J, Sarnola K, Ruotsalainen S, Moilanen L, Lepistö P, Laakso M, Kuusisto J. The metabolic syndrome predicts incident congestive heart failure: a 20-year follow-up study of elderly Finns. Atherosclerosis. 2010 May;210(1):237-42.

37 K.G.M.M. Alberti, R.H. Eckel, S.M. Grundy, P.Z. Zimmet, J. I. Cleeman, K.A. Donato, J.-C. Fruchart, W. P.T. James, C.M. Loria, Si.C. Smith Jr, Harmonizing the Metabolic Syndrome a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009; 120:1640-1645.

- Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data

Table 7. Metabolic syndrome criteria.

Measure	Categorical Cut Points
Elevated waist circumference*	IDF cut points ≥ 94 cm in males; ≥ 80 cm in females (for European population)
Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator)	≥ 150 mg/dL (1.7 mmol/L)
Reduced HDL-C OR (drug treatment for reduced HDL-C is an alternate indicator†)	< 40 mg/dL (1.0 mmol/L) in males; < 50 mg/dL (1.3 mmol/L) in females
Elevated blood pressure OR (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	systolic ≥ 130 and/or diastolic ≥ 85 mm Hg
Elevated fasting glucose‡ OR (drug treatment of elevated glucose is an alternate indicator)	≥ 100 mg/dL

*It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available
†The most commonly used drugs for elevated triglycerides and reduced HDL-C are fibrates and nicotinic acid. A patient taking 1 of these drugs can be presumed to have high triglycerides and low HDL-C. High-dose _-3 fatty acids presumes high triglycerides.
‡Most patients with type 2 diabetes mellitus will have the metabolic syndrome by the proposed criteria.

4.1.4.2. Study population Group 2

Subjects with a diagnosis of either chronic kidney disease or chronic heart failure. Those patients who meet the following inclusion and exclusion criteria will be eligible for participation in the study group 2.

Inclusion criteria for Group 2

- Written informed consent (and assent when applicable) obtained from subject or subject's legal representative and ability for subject to comply with the requirements of the study.
- Ability for subject to comply with the requirements of the study, including basic ability to handle personal sensors and computer equipment required for the CARRE service.
- Male or female between 18-65 years old.
- Diagnosed CKD stage 3a or CKD stage 2 with albuminuria or diagnosed CHF (systolic), NYHA class II or III[38]

Exclusion criteria for Group 2

[38] The Criteria Committee of the New York Heart Association. (1994). Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. (9th ed.). Boston: Little, Brown & Co. pp. 253–256.

- Any stage CKD for patient with CHF (systolic)
- Any stage CHF (systolic for patient CKD
- CKD stage 1, 3b-5, CKD stage 2 without albuminuria,for patients with diagnosed CKD stage 3a or CKD stage 2 with albuminuria
- NYHA I or IV, for patients diagnosed with chronic (systolic) heart failure, NYHA class II or III
- Type 1 diabetes or gestational diabetes
- Advanced liver disease and/or cirrhosis
- Cancer
- Uncontrolled thyroid disorders
- Exacerbated chronic inflammatory disorders (e.g. rheumatoid arthritis)
- Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)
- Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis);
- CKD stage 1, 3b-5, CKD stage 2 without albuminuria
- NYHA I or IV
- Pregnancy
- Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data

4.1.5. Procedures and randomization

CARRE Pilot Study is a randomized single-blind, controlled pilot study.

4.1.5.1. Study design

The study design is shown in Figure 31. CARRE evaluation group (CARRE group) and Control group will be balanced by age, gender and number of patients with heart failure or chronic kidney disease (in Group 2). The same protocol will be used in 2 pilot sites. The intervention flow chart is shown in Figure 32.

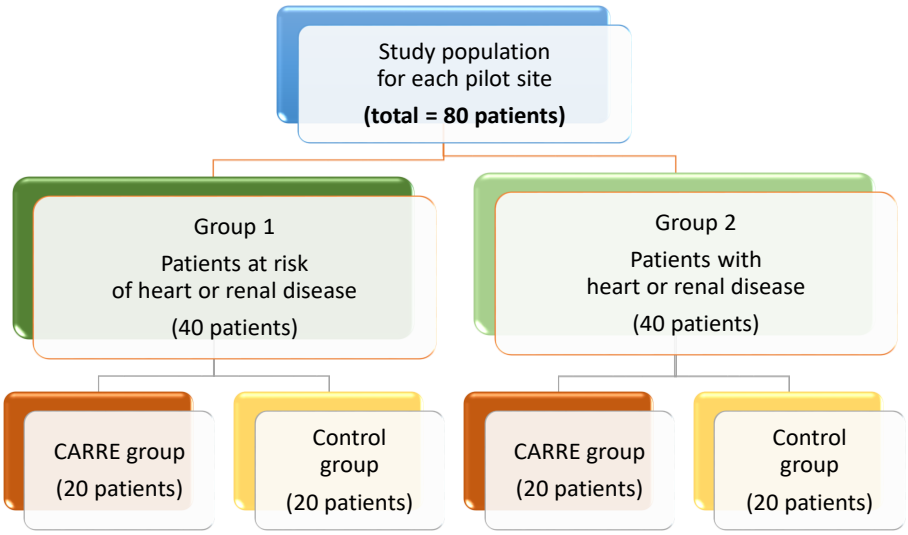

Figure 31. Study population groups for each pilot site.

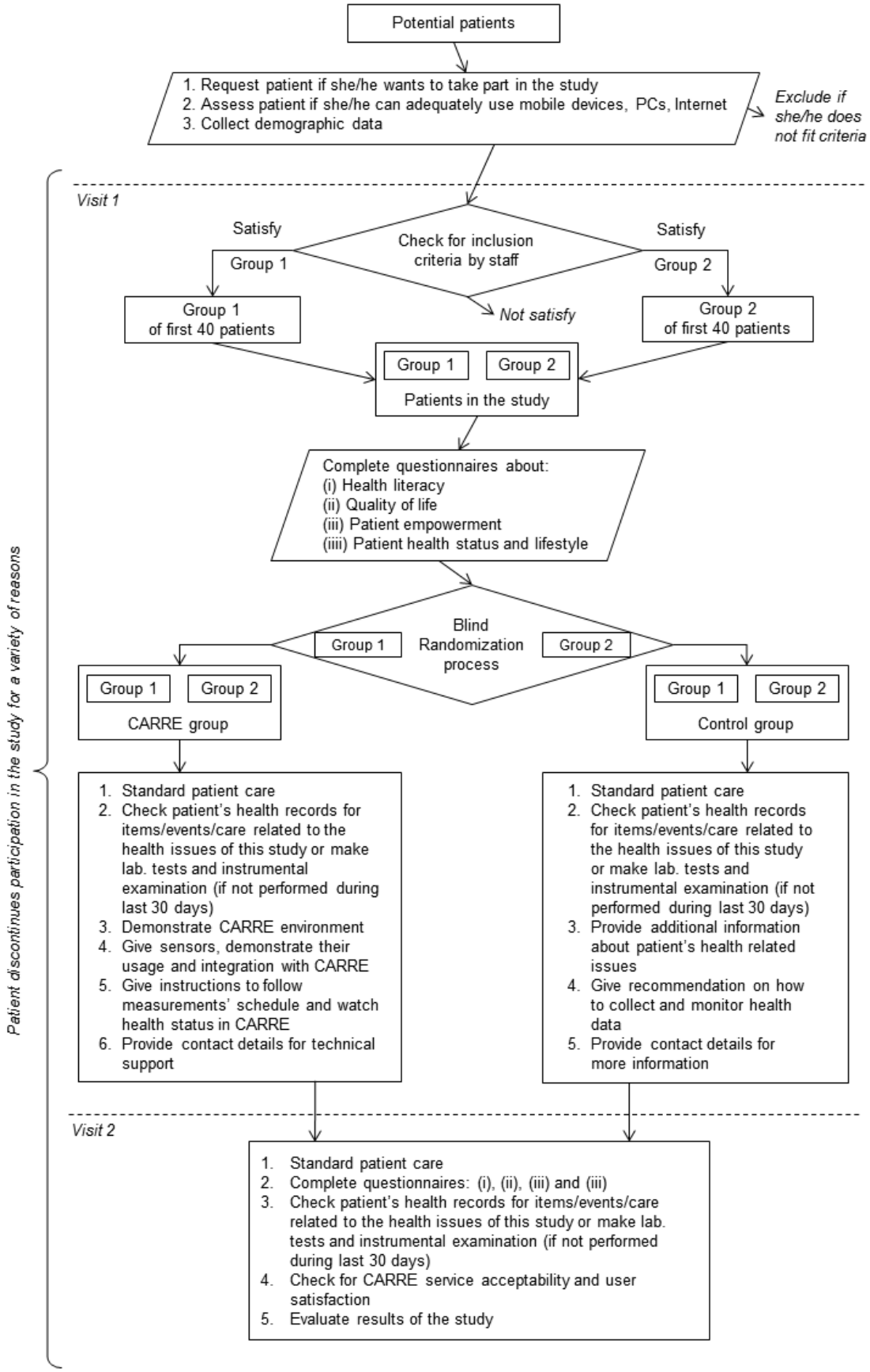

Figure 32. Overview of the clinical investigation flow chart.

4.1.5.2. Informed Consent Form

Patient informed consent will be obtained in accordance with local regulations.

4.1.5.3. Patient identification and numbering

To the confidentiality assurance issues each patient is uniquely identified in the study by 3 digit number which is a combination of his/her site number and patient number (e.g. 101). The site number consists of one digit (DUTH – "1"; VUL SK – "2"). After the patient will sign the informed consent form, the Investigator or his/her staff will then assign the site patient number, which is a 2-digit sequential number that begins with "0" (e.g., 01, 02, 03, etc.).

4.1.6. Criteria for evaluation

4.1.6.1. Primary efficacy points

Population Group 1

1) The between-group change in the SUSTAINS empowerment questionnaire.
2) The between-group change in the SF-36 questionnaire.
3) The between-group change in metabolic syndrome prevalence at the end of the study.
4) The between-group change in the number of metabolic syndrome components at the end of the study.

Population Group 2

1) The between-group change in the SUSTAINS empowerment questionnaire.
2) The between-group change in the SF-36 questionnaire.
3) Development of cardiorenal syndrome (chronic dysfunction in one organ induces acute or chronic dysfunction of the other)
4) Hospitalization due to renal or cardiac event.
5) The between-group change of eGFR and/or albuminuria.
6) The between-group change of Ejection Fraction (quantitative evaluation of left ventricular systolic function using biplane *Simpson's* method).

4.1.6.2. Secondary Efficacy endpoints

Population Group 1

1) The within-group intervention acceptability and user satisfaction.
2) The within- and between-group variations in lifestyle habits (smoking, physical activity, adherence to self-monitoring and therapy).
3) The within- and between-group variations in the number or dose of essential drugs.
4) The within- and between-group variations using the clinical and laboratory parameter measured at regular patient visits in clinical diagnostic centers. These include the following:
   - Weight
   - Waist circumference
   - Body Mass Index (BMI)
   - Fat mass (%)
   - Systolic pressure
   - Diastolic pressure
   - Total cholesterol

- Pulse
- Fasting glucose
- Glycohemoglobin (Hb_{AIC})
- Total cholesterol
- HDL cholesterol
- LDL cholesterol
- Triglycerides
- Uric Acid
- Creatinine
- Albumine /creatinine in urine sample

Population Group 2

1) The within-group intervention acceptability and user satisfaction.
2) The within- and between-group variations in lifestyle habits (smoking, physical activity, adherence to self-monitoring and therapy).
3) The within- and between-group variations in the number or dose of essential drugs.
4) The within- and between-group variations using the clinical and laboratory parameter measured at regular patient visits in clinical diagnostic centers. These include the following:
   - Weight
   - Waist circumference
   - Body Mass Index (BMI)
   - Fat mass (%)
   - Systolic pressure
   - Diastolic pressure
   - Pulse
   - Fasting glucose
   - Total cholesterol
   - HDL cholesterol
   - LDL cholesterol
   - Triglycerides
   - Uric Acid
   - Creatinine
   - Albumine /creatinine in urine sample
   - Glycohemoglobin (Hb_{AIC})
5) The within and between group left ventricular diastolic function (echocardiographic parameters: 1) E/A, 2) Deceleration Time, 3) IVRT, 4) Medial Annulus, 5) Lateral Annulus, 6) Left Atrium size (according to her/his medical file or/and laboratory tests).
6) The within- and between-group variations in 6 minutes walk test.

4.1.7. Evaluation by visit

4.1.7.1. Visit 1 (T_0, Screening, Baseline visit)

At Visit 1, subject's eligibility for entering the study will be assessed by the Investigator by evaluating all inclusion/exclusion criteria. Subject will be introduced to the study and a patient informed consent will be signed for participation in the study. All the participants must provide informed consent before any study-specific procedure (and randomization) is performed. Each subject will be assigned with a unique screening number (see Patient identification and numbering).

Staff should:

1) Fill in Screening Form and Randomize the patient.
2) Fill in Clinical Data Collection Form: perform measurements and collect required medical records (clinical and laboratory parameters, instrumental examination and number and dose of essential drugs)
3) Schedule patient for Visit 2.

Subjects should fill in following questionnaires:

1) Patient Visit Questionnaire (health status, lifestyle habits (physical activity, diet, smoking, alcohol consumption)
2) SF-36 questionnaire
3) SUSTAINS empowerment questionnaire

Patient baseline clinical and sociodemographic characteristics are aimed to be balanced in comparison groups at the involvement phase in each center.

4.1.7.2. After randomisation

CARRE evaluation group arm: After assignment to this group patients should get the following:

- Basic training how to work with CARRE user interface
- Training how to use telemedicine devices at home:
  - all: BP monitor, scale, physical activity tracker;
  - according to the clinical status (if are diagnosed with type 2 diabetes mellitus: glucometers)
- Obtain contact details of technical support

Control group arm: After assignment to this group, patients should get the following:

- Advice measurements and data collection with their own devices in a traditional way (paper notes/smartphone application, if they have got it)
- Obtain contact details in case patients may need more information about the study.

4.1.7.3. Visit 2 (T_{end}, Study termination)

The aim of this study termination visit is to assess the efficacy of CARRE service in increasing health literacy and its ability to empower patients and to evaluate possible changes of patient`s medical condition and his/her quality of life during study period.

Staff should:

1) Fill in Clinical Data Collection Form: perform measurements and collect required medical records (clinical and laboratory parameters, instrumental examination and number and dose of essential drugs)
2) Run all assessment instruments and final evaluation

Subjects should fill in following questionnaires:

1) Patient Visit Questionnaire (health status, lifestyle habits, physical activity, diet, smoking, alcohol consumption)
2) SF-36 questionnaire
3) SUSTAINS empowerment questionnaire

4.1.7.4. Early Withdrawal Visit

Staff should:

1) Fill in study Drop Out Report Form
2) Fill in Clinical Data Collection Form: perform measurements and collect required medical records (clinical and laboratory parameter, number and dose of essential drugs)

Subjects (if they agree) should fill in following questionnaires:

1) Patient Visit Questionnaire (health status, lifestyle habits, physical activity, diet, smoking, alcohol consumption)
2) SF-36 questionnaire
3) SUSTAINS empowerment questionnaire

4.1.7.5. Discontinuation and replacement of subjects

All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. Reasonable attempts will be made by the Investigator to provide a reason for subject withdrawals.

A subject may be discontinued from the study at any time if the subject or the Investigator feels that it is not in the subject's best interest to continue. The following is a list of possible reasons for the study discontinuation:

- Subject withdrawal of consent (or assent)
- Subject is not compliant with study procedures
- Protocol violation requiring discontinuation of the study
- Lost to follow-up

All subjects who discontinue the study should come in for an early discontinuation visit as soon as possible and then should be encouraged to complete all remaining scheduled visits and procedures.

4.1.7.6. Withdrawal of Subjects from the Study

A subject may be withdrawn from the study at any time if the subject or the Investigator feels that it is not in the subject's best interest to continue. All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice.

4.1.7.7. Replacement of Subjects

Subjects who withdraw from the study will be replaced.

4.1.8. Statistics and scores

4.1.8.1. Statistical assumptions

In the following sections the results derived from the participants testing with the various questionnaires across the two visits are presented. Then, the findings derived from the comparison between the scores from the two visits will be presented. It has to be reminded that the rationale of the pilot study was based on an experimental design whereas two groups (control and experimental-CARRE) were tested in two successive period of time. Both groups were tested on the basis of the same scale across the two visits while the experimental group participated in the interval in the CARRE program.

The ideal pattern of a successful experiment is the following (see Table 8 for symbols).

- C1 has to be statistically equal to E1 (homogeneity among study and control group, establish equal baseline);
- C1 statistically equal to C2 (control group, i.e. no exposure, shows no impact);

- C2 statistically different from E2 (exposure in CARRE group results in impact); and
- E1 statistically different from E2.(exposure in CARRE group results in impact).

Table 8.Symbols used for to indicate the observable value in different groups and visits.

Groups	Visit 1 before experiment	Visit 2 after experiment
Control	C1	C2
CARRE (Experimental)	E1	E2

Note: E and C are the respective scores of the various assessment instruments used in the study.

4.1.8.2. Quality of life questionnaire scores

In the field of healthcare, quality of life is often regarded in terms of how a certain ailment affects a patient on an individual level. This may be a debilitating weakness that is not life-threatening; life-threatening illness that is not terminal; terminal illness; the predictable, natural decline in the health of an elder; an unforeseen mental/physical decline of a loved one; or chronic, end-stage disease processes.

The most common used questionnaires for Quality of life measurement is the Short Form (36) Health Survey is a 36-item, patient-reported survey of patient health. In order to compare our results between the control and the CARRE intervention group and within the groups, we calculated the SF-36 score according to QualityMetric Scoring Software v5.0. This software provides two scores, the physical health summary $\mathrm{PHs}_{\mathrm{score}}$ and the mental health summary $\mathrm{MHs}_{\mathrm{score}}$.

4.1.8.3. Health literacy questionnaire scores

Based on a recent critical appraisal of 51 questionnaires[39], we decided to use a combination of European Health Literacy Questionnaire enriched with questions from Lipkus Expanded Health Numeracy Scale.

The European Health Literacy Questionnaire consists from 29 questions with a scale from "very difficult, difficult, easy, very easy". In our version we choose the 19 most relevant questions (see Annex 2) and transformed the answers as follows: very difficult = 1, difficult = 2, easy = 3, very easy = 4 and then we calculated the HL score according to the following formula[40]:

$$HLa_{score} = (mean(per\ Item) - 1) \times \frac{50}{3}$$

The Lipkus Expanded Health Numeracy Scale consists from 10 questions with answers "correct and incorrect". We transform the answers as incorrect to 0 and correct to 1, and then we calculated the HL score according the following formula:

$$HLb_{score} = count(correct\ Item) \times \frac{50}{10}$$

[39] JN. Haunab, MA. Valerioc, LA. McCormackd, KSørensene & MK. Paasche-Orlowf, Health Literacy Measurement: An Inventory and Descriptive Summary of 51 Instruments, Journal of Health Communication: International Perspectives, Volume 19, Supplement 2, 2014

[40] Pelikan JM, Röthlin F, Canahl K. Introduction to HL measurement procedures of the HLS-EU study, 2nd European HL Conference, Aarhus,10.4.2014. 2014.

These two scores have a minimum of 0 and a maximum of 50 points.

The final total score of health literacy is calculated by the mean score of these two scores, with a minimum of 0 and a maximum of 50, and is given from the following formula:

$$HLt_{score} = \frac{HLa_{score} + HLb_{score}}{2}$$

4.1.8.4. Empowerment (EMP) questionnaire scores

The assessment of patient empowerment in CARRE was based on the instrument developed in the EU funded SUSTAINS project questionnaire[41]. The background to the SUSTAINS project has three drivers that SUSTAINS contributes to: a) enabling and strengthening empowerment of patients; b) enabling better medical results; c) enabling a more efficient use of healthcare resources and containing costs. SUSTAINS project questionnaire consists from 19 questions where the answers are numeric from 1 to 10.

In order to compare our results between the control and the CARRE intervention group and within the groups we calculated the score according to a formula adjusted to SUSTAINS project questionnaire:

$$EMp_{score} = (mean(per\ Item) - 1) \times \frac{50}{9}$$

The final score of this formula has a minimum of 0 and a maximum of 50 points.

4.1.8.5. System Usability Score

To calculate the SUS score, the participants scores for each questions are summed. Each item's score contribution will range from 0 to 4. For items 1, 3, 5, 7 and 9 the score contribution is the scale position minus 1. For items 2, 4, 6, 8 and 10, the contribution is 5 minus the scale position. At the end we multiply the sum of the scores by 2.5 to obtain the overall value of SU.SUS scores have a range of 0 to 100[42]. Research indicates that a mean SUS score above 60 corresponds to an acceptable system[43].

4.1.9. Protocol Violations

A protocol violation occurs when the subject or the Investigator fails to adhere to significant protocol requirements affecting the inclusion, exclusion, subject safety and primary endpoint criteria. When a protocol violation occurs, it will be discussed with the Investigator and a Protocol Violation Form detailing the violation will be generated. This form will be signed by the Investigator.

4.1.10. Administrative, Ethical, Regulatory Considerations

The study will be conducted according to local regulations pertaining for each pilot site.

To maintain confidentiality, all laboratory specimens, evaluation forms, reports and other records will be identified by a coded number only (anonymized). All study records will be kept in a locked file cabinet and code sheets linking a patient's name to a patient identification number will be stored separately in another locked file cabinet. Clinical information will not be released without written permission of the subject. The Investigator must also comply with all applicable privacy regulations.

Patients' medical data related to cardiorenal syndrome collected from CARRE sensors or Manual Entry Form will be stored on the servers hosted in pilot sites in Greece (DUTH) and Lithuania (VULSK) respectively with appropriate technical organisational measures taken to protect the information. Other CARRE project partners

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[41] O. Unver, W. Atzori, Document D3.2 – Questionnaire for Patient Empowerment Measurement Version 1.0, SUSTAINS: Support USers To Access INformation and Services, January 2013, EU CT PSP Grant Agreement No 29720

[42] John Brooke. SUS - A quick and dirty usability scale. Redhatch Consulting Ltd., 12 Beaconsfield Way, Earley, READING RG6 2UX United Kingdom

[43] A. Bangor, P. Kortum, J. Miller, Determining what individual SUS sores mean: adding an adjective rating scale, Jornal of Usability Studies,4(3),114-123, 2009

will only be granted access to CARRE medical data for study evaluation purposes after data anonymization will take place taking into account local privacy regulations.

4.2. Results

4.2.1. Study protocol implementation

Building of Pilot Study Protocol was started early in February in order to acquire approval from Ethics Committees and other related Boards/Bodies of the University Hospitals and Healthcare structure in VULSK and DUTH. Study documents were prepared by both pilot site investigators.

- The Scientific Council of the Regional University Hospital of Alexandroupoli, Greece following the recommendation of the Hospital Bioethics Committee approved the CARRE protocol on 20 April 2016 (No. ΕΣ4/20-4-2016)
- The Bioethics Committee of Democritus University of Thrace, DUTH, approved the CARRE protocol on 2 June 2016 (No. ΕΗΔΕ 10/02 Ιουνίου 2016 ΘΕΜΑ 2β)
- The Bioethical committee of Vilnius Regional Biomedicine Research approved the permission to conduct the Pilot Study on 7thof June 2016 (No.158200-16-848-362).

In DUTH the participant recruitment started in August and involved chronic patients conducting their regular visit at the outpatient clinics of three department of the General University Hospital of Alexandroupolis, Department of Cardiology, Department of Nephrology and Department of Obesity and Metabolic Syndrome. From the Department of Obesity and Metabolic Syndrome 25 patients (METS) enrolled in the study, from the Department of Cardiology 12 patients (CKD) and from the Department of Nephrology 6 patients (CHF). The enrolment lasted for 22 working days. It should be noted that the timing of recruitment during August created the following problem. In Greece, due to the extremely hot weather and vacation time, this period is not ideal for regular patient visits. As a result, chronic patients are not scheduled for their regular visits during this period (unless for emergency events), so the Greek pilot was not able to recruit all the full number of scheduled participants. The recruitment continued well into fall, however, this resulted in less than adequate available time for CARRE use by the participants. So, the GA decided to go on with the pilot and assess quality of life, health literacy, empowerment and system user satisfaction in an intermediate visit at the end of October 2016 and report the findings in this document, while prolong the pilot for at least two more months so as to allow some meaningful time for any expected changes in the health status of the participants. These are to be collected after the end of the project and reported (if possible) during the final year review and in a journal publication presenting all the results of the pilot deployment and evaluation. During the course of the study there were 2 drop outs, both during the follow up visit, so there was no time to substitute participants within the time limit of the project duration.

In VULSK the participant recruitment started at the end of July. The enrolment took 19 working days. It was organised in two centres: Centre of Cardiology and Angiology and Centre of Nephrology. In the Centre of Cardiology and angiology in Preventative Cardiology Department 40 patients to form Group 1 (patients with Metabolic Syndrome (MetS)) were enrolled. Group 1 was enrolled from 26 July 2016 till 12 August 2016.A part of Group 2 was formed in Department of Out-patient Cardiology in VULSK: 20 patients with Chronic Heart Failure were enrolled from 26 July 2016 till 09 August 2016. The rest of Group 2 was formed in Centre of Nephrology in Cabinets of Out-patient Nephrology (20 patients with Chronic Kidney Disease) from 29 July 2016 till 19 August 2016. During study period (till Interim Visit) there were two drop outs: they both occurred in Group 2 CARRE arm (one patient with CHK and one with CHF). The reason of study discontinuation was patient consent withdrawal in both cases. Both patients were replaced according the Protocol procedures.

During Visit 1, the investigator evaluated whether the subject was eligible to take part in the 6 month study taking into account study inclusion and exclusion criteria and filling in the Screening Form. The patient was introduced to the study as long as he/she had signed a participant informed consent form for participation in the study. During the same visit Patient Visit Questionnaire, SF-36 questionnaire, SUSTAINS empowerment questionnaire were filled in by study participant. The investigator carried out the relevant measurements and collected required medical records (clinical and laboratory parameters, instrumental examination and number and dose of essential drugs), filled in Clinical Data Collection Form and scheduled the participant for the next visit. The enrolled participants completed all baseline assessment and were allocated to either CARRE or

control group, each was assigned with a unique screening number. Study participants assigned to CARRE group have received leaflets related to their medical condition. They also were trained how to work with CARRE user interface and how to use smart devices (BP monitor, scale, physical activity tracker and glucometers, if diagnosed with type 2 diabetes mellitus) at home. Control group participants were given information leaflets relevant to their disease and were advised how to properly measure their health parameters (e.g. body weight, blood pressure) with their own devices in a routine way.

In October 2016 an interim visit (at DUTH) and phone survey (at VULSK) were arranged for study participants in order to fill-in SF-36 questionnaire, SUSTAINS empowerment questionnaire and System Usability Scale Survey.

In December 2016 study end visit is scheduled to evaluate changes in the SF-36 questionnaire, SUSTAINS empowerment questionnaire and System Usability Scale Survey. Patient Visit Questionnaire (VULSK) is also to be filled-in, the same measurements performed and medical records evaluated as during the Visit 1 in order to detect changes in study participants' primary and secondary endpoints.

4.2.2. Statistical analysis

Continuous variables were expressed as means and standard deviations (SD), whereas categorical variables were expressed as frequencies and percentages. Comparisons between groups were made using chi-square or Fisher exact test for categorical data and *t* test for independent samples for continuous data. Within group baseline and interim visit comparisons were made with *t* test for matched pairs.

All data were analyzed using SPSS 20 software. Propensity score matching was performed using the MatchIt package of the R program. P-values less than 0.05 (two-tailed) were considered statistically significant. Where needed, data were balanced using the propensity score matching method (PSM)[44].

4.2.3. Characteristics of study population

The descriptive characteristics of the study groups are given below: **Error! Reference source not found.** presents demographics for the study population for DUTH and VULSK pilots separately, and Table 10 the demographics of the pooled population from both pilots.

[44] Rosenbaum P.R.; Rubin, D.B. The Central Role of the Propensity Score in Observational Studies for Causal Effects. Biometrika. 70 (1): 41–55, 1983.

Table 9. Demographics of study group in DUTH and VULSK pilot separately.

	DUTH pilot		VUSLK pilot	
Total Population	**Control**	**CARRE**	**Control**	**CARRE**
N	14	26	29	29
Age (yrs)	54.5 ± 7.2	47.3 ± 11.2	51.5 ± 7.0	50.2 ± 10.1
Female	3 (21%)	14 (54%)	9 (31%)	7 (24%)
Educational level				
Secondary education	13 (93%)	19 (73%)	14 (48%)	13 (45%)
Tertiary education	1 (7%)	7 (27%)	15 (52%)	16 (55%)
Metabolic syndrome				
N	5	19	14	15
Age (yrs)	56.6 ± 5.5	46.7 ± 10.0	49.8 ± 6.7	50.0 ± 7.2
Female	2 (40%)	12 (63%)	5 (36%)	3 (20%)
Educational level				
Secondary education	4 (80%)	12 (63%)	2 (14%)	6 (40%)
Tertiary education	1 (20%)	7 (37%)	12 (86%)	9 (60%)
HF or CKD				
N	9	7	15	14
Age (yrs)	53.3 ± 8.0	49.1 ± 14.6	53.1 ± 7.1	50.4 ± 12.8
Female	1 (11%)	2 (29%)	4 (27%)	4 (29%)
Educational level				
Secondary education	9 (100%)	7 (100%)	12 (80%)	7 (50%)
Tertiary education	0 (0%)	0 (0%)	3 (20%)	7 (50%)

Table 10. Demographics of pooled study population for both pilots.

Total Population	**Control**	**CARRE**
N	43	55
Age (yrs)	52.5 ± 7.1	48.9 ± 10.6
Female	12 (28%)	21 (38%)
Educational level		
Secondary education	27 (63%)	32 (58%)
Tertiary education	16 (37%)	23 (42%)
Metabolic syndrome		
N	19	34
Age (yrs)	51.6 ± 6.9	48.1 ± 8.9
Female	7 (37%)	15 (44%)
Educational level		
Secondary education	6 (32%)	18 (53%)
Tertiary education	13 (68%)	16 (47%)
HF or CKD		
N	24	21
Age (yrs)	53.2 ± 7.3	50.0 ± 13.0
Female	5 (21%)	6 (29%)
Educational level		
Secondary education	21 (87%)	14 (67%)
Tertiary education	3 (13%)	7 (33%)

4.2.3.1. Quality of life, health literacy and empowerment at baseline (control vs. CARRE)

Table 11 shows comparative characteristics for control and study arms for DUTH pilot at baseline in terms of quality of life, health literacy and empowerment. The differences between the two study arms (control and CARRE) in each of various measures were not significant for the study population in DUTH pilot. These results show that both control and CARRE arms are equivalent at baseline, i.e. in the visit before the intervention, in terms of the scores measuring the variables under investigation, namely quality of life, health literacy and empowerment.

Table 11. Quality of life, health literacy and empowerment scores for the study population at baseline (visit1) for DUTH pilot.

Visit 1: C1 – E1 for DUTH*		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2)[&]	p[†]
Quality of Life	PCS	43.5 ± 10.1	47.8 ± 9.2	-1.377	0.177
	MCS	42.5 ± 8.1	42.0 ± 12.7	0.135	0.894
Health Literacy	HLT	21.6 ± 12.4	28.3 ± 9.0	-1.968	0.056
Empowerment	EMP	24.0 ± 12.0	31.5 ± 11.5	-1.938	0.060
METS group					
Quality of Life	PCS	48.8 ± 8.0	48.0 ± 7.8	0.205	0.839
	MCS	42.8 ± 1.4	40.4 ± 13.7	0.389	0.701
Health Literacy	HLT	27.9 ± 7.1	30.5 ± 8.1	-0.642	0.528
Empowerment	EMP	27.5 ± 8.8	30.8 ± 11.1	-0.605	0.552
HF/CKD group					
Quality of Life	PCS	40.5 ± 10.2	47.3 ± 13.2	-1.163	0.264
	MCS	42.3 ± 10.3	46.4 ± 8.7	-0.829	0.421
Health Literacy	HLT	18.0 ± 13.7	22.3 ± 9.4	-0.713	0.487
Empowerment	EMP	22.0 ± 13.6	33.4 ± 13.5	-1.675	0.116

** C1 = control arm before (visit 1), E1 = CARRE arm before (visit 1)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[&] total N-2 = 38, METs N-2=22. HF/CKD N-2=14

Table 12 shows the scores for the study population for the VULSK pilot. The differences between the two arms in measures of mental quality of life score (MCS) and empowerment (EMP) were not statistically significant ($p > 0.05$), but the differences in measures of physical quality of life score (PCS) and health literacy (HLT) were significant ($p < 0.05$). This signifies a biased between the two study arms at baseline (based on Table 8). To remedy this, we used propensity score matching (R package 'MatchIt'[45]) on measures (PCS, MCS, HLT, EMP) and demographics (age, sex, education level, disease group) to reduce selection bias and construct balanced control and experimental-CARRE groups. This resulted in removal of 11 patients from CARRE group and 11 patients from Control Group (27.5% removal of the sample). The scores for the different measures for the final VULSK study population of 58 participants after propensity matching are presented in Table 13. These results show that both control and CARRE arms for VULSK pilot are equivalent at baseline, i.e. in the visit before the intervention, in terms of the scores measuring the variables under investigation, namely quality of life, health literacy and empowerment.

[45] Ho DE, Imai K, King G, Stuart EA. Matching as nonparametric preprocessing for reducing model dependence in parametric causal inference. Political analysis. 2007 Jun 20;15(3):199-236.

Table 12. Quality of life, health literacy and empowerment scores for the study population at baseline (visit1) for VULSK pilot (N=80).

Visit 1: C1 – E1 for VUSLK*		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2)[&]	p[†]
Quality of Life	**PCS**	47.8 ± 7.5	51.6 ± 6.3	-2.402	**0,019**[#]
	MCS	44.4 ± 7.3	43.9 ± 7.8	0,293	0,771
Health Literacy	**HLT**	26.91 ± 7.7	32.3 ± 7.7	-3,122	**0,003**
Empowerment	EMP	38.1 ± 7.5	37.5 ± 7.0	0,365	0,716

** C1 = control arm before (visit 1), E1 = CARRE arm before (visit 1)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[#] bold red lettering highlights significant differences (p<.05)

[&] total N-2 = 78

Table 13. Quality of life, health literacy and empowerment scores for the study population at baseline (visit1) for VULSK pilot after propensity score matching – resulting N=58.

Visit 1: C1 – E1 for VUSLK*		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2) [&]	p[†]
Quality of Life	PCS	49.4 ± 7.7	50.0 ± 6.4	-0.312	0.756
	MCS	44.4 ± 7.2	44.0 ± 8.5	0.186	0.853
Health Literacy	HLT	29.4 ± 5.8	30.7 ± 7.8	-0.672	0.504
Empowerment	EMP	37.9 ± 7.2	36.3 ± 7.1	0.861	0.393
Metabolic Syndrome group					
Quality of Life	PCS	50.4 ± 5.3	52.0 ± 3.2	-0.997	0.328
	MCS	45.9 ± 6.5	47.8 ± 8.2	-0.686	0.499
Health Literacy	HLT	31.4 ± 5.2	32.2 ± 8.8	-0.305	0.763
Empowerment	EMP	35.7 ± 7.7	33.9 ± 8.5	0.588	0.562
HF or CKD group					
Quality of Life	PCS	48.5 ± 9.5	47.8 ± 8.2	0.202	0.842
	MCS	42.9 ± 7.6	39.9 ± 7.0	1.119	0.273
Health Literacy	HLT	27.6 ± 5.9	29.0 ± 6.6	-0.590	0.560
Empowerment	EMP	39.9 ± 6.1	38.8 ± 4.1	0.576	0.570

** C1 = control arm before (visit 1), E1 = CARRE arm before (visit 1)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[&] total N-2 = 56, METs N-2=27, HF/CKD N-2=27

Table 14 shows comparative characteristics for control and study arms for the entire study population after VULSK population propensity matching at baseline in terms of quality of life, health literacy and empowerment. The differences between the two study arms (control and CARRE) in each of various measures were not significant for the study population. These results show that both control and CARRE arms are equivalent at baseline, i.e. in the visit before the intervention, in terms of the scores measuring the variables under

investigation, namely quality of life, health literacy and empowerment.and for the pooled population of both pilot sites.

Table 14. Quality of life, health literacy and empowerment scores for the pooled study population at baseline (visit1) for both pilot sites.

Visit 1: C1 – E1* for total population		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2)[&]	p[†]
Quality of Life	PCS	47.5 ± 8.9	49.0 ± 7.9	-0.876	0.383
	MCS	43.8 ± 7.4	43.0 ± 10.6	0.376	0.708
Health Literacy	HLT	26.9 ± 9.2	29.5 ± 8.4	-1.494	0.139
Empowerment	EMP	33.3 ± 11.1	34.0 ± 9.7	-0.316	0.752
Metabolic Syndrome group					
Quality of Life	PCS	50.0 ± 5.9	49.8 ± 6.4	0.121	0.904
	MCS	45.1 ± 5.7	43.7 ± 12.0	0.491	0.626
Health Literacy	HLT	30.5 ± 5.7	31.2 ± 8.3	-0.361	0.719
Empowerment	EMP	33.6 ± 8.6	32.2 ± 10.0	0.507	0.614
HF or CKD group					
Quality of Life	PCS	45.5 ± 10.3	47.7 ± 9.8	-0.717	0.477
	MCS	42.7 ± 8.5	42.0 ± 8.0	0.268	0.790
Health Literacy	HLT	24.0 ± 10.4	26.8 ± 8.1	-0.980	0.333
Empowerment	EMP	33.2 ± 12.9	37.0 ± 8.5	-1.151	0.256

** C1 = control arm before (visit 1), E1 = CARRE arm before (visit 1)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[&] total N-2 = 96, METs N-2=51, HF/CKD N-2=43

4.2.3.2. Quality of life, health literacy and empowerment after intervention (control vs. CARRE)

The results from the assessment of quality of life (PCS and MCS), health literacy (HLT) and empowerment for the two study arms, control and CARRE, after intervention (visit 2) for the DUTH pilot are presented in Table 15. Considering the total study population at DUTH pilot, the results show that there was no significant difference between the two groups in the quality of life scores, both PCS score ($M_{control}$ = 45.1, M_{CARRE} = 48.9) t (38) = -1.410, p > 0.05 and in the MCS score ($M_{control}$ = 40.8, M_{CARRE} = 41.6) t (38) = -0.192, p > 0.05. On the contrary, there were significant differences between the two groups in the he;ath literacy score HLT ($M_{control}$ = 22.0, M_{CARRE} = 30.5) t (38) = -2.707, p < 0.05 and empowerment score EMP ($M_{control}$ = 24.2, M_{CARRE} = 36.2) t (38) = -3.757, p = 0.001. These results show that the CARRE service had positive effects on the participants of the experimental arm (CARRE group) in terms of health literacy and empowerment as compared to the control arm.

Table 15. Quality of life, health literacy and empowerment scores for the study population after intervention (visit 2) for DUTH pilot.

Visit 2: C2 – E2* for DUTH		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2)[&]	p[†]
Quality of Life	PCS	45.1 ± 9.9	48.9 ± 6.8	-1.410	0.167
	MCS	40.8 ± 9.0	41.6 ± 13.8	-0.192	0.849
Health Literacy	**HLT**	22.0 ± 12.6	30.5 ± 7.2	-2.707	**0.010**[#]
Empowerment	**EMP**	24.2 ± 12.3	36.2 ± 8.0	-3.757	**0.001**
Metabolic Syndrome group					
Quality of Life	PCS	50.9 ± 3.9	47.6 ± 6.1	1.133	0.270
	MCS	39.1 ± 7.3	40.1 ± 15.0	-0.152	0.880
Health Literacy	HLT	28.6 ± 6.6	31.0 ± 7.4	-0.647	0.525
Empowerment	EMP	27.8 ± 9.1	35.1 ± 8.1	-1.752	0.094
HF or CKD group					
Quality of Life	PCS	41.9 ± 10.9	52.2 ± 8.1	-2.082	0.056
	MCS	41.8 ± 10.1	45.7 ± 9.7	-0.775	0.451
Health Literacy	HLT	18.4 ± 14.0	29.1 ± 7.0	-1.858	0.084
Empowerment	**EMP**	22.1 ± 13.8	39.2 ± 7.6	-2.938	**0.011**

** C2 = control arm after (visit 2), E2 = CARRE arm after (visit 2)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[#] bold red lettering highlights significant differences (p<.05)

[&] total N-2 = 38, METs N-2=22, HF/CKD N-2=14

The results from the assessment of quality of life (PCS and MCS), health literacy (HLT) and empowerment for the two study arms, control and CARRE, after intervention (visit 2) for the VULSK pilot are presented in Table 16. Considering the total study population at DUTH pilot, the results show that there was no significant difference between the two arms for the general population and the metabolic syndrome patients group. However, there was a significant difference between the two arms for the patient population with HF or CD in the health literacy score HLT ($M_{control}$ = 27.8, M_{CARRE} = 34.2) t (56) = -2.091, p < 0.05. These results show that the CARRE service had positive effects on the participants of the HF or CKD (heart failure or chronic kidney disease) experimental arm (CARRE group) in terms of health literacy as compared to the respective control arm.

Table 16. Quality of life, health literacy and empowerment scores for the study population after intervention (visit 2) for VULSK pilot.

Visit 2: C2 – E2* for VULSK		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2)[&]	p[†]
Quality of Life	PCS	47.1 ± 11.2	50.7 ± 6.2	-1.506	0.138
	MCS	43.6 ± 5.8	45.1 ± 8.3	-0.776	0.441
Health Literacy	HLT	30.6 ± 8.3	34.2 ± 7.3	-1.731	0.089
Empowerment	EMP	36.3 ± 8.4	37.2 ± 5.0	-0.493	0.624
Metabolic Syndrome group					
Quality of Life	PCS	50.0 ± 9.3	51.8 ± 5.7	-0.632	0.533
	MCS	46.2 ± 4.3	48.6 ± 8.6	-0.946	0.353
Health Literacy	HLT	33.6 ± 6.6	34.2 ± 7.5	-0.206	0.838
Empowerment	EMP	35.2 ± 8.8	37.5 ± 5.5	-0.848	0.404
HF or CKD group					
Quality of Life	PCS	44.4 ± 12.5	49.5 ± 6.8	-1.359	0.186
	MCS	41.3 ± 6.1	41.3 ± 6.4	-0.036	0.971
Health Literacy	**HLT**	27.8 ± 8.9	34.2 ± 7.3	-2.091	**0.046**[#]
Empowerment	EMP	37.3 ± 8.1	36.8 ± 4.5	0.192	0.849

** C2 = control arm after (visit 2), E2 = CARRE arm after (visit 2)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[#] bold red lettering highlights significant differences (p<.05)

[&] total N-2 = 56, METs N-2=27, HF/CKD N-2=27

The results from the assessment of quality of life (PCS and MCS), health literacy (HLT) and empowerment (EMP) for the two study arms, control and CARRE, after intervention (visit 2) for the pooled data from both pilots are presented in Table 17. Considering the total study population, the results show that there was no significant difference between the two groups in the quality of life scores, both PCS score and in the MCS score. On the contrary, there were significant differences between the two groups in the health literacy score HLT ($M_{control}$ = 27.8, M_{CARRE} = 32.4), t(96) = -2.527, $p < 0.05$ and empowerment score EMP ($M_{control}$ = 32.3, M_{CARRE} = 36.7) t(96) = -2.419, $p < 0.05$. These results show that the CARRE service had positive effects on the participants of the experimental arm (CARRE group) in terms of health literacy and empowerment as compared to the control arm. Considering the two different study groups of the pooled data in more detail, namely metabolic syndrome patients (group 1) and heart failure or chronic kidney disease (HF or CKD, group 2), we find no significant differences between control and study arms after intervention for the metabolic syndrome group patients. However, for the study group of HF/CKD patients, there were significant differences between the two groups in the health literacy score HLT ($M_{control}$ = 27.8, M_{CARRE} = 32.4), t(43) = -2.527, $p < 0.05$ and empowerment score EMP ($M_{control}$ = 32.3, M_{CARRE} = 36.7), t(43) = -2.419, $p < 0.05$.

Table 17. Quality of life, health literacy and empowerment scores for the for the pooled study population after intervention (visit 2) for both pilot sites.

Visit 2: C2 – E2* for VUSLK		**Control**	**CARRE**	**t test**	
Total Population		Mean ± SD	Mean ± SD	t (df=N-2)[&]	p[†]
Quality of Life	PCS	46.5 ± 10.7	49.8 ± 6.5	-1.921	0.058
	MCS	42.7 ± 7.0	43.5 ± 11.3	-0.373	0.710
Health Literacy	**HLT**	27.8 ± 10.6	32.4 ± 7.4	-2.527	**0.013**[#]
Empowerment	**EMP**	32.3 ± 11.2	36.7 ± 6.5	-2.419	**0.017**
Metabolic Syndrome group					
Quality of Life	PCS	50.2 ± 8.1	49.5 ± 6.2	0.390	0.698
	MCS	44.3 ± 6.0	43.9 ± 13.1	0.138	0.891
Health Literacy	HLT	32.3 ± 6.8	32.4 ± 7.5	-0.033	0.973
Empowerment	EMP	33.3 ± 9.3	36.2 ± 7.1	-1.279	0.207
HF or CKD group					
Quality of Life	**PCS**	43.5 ± 11.7	50.4 ± 7.2	-2.354	**0.023**
	MCS	41.5 ± 7.6	42.8 ± 7.7	-0.579	0.565
Health Literacy	**HLT**	24.3 ± 11.8	32.5 ± 7.4	-2.758	**0.008**
Empowerment	EMP	31.6 ± 12.7	37.6 ± 5.6	-1.999	0.052

** C2 = control arm after (visit 2), E2 = CARRE arm after (visit 2)*

[†] p values obtained by comparing differences in the variable values between control and CARRE arms using independent samples t-test

[#] bold red lettering highlights significant differences (p<.05)

[&] total N-2=96, METs N-2=51, HF/CKD N-2=43

4.2.3.3. Quality of life, health literacy and empowerment before and after intervention (for control & CARRE)

Table 18 shows the mean differences before (visit 1) and after the intervention (visit 2) for the measures of quality of life (PCS and MCS), health literacy (HLT) and empowerment (EMP) for both study arms for the DUTH pilot. Statistical significance of the differences was assessed via matched pair t test. The results show no significant difference for any of the measured quantities for the control arm. Regarding the CARRE arm, results show no significant difference before and after the intervention for both measures of the quality of life (PCS an MCS) and health literacy (HLT). However, we found a significant difference for the empowerment (EMP) of the total CARRE arm population for the DUTH pilot. Considering the two disease groups, empowerment (EMP) was significantly increased in the metabolic syndrome group, while the HF/CKD group showed significantly increased health literacy (HLT).

Table 18. Quality of life, health literacy and empowerment scores for the study population before and after intervention (visit 2 – visit 1) for DUTH pilot.

Visit 2 – Visit 1: for DUTH C2 – C1 & E2 – E1*		**Control**		**CARRE**	
Total Population		mean difference	p†	mean difference	p†
Quality of Life	PCS	1.642	0.167	1.034	0.426
	MCS	-1.654	0.242	-0.360	0.842
Health Literacy	HLT	0.482	0.065	2.192	0.114
Empowerment	**EMP**	0.188	0.168	4.725	**0.000**#
Metabolic Syndrome group					
Quality of Life	PCS	2.074	0.374	-0.385	0.621
	MCS	-3.744	0.374	-0.256	0.918
Health Literacy	HLT	0.674	0.238	0.487	0.734
Empowerment	**EMP**	0.292	0.374	4.326	**0.002**
HF or CKD group					
Quality of Life	PCS	1.402	0.347	4.886	0.283
	MCS	-0.492	0.347	-0.644	0.410
Health Literacy	**HLT**	0.376	0.206	6.817	**0.038**
Empowerment	EMP	0.130	0.347	5.806	0.095

** C2 = control arm after (visit 2), E2 = CARRE arm after (visit 2)*

† p values obtained by comparing values within each arm using paired samples t-test

 # bold red lettering highlights significant differences (p<.05)

Table 19 shows the mean differences before (visit 1) and after the intervention (visit 2) for the measures of quality of life (PCS and MCS), health literacy (HLT) and empowerment (EMP) for both study arms for the VULSK pilot. Statistical significance of the differences was assessed via matched pair t test. The results show no significant difference for any of the measured quantities for the control arm. Regarding the CARRE arm, results show no significant difference before and after the intervention for both measures of the quality of life (PCS an MCS) and empowerment (EMP). However, we found a significant difference for health literacy (HLT) of the total CARRE arm population for the VULSK pilot. Considering the two disease groups, empowerment (EMP) was significantly increased in the metabolic syndrome group, while the HF/CKD group showed significantly increased health literacy (HLT). This finding is consistent with the respective finding of the DUTH pilot (see Table 18).

Table 19. Quality of life, health literacy and empowerment scores for the study population before and after intervention (visit 2 – visit 1) for VUSLK pilot.

Visit 2 – Visit 1: for VUSLK C2 – C1 & E2 – E1*		**Control**		**CARRE**	
Total Population		mean difference	p†	mean difference	p†
Quality of Life	PCS	-2.337	0.076	0.676	0.487
	MCS	-0.744	0.605	1.102	0.291
Health Literacy	**HLT**	1.197	0.371	3.536	**0.013**#
Empowerment	EMP	-1.574	0.113	0.926	0.340
Metabolic Syndrome group					
Quality of Life	PCS	-0.423	0.758	-0.243	0.838
	MCS	0.226	0.870	0.746	0.598
Health Literacy	HLT	2.293	0.127	2.015	0.192
Empowerment	**EMP**	-0.489	0.731	3.589	**0.007**
HF or CKD group					
Quality of Life	PCS	-4.124	0.063	1.661	0.303
	MCS	-1.649	0.514	1.484	0.360
Health Literacy	**HLT**	0.173	0.938	5.165	**0.039**
Empowerment	EMP	-2.586	0.071	-1.927	0.123

** C2 = control arm after (visit 2), E2 = CARRE arm after (visit 2)*

† p values obtained by comparing values within each arm using paired samples t-test

 # bold red lettering highlights significant differences (p<.05)

Table 20 shows the mean differences before (visit 1) and after the intervention (visit 2) for the measures of quality of life (PCS and MCS), health literacy (HLT) and empowerment (EMP) for both study arms for the pooled data of both pilots. Statistical significance of the differences was assessed via matched pair t test. The results show no significant difference for any of the measured quantities for the control arm. Regarding the CARRE arm, results show no significant difference before and after the intervention for both measures of the quality of life (PCS an MCS). However, we found a significant difference for health literacy (HLT) and empowerment (EMP) of the total CARRE arm population for the pooled data. Considering the two disease groups, empowerment (EMP) was significantly increased in the metabolic syndrome group, while the HF/CKD group showed significantly increased health literacy (HLT).

Table 20. Quality of life, health literacy and empowerment scores for the pooled study population before and after intervention (visit 2 – visit 1) for both pilots.

Visit 2 – Visit 1: C2 – C1 & E2 – E1* for pooled data		**Control**		**CARRE**	
Total Population		mean difference	p†	mean difference	p†
Quality of Life	PCS	-1.042	0.287	0.845	0.284
	MCS	-1.040	0.326	0.411	0.683
Health Literacy	**HLT**	0.964	0.283	2.900	**0.003**#
Empowerment	**EMP**	-1.000	0.137	2.722	**0.001**
Metabolic Syndrome group					
Quality of Life	PCS	0.234	0.838	-0.322	0.627
	MCS	-0.818	0.567	0.186	0.901
Health Literacy	HLT	1.867	0.091	1.161	0.261
Empowerment	**EMP**	-0.284	0.785	4.001	**0.000**
HF or CKD group					
Quality of Life	PCS	-2.052	0.176	2.736	0.122
	MCS	-1.215	0.437	0.774	0.481
Health Literacy	**HLT**	0.249	0.856	5.716	**0.003**
Empowerment	EMP	-1.568	0.082	0.650	0.660

** C2 = control arm after (visit 2), E2 = CARRE arm after (visit 2)*

† p values obtained by comparing values within each arm using paired samples t-test

 # bold red lettering highlights significant differences (p<.05)

4.2.3.4. System Usability Assessment – SUS scores

Table 21 shows the mean System Usability Score (SUS) as assessed for the total CARRE intervention arm (N=66) and for each individual pilot CARRE arm. Overall, SUS had a mean value of 67.7±12.8. The frequency distribution of individual participants' responses for both pilots together, DUTH pilot, and VUSLK pilot are shown in Figure 33, Figure 34 and Figure 35 respectively.

For DUTH pilot, the frequency distribution shows a clustering of responses in the range from 56 to 78 (95% within 2*SD), with one outlier in the very low values (SUS=27.5) and one in the higher values (SUS=92.5). For VUSLK pilot, the frequency distribution shows a clustering of responses in the range from 55 to 83 (95% within 2*SD), with one outlier in the very low values (SUS=27.5) and two in the higher values (SUS=100).

Table 21. System usability mean scores.

	N (%)	SUS (mean ± SD)
total population	55 (100%)	67.7 ± 12.8
DUTH	26 (47.3%)	67.0 ± 11.4
VULSK	29 (52.7%)	68.3 ± 14.5

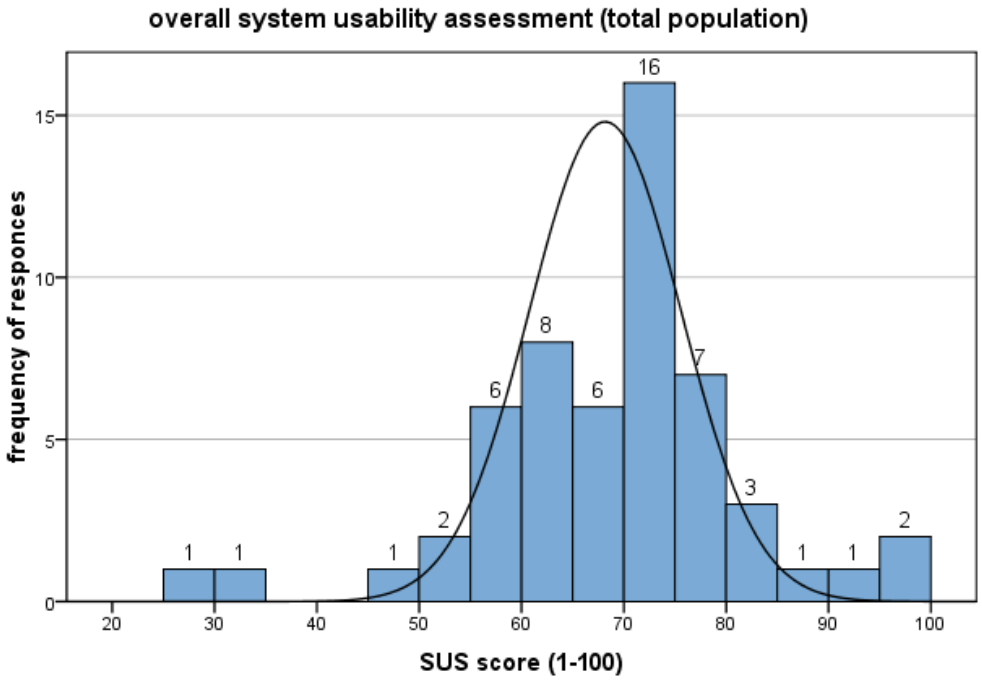

Figure 33. Frequency distribution of individual SUS scores for the total CARRE arm population from both pilots (N=55).

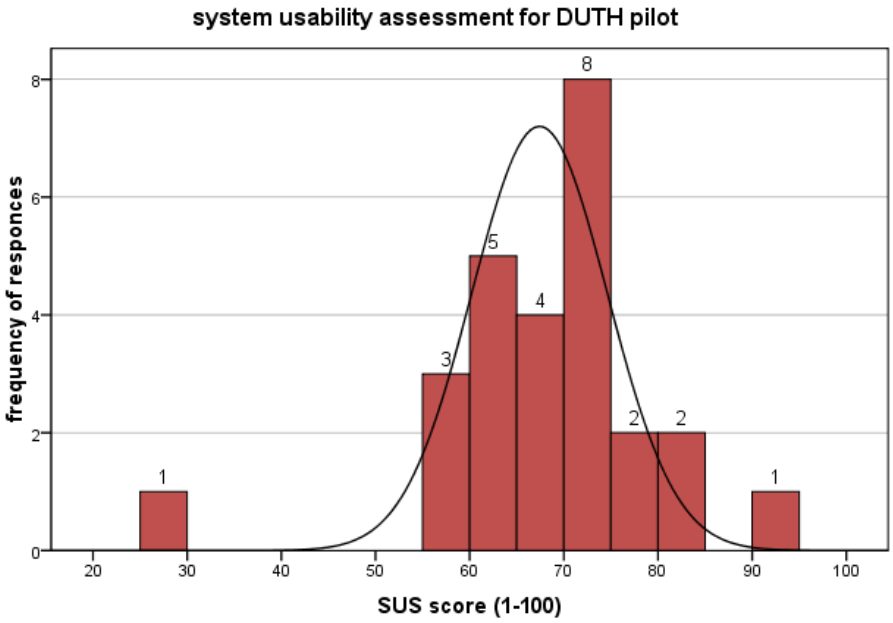

Figure 34.Frequency distribution of individual SUS scores for the CARRE arm population in DUTH pilot (N=26).

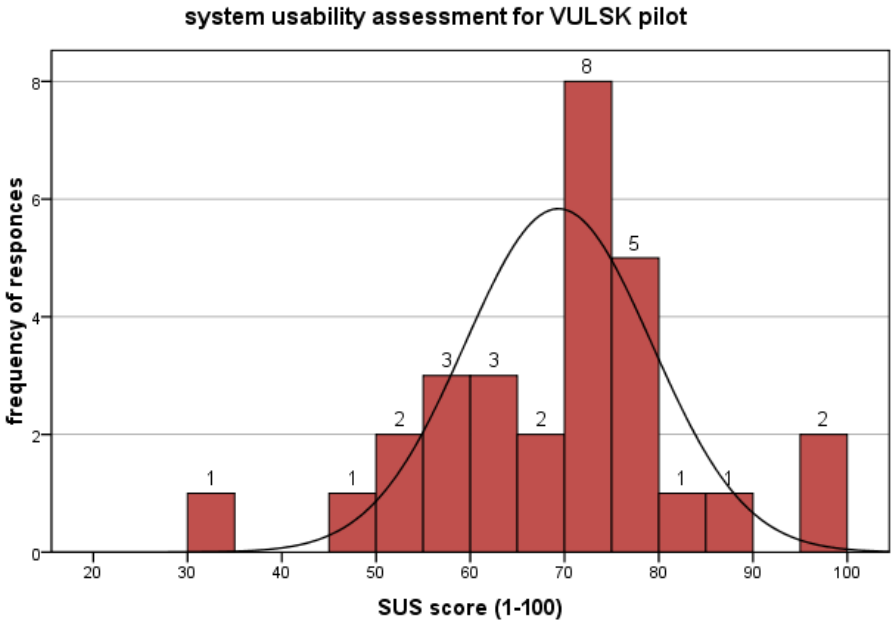

Figure 35.Frequency distribution of individual SUS scores for the CARRE arm population in VUSLK pilot (N=29).

5. Discussion

5.1. Pilot evaluation

Connected health systems hold great promise for supporting team-based care and improved health outcomes[46]. It is known that metabolic syndrome confers an increased risk of cardiovascular morbidity and mortality[47], and its risk assessment and full rate management, also, as adequate control of chronic kidney disease or/and chronic heart failure, is crucial for promoting longevity and avoidance of complications. The early findings of this randomized, single-blind controlled pilot study revealed that during the CARRE service positively influenced participants in the interventional arm, when applied for about two months, increasing health literacy and empowerment.

CARRE service was assessed for the impact on quality of life, health literacy and empowerment via a randomized control investigational study involving two different pilot deployments in DUTH and VUSLK. Both study arms, control and CARRE, were tested based on the same scale across two visits while the CARRE group was exposed in the CARRE service in between visits. Because of the short period (<2 months) between the two visits, changes in clinical outcomes (e.g. lab test values) were not expected and were not assessed – these will be assessed in a third visit (>4 months from study start). Therefore, during the interim visit (visit 2) participants were tested for possible changes on their quality of life, health literacy and empowerment (3 of 4 primary efficacy points end points according the study protocol) and intervention acceptability and user satisfaction (the only non-clinical parameter from secondary efficacy end points).

Overall, the control arm showed no statistically significant differences on all measured scores between visits. Table 22 summarized the differences between visits on the measured scores for the CARRE exposed arm expressed as a percentage of the initial value for each score:

$$value\ in\ the\ table = \frac{E_2 - E_1}{E_1} \times 100\%$$

where E_1 is the score value of the CARRE arm at baseline and E_2 is the score value of the CARRE arm at visit 2, after CARRE intervention. The overall results of the pooled population of both pilots show an overall statistically significant increase in health literacy by 9.8% and an increase in empowerment by 8.0%. Considering the two different disease groups, empowerment is statistically increased by a 12.4% only in the metabolic syndrome group (group 1), while health literacy is statistically increased by 21.3% only in the group with heart failure of chronic kidney disease.

In terms of system usability, participants reported an above average assessment of a SUS mean score of 68, corresponding to an acceptable system.

Patient empowerment has emerged as a new paradigm that can help improve medical outcomes while lowering costs of treatment. The concept seems particularly promising in the management of chronic diseases[48]. We`re glad to show CARRE system service has increased participants empowerment and in CARRE arm between two visits.

Adequate health literacy has been demonstrated as an important component of chronic disease management by reducing risk factors, recurrence, and further complications[49]. Preliminary results show statistically

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[46] Aberger EW, Migliozzi D, Follick MJ, Malick T, Ahern DK. Enhancing Patient Engagement and Blood Pressure Management for Renal Transplant Recipients via Home Electronic Monitoring and Web-Enabled Collaborative Care. Telemedicine Journal and e-Health. 2014;20(9):850-854. doi:10.1089/tmj.2013.0317.

[47] Bo Isomaa, Peter Almgren, Tiinamaija Tuomi, Björn Forsén, Kaj Lahti, Michael Nissén, Marja-Riitta Taskinen, Leif Groop. Cardiovascular Morbidity and Mortality Associated With the Metabolic Syndrome Diabetes Care Apr 2001, 24 (4) 683-689; DOI: 10.2337/diacare.24.4.683 .

[48] Chatzimarkakis J. Why Patients Should Be More Empowered: A European Perspective on Lessons Learned in the Management of Diabetes. *Journal of Diabetes Science and Technology*. 2010;4(6):1570-1573.

[49] González-Chica DA, Mnisi Z, Avery J, et al. Effect of Health Literacy on Quality of Life amongst Patients with Ischaemic Heart Disease in Australian General Practice. Hernandez-Lemus E, ed. *PLoS ONE*. 2016;11(3):e0151079. doi:10.1371/journal.pone.0151079.

significant increase on participants` health literacy in Interventional (CARRE) arm compare to control arm. This undoubtedly shows CARRE system service profit for its users.

Table 22. Mean differences between the two visits on quality of life (PCS and MCS), health literacy (HLT) and empowerment (EMP) for the CARRE arm, calculated as a percentage of the value at baseline.

Visit 2 – Visit 1: E2 – E1* [(E2 - E1)/E1]*100%	**PCS**	**MCS**	**HLT**	**EMP**
DUTH				
Total Population	2.2%	-0.9%	7.7%	**15.0%**
Metabolic Syndrome	-0.8%	-0.6%	1.6%	**14.0%**
HF or CKD	10.3%	-1.4%	**30.5%**	17.4%
VULSK				
Total Population	1.4%	2.5%	**11.5%**	2.6%
Metabolic Syndrome	-0.5%	1.6%	6.3%	**10.6%**
HF or CKD	3.5%	3.7%	**17.8%**	-5.0%
POOLED				
Total Population	1.7%	1.0%	**9.8%**	**8.0%**
Metabolic Syndrome	-0.6%	0.4%	3.7%	**12.4%**
HF or CKD	5.7%	1.8%	**21.3%**	1.8%

** E2 = CARRE arm after (visit 2), E1 = CARRE arm at baseline (visit 1)*

[#] *bold red lettering highlights significant differences (p<.05), p values obtained by comparing values within each arm using paire*d samples *t-test, see Table 18, Table 19, and Table 20* for values of mean differences and p values.

The findings from large meta-analyses suggest that the effectiveness of Internet-based interventions is associated with more extensive use of theory, inclusion of more behaviour change techniques, and use of additional methods of interacting with participants[50]. Moreover, Jahangiry L, Shojaeizadeh D. *et al*. study showed that the use of an interactive website that is frequently updated for informational content with e-mail notifications, interactive risk assessment tools, and tracking tools appeared to contribute to a change in lifestyle and had a positive effect on metabolic syndrome components[51]. CARRE service judged to be very valuable and perspective as it is very complex system: visual analysis visualizes related risk factors according to the patient's health and lifestyle status (which one may enter on PHR or can be received from his/her used smart devices) and visualizes the changes that may happen if the user changes the lifestyle or medical indicators. Furthermore, decision support systems support patient application with appropriate personal recommendation and advices to his/her lifestyle.

[50] Webb TL, Joseph J, Yardley L, Michie S. Using the Internet to Promote Health Behavior Change: A Systematic Review and Meta-analysis of the Impact of Theoretical Basis, Use of Behavior Change Techniques, and Mode of Delivery on Efficacy. Eysenbach G, ed. *Journal of Medical Internet Research*. 2010;12(1):e4. doi:10.2196/jmir.1376.

[51] Jahangiry L, ShojaeizadehD, Mahdieh AF, Yaseri M, Mohammad K, Najafi M, Montazeri A. Interactive web-based lifestyle intervention and metabolic syndrome: findings from the Red Ruby (a randomized controlled trial). Trials, 2015, 16:418. DOI: 10.1186/s13063-015-0950-4.

As these are the results of interim visit, significant improvements are expected not only on participants quality of life, empowerment and health literacy, but also on clinical participants findings after longer observation period (e.g. 6 month, as previous studies[52] reveal).

5.2. CARRE strengths meet today`s eHealth challenges

CARRE addresses the specific medical domain of cardiorenal disease comorbidities provided proof-of-concept via deployment and validation in healthcare settings during the evaluation process. CARRE research first fosters understanding of the complex interdependent nature of the comorbid condition in general and as specialized for the specific patient, then calculates informed estimations for disease progression and comorbidity trajectories, and compiles a variety of personalized alerting, planning and educational services so that patients (and professionals) are empowered, and can, eventually, makes shared informed decisions.

Looking at CARRE system according Cornford, Doukidis and Forster[53] proposed evaluation framework for telemedicine and eHealth interventions we can summarise the results of CARRE system service evaluation (see Figure 36. Overview of the project evaluation phases and results as presented in D.7.1. Green indicates what has been achieved, yellow expected result after short term (evaluation continues beyond the project); grey indicates what however requires large scale, long term deployment and is mostly outside the scope of the project's work plan..

	CARRE system functions	Human perspectives			Context and Environment
		Experts	Patients	Admins	
Structure	aggregators and interfaces functioning	changes to working conditions and practices; new skills, and abilities	new skills, and abilities		
Process	service operation correct & valid	induced changes in function and satisfaction	Induced changes in self-management and satisfaction		
Outcome	service usable	effectiveness	perceived quality of care and life	improving specific clinical parameters	potential to improve the health status and quality of life

Figure 36. Overview of the project evaluation phases and results as presented in D.7.1. Green indicates what has been achieved, yellow expected result after short term (evaluation continues beyond the project); grey indicates what however requires large scale, long term deployment and is mostly outside the scope of the project's work plan.

The ultimate goal of the CARRE service is to provide the means for patients with comorbidities to take an

[52] Jahangiry L, ShojaeizadehD, Mahdieh AF, Yaseri M, Mohammad K, Najafi M, Montazeri A. Interactive web-based lifestyle intervention and metabolic syndrome: findings from the Red Ruby (a randomized controlled trial). Trials, 2015, 16:418. DOI: 10.1186/s13063-015-0950-4.

[53] Cornford, T., Doukidis, G.I., and Forster, D., 1994. Experience with a structure, process and outcome framework for evaluating and information system. Omega, Int. J. Manag. Science, 22, 5, 491-504.

active role in care processes, including self-care and shared decision making. Being able to contribute to health behavior programs, feeling valued and able to experience personal growth are vital factors to engage mental health service users in health programs. Clinicians and health care policy makers need to account for these considerations to improve success of health improvement initiatives for this population[54].

Moreover, the results of the CARRE service evaluation show the increase of empowerment and health literacy (in DUTH co-occurrence). The impacts of health literacy and patient empowerment are deeply intertwined. High literacy does not necessarily entail empowerment and vice versa, and mismatches of the two can have deleterious consequences. High levels of health literacy without a corresponding high degree of patient empowerment creates an unnecessary dependence of patients on health professionals, while a high degree of empowerment without a corresponding degree of health literacy poses the risk of dangerous health choices[55]. This is an importnt CARRE service advantage as there recently has been declared that communication programs must include the empowerment that motivates consumers to engage and the literacy that enables them to make informed and reasoned choices[56].

eHealth interventions that are interactive, interoperable, personally engaging, contextually tailored, with the ability to be delivered to mass audiences can really make a difference in enhancing the quality of health care and health promotion efforts[57]. The findings from large metanalyses suggest that the effectiveness of Internet-based interventions is associated with more extensive use of theory, inclusion of more behaviour change techniques, and use of additional methods of interacting with participants[58]. The CARRE service provides visual and quantitative model of disease progression pathways and comorbidities trajectories, based on current medical evidence; personalizes the risk model to each individual based on his personal medical data and real-time sensor measurement to support disease status awareness; uses the personalized model in conjunction with real time monitoring to create a set of alarms to enable patient engagement and provides advanced decision support services and mind change interventions based on the real-time coupling of medical evidence and personal health status.

It is generally recognised based on evidence that an effective risk assessment process is the cornerstone of any effective **disease management** and health care policy. Risk factor assessment is the first step in primary prevention and guides treatment strategy because the intensity of the preventive recommendations is tailored to a patient's level of risk[59]. As in CARRE service particular attention is paid for the risk factors that patient exposes (related to cardiorenal syndrome), calculation of his/her risk and mitigation of that risk. During the project activities, unique CARRE ontologies were created (risk factor database and/or the possibility aggregated educational material) to timely identify major concerns about patients' health condition levels and inform the user, i.e. patient. The DSS sends alerts, including medical check-ups, monitoring, increased risk of disease progression and transition, and suggestions on behaviour change.

5.3. Implications of the CARRE service intervention

CARRE service can potentially impact traditional care pathways in several ways:

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[54] Graham C, Rollings C, de Leeuw S, Anderson L, Griffiths B, Long N. A Qualitative Study Exploring Facilitators for Improved Health Behaviors and Health Behavior Programs: Mental Health Service Users' Perspectives. *The Scientific World Journal*. 2014;2014:870497. doi:10.1155/2014/870497.

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[58] Webb TL, Joseph J, Yardley L, Michie S. Using the Internet to Promote Health Behavior Change: A Systematic Review and Meta-analysis of the Impact of Theoretical Basis, Use of Behavior Change Techniques, and Mode of Delivery on Efficacy. Eysenbach G, ed. *Journal of Medical Internet Research*. 2010;12(1):e4. doi:10.2196/jmir.1376.

[59] Jahangiry L, ShojaeizadehD, Mahdieh AF, Yaseri M, Mohammad K, Najafi M, Montazeri A. Interactive web-based lifestyle intervention and metabolic syndrome: findings from the Red Ruby (a randomized controlled trial). Trials, 2015, 16:418. DOI: 10.1186/s13063-015-0950-4.

CARRE can increase health awareness and motivate person to adopt a healthier lifestyle, monitor themselves efficiently and plan personally for better odds in terms of disease progression and transition. The induced impact includes:

- empowered patients with higher health literacy;
- lifestyle managed based on personalized, quantitative evidence;
- prolongation of the period in a low risk zone;
- cost effectiveness (economic aspects of self-management of lifestyle related disease prevention).

CARRE can motivate person to consult the doctor earlier triggered by individualised visual and quantitative model of disease progression pathways and comorbidities trajectories, based on current medical evidence. The induced impact includes:

- empowered patients with higher health literacy;
- early primary prevention (patient visits doctor at earlier stages of the disease when s/he is still at risk of developing disease);
- accurate data collection (patient at once can provide correct measurement values, information on physical activity to health care specialist);
- cost effectiveness (economic aspects of early prevention).

CARRE can defer to the medical specialist an empowered person with better health literacy and appropriate tool would induce desirable behavioural change. The induced impact includes:

- empowered patient with higher health literacy;
- prolongation of the period in a low risk zone;
- expected increased compliance to medical prescriptions and recommendations;
- cost effectiveness (economic aspects of early prevention).

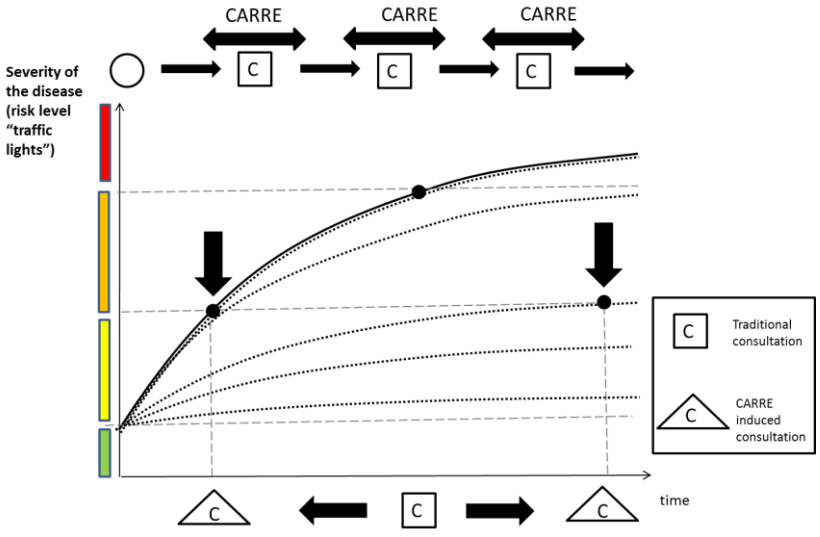

Figure 37. CARRE potential to induce changes in care pathways.

CARRE service can also prove beneficial when applied during the consultation with health care specialists, as it would help on further disease management (understand current condition as presenting a risk factor for major complications; educational interventions; establish treatment goals; recognise of a possible deregulation of the primary disease or early symptoms or signs of a possible complication; re-evaluate therapy and

treatment goals in case of deterioration or new complications; adherence to therapy; other risk factors modification, understand hierarchy of the most important risk factors that have to be modified and monitored). Figure 37 figure shows that traditionally patient comes for a consultation to doctor`s office when the disease or organ damage already exists. Usually a period of time passes from the moment a particular person experiences the first signs of the disease (is at risk of, or has combination of several risk factors) until the onset of the disease. The induced impact includes:

- empowered patient with higher health literacy;
- stabilisation of the current disease state, prevention of the progression;
- better adherence to treatment and compliance on monitoring; and
- cost effectiveness (economic aspects of optimal therapy and management choice).

Self-management support and empowerment interventions are becoming more common as a structured way of helping patients learn to better manage at risk of chronic disease development[60] and even when they have already developed chronic disease[61]. Probably the biggest concern for the application of CARRE would not be approach from the patient's or health specialist's point of view, but the attitude of the stakeholders that come from different parts of the healthcare system with different value systems, different perceptions of risk and different expectations for personal eHealth applications.

[60] Jahangiry L, ShojaeizadehD, Mahdieh AF, Yaseri M, Mohammad K, Najafi M, Montazeri A. Interactive web-based lifestyle intervention and metabolic syndrome: findings from the Red Ruby (a randomized controlled trial). Trials, 2015, 16:418. DOI: 10.1186/s13063-015-0950-4

[61] Franek J. Self-Management Support Interventions for Persons With Chronic Disease: An Evidence-Based Analysis. Ontario Health Technology Assessment Series. 2013;13(9):1-60.

Annex 1

Investigational Protocol Forms

This annex presents the various instruments (questionnaires) used in the evaluation of CARRE service in the two pilot deployments. In particular:

(1) Screening from for participant inclusion in group 1: metabolic syndrome

(2) Screening from for participant inclusion in group 2: HF/CKD

(3) Clinical data collection form for metabolic syndrome patients

(4) Clinical data collection form for heart failure patients

(5) Clinical data collection form for chronic kidney disease patients

(6) Drop out report form

(7) Patient consent forms in Greek

(8) Patient consent forms in Lithuanian

1. Screening form for inclusion in group 1: metabolic syndrome

SCREENING FORM FOR GROUP 1

1. PERSONAL DATA	Patient ID:
	Date:

Patient`s name, surname_____

Adress_____

Telephone number_____ Mobile _____

E-mail address_____ Facebook account:_____

National Insurance ID _____

Educational level _____

Current diagnosis_____

2. DEMOGRAPHICS

2.1 Gender [ ] female [ ] male

2.2 Date of birth:

3. ACCESS TO TECHNOLOGY

3.1 Personal computer No☐ Yes ☐ operating system: Windows ☐ iOS ☐

3.2 Smartphone No☐ Yes ☐ operating system: Android ☐ iOS ☐

3.3 Internet connection Yes ☐ No☐

3.4 Devices:

Scale	Yes ☐	No☐
Blood pressure monitor	Yes ☐	No☐
Activity meter	Yes ☐	No☐
Glucometer	Yes ☐	No☐

4. INCLUSION CRITERIA (GENERAL)

Written informed consent obtained on date:	YES [ ] PROCEED NO [ ] STOP
Male or female between 18-65 years old.	YES [ ] PROCEED NO [ ] STOP
E-literacy	
Patient or household member has sufficient competence to handle computer equipment	YES [ ] PROCEED NO [ ] STOP
Patient or household member has sufficient competence to use internet	YES [ ] PROCEED NO [ ] STOP
Patient or household member has sufficient competence to handle personal sensors	YES [ ] PROCEED NO [ ] STOP

5. INCLUSION CRITERIA (MEDICAL)

Waist circumference ≥ 94 cm in males; ≥ 80 cm in females	YES [ ]	NO [ ]
Triglycerides ≥ 150 mg/dL (1.7 mol/L) OR drug treatment for elevated triglycerides	YES [ ]	NO [ ]
HDL-C < 40 mg/dL (1.0 mmol/L) in males; < 50 mg/dL (1.3 mmol/L) in females) OR drug treatment for reduced HDL-C	YES [ ]	NO [ ]
Blood pressure systolic ≥ 130 and/or diastolic ≥ 85 mm Hg OR antihypertensive drug treatment (in patients with hypertension diagnosis)	YES [ ]	NO [ ]
fasting glucose ≥ 100 mg/dL (≥ 5.6 mmol/L) OR drug treatment of elevated glucose	YES [ ]	NO [ ]
if three of the above are YES [ ] if three or more of above are NO [ ]		PROCEED STOP

6. EXCLUSION CRITERIA

Diagnosed renal or cardiac disease, causing CKD or CHF	NO [ ]	YES [ ]
Type 1 diabetes or gestational diabetes	NO [ ]	YES [ ]
Advanced liver disease and/or cirrhosis	NO [ ]	YES [ ]
Cancer	NO [ ]	YES [ ]
Uncontrolled thyroid disorders	NO [ ]	YES [ ]
Exacerbated chronic inflammatory disorders rheumatoid arthritis	NO [ ]	YES [ ]
Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)	NO [ ]	YES [ ]
Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis);	NO [ ]	YES [ ]
Pregnancy	NO [ ]	YES [ ]
Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data	NO [ ]	YES [ ]
if all of the above are NO [ ] if at least one of the above is YES [ ]		PROCEED STOP

Go further ONLY if all criteria are satisfied! DONE THAT [ ]

7. Based on randomized study envelop (as opened by patient):

Assign patient to: [ ] control group [ ] CARRE intervention group

2. Screening form for inclusion in group 2: HF/CKD

SCREENING FORM FOR GROUP 2

1. PERSONAL DATA	Patient ID:
	Date:

Patient`s name, surname_____

Adress_____

Telephone number_____ Mobile _____

E-mail address_____ Facebook account:_____

National Insurance ID _____

Educational level _____

Current diagnosis_____

2. DEMOGRAPHICS

2.1 Gender [ ] female [ ] male

2.2 Date of birth:

4. ACCESS TO TECHNOLOGY

3.1 Personal computer No☐ Yes ☐ operating system: Windows ☐ iOS ☐

3.2 Smartphone No☐ Yes ☐ operating system: Android ☐ iOS ☐

3.3Internet connection Yes ☐ No☐

3.4 Devices:

Scale	Yes ☐	No☐
Blood pressure monitor	Yes ☐	No☐
Activity meter	Yes ☐	No☐
Glucometer	Yes ☐	No☐

4. INCLUSION CRITERIA (GENERAL)

Written informed consent obtained on date:	YES [ ] PROCEED NO [ ] STOP
Male or female between 18-65 years old.	YES [ ] PROCEED NO [ ] STOP
E-literacy	
Patient or household member has sufficient competence to handle computer equipment	YES [ ] PROCEED NO [ ] STOP
Patient or household member has sufficient competence to use internet	YES [ ] PROCEED NO [ ] STOP
Patient or household member has sufficient competence to handle personal sensors	YES [ ] PROCEED NO [ ] STOP

5. INCLUSION CRITERIA (MEDICAL)

Diagnosed and adequately treated for renal disease which has already caused diagnosed chronic kidney disease (Stage 2 with albuminuria) or diagnosed and adequately treated chronic kidney disease (Stage 3a)	YES [ ]	NO [ ]
Diagnosed chronic heart failure (systolic), NYHA class II or III	YES [ ]	NO [ ]
if one of the above is YES [ ] if both of the above are NO [ ]		PROCEED STOP

6. EXCLUSION CRITERIA

CKD stage 1, 3b-5, CKD stage 2 without albuminuria (at screening)	NO [ ]	YES [ ]
NYHA I or IV (at screening)	NO [ ]	YES [ ]
Any stage CHF (systolic), for patients with CKD (at screening)	NO [ ]	YES [ ]
Any stage CKD for patients with CHF (systolic) (at screening)	NO [ ]	YES [ ]
Type 1 diabetes or gestational diabetes	NO [ ]	YES [ ]
Advanced liver disease and/or cirrhosis	NO [ ]	YES [ ]
Cancer	NO [ ]	YES [ ]
Uncontrolled thyroid disorders	NO [ ]	YES [ ]
Exacerbated chronic inflammatory disorders rheumatoid arthritis	NO [ ]	YES [ ]
Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)	NO [ ]	YES [ ]
Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis);	NO [ ]	YES [ ]
Pregnancy	NO [ ]	YES [ ]
Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data	NO [ ]	YES [ ]
if all of the above are NO [ ] if at least one of the above is YES [ ]		PROCEED STOP

Go further ONLY if all criteria are satisfied! DONE THAT [ ]

7. Based on randomized study envelop (as opened by patient):

Assign patient to: [ ] control group [ ] CARRE intervention group

3. Clinical data collection form for metabolic syndrome patients

CLINICAL DATA COLLECTION FORM FOR GROUP 1

Visit:

Patient ID: **Date:**

Investigator:

1. METABOLIC SYNDROME DIAGNOSIS

1.1. Metabolic syndrome diagnosed during this study ☐

1.2. Metabolic syndrome diagnosed earlier ☐

- Less than 1 years ago ☐
- Between 1 to 2 years ☐
- Between 2 to 5 years ☐
- More than 5 years ago ☐

2. Findings related to metabolic syndrome

Criteria	Current patient value
Waist circumference ≥ 94 cm in males; ≥ 80 cm in females	cm
Triglycerides ≥ 150 mg/dL (1.7 mol/L) OR drug treatment for elevated triglycerides	mmol/l ☐
HDL-C < 40 mg/dL (1.0 mmol/L) in males; < 50 mg/dL (1.3 mmol/L) in females) OR drug treatment for reduced HDL-C	mmol/l ☐
Blood pressure systolic ≥ 130 and/or diastolic ≥ 85 mm Hg OR antihypertensive drug treatment	systolic: mmHg diastolic: mmHg ☐
fasting glucose ≥ 100 mg/dL (≥ 5.6 mmol/L) OR drug treatment of elevated glucose	mmol/l ☐

3. Other biometric measurements

Weight: Kg	Fat mass: %	Fat mass measurement method:
Height: cm	BMI:	
Pulse rate: beats/min		

4. Drug treatment

	Class	Dosage
Antidiabetic agents		
☐	Biguanides (e.g. metformin)	
☐	Sulfonylureas (e.g. glimepiride)	
☐	Meglitinides (e.g. repaglinide)	
☐	Thiazolidinediones (e.g. pioglitazone)	
☐	dipeptidyl peptidase IV inhibitors (e.g. sitagliptin),	
☐	α-glucosidase inhibitors (e.g. acarbose)	
☐	Insulin	
☐	Other	
Cholesterol medication		
☐	Statins (e.g. atorvastatin,simvastatin)	
☐	Fibrates (e.g. fenofibrate)	
☐	Niacin	
☐	Bile acid binding resins (e.g. cholestipol, cholestyramine)	
☐	Cholesterol absorption inhibitor (e.g. ezetimibe)	
☐	Combination cholesterol absorption inhibitor and statin	
☐	Omega-3 fatty acids	
☐	Other	
Blood pressure medication		
☐	ACE inhibitors (e.g. ramipril)	
☐	Beta-blockers (e.g. metoprolol)	
☐	Angiotensin II receptor blockers (e.g. losartan)	
☐	Calcium channel blockers (e.g. amlodipine)	
☐	Diuretics (e.g. indapamide)	
☐	Other	
Other medication		
☐	Aldosterone receptor antagonist (e.g. spironolactone)	
☐	Alpha blockers (e.g. doxazosin mesylate)	
☐	Combined alfa and beta blockers (e.g. carvedilol)	
☐	Central alpha agonists (e.g. moxonidine)	
☐	Renin inhibitors(e.g. aliskiren)	
☐	Other	

5. LABORATORY TESTS

Parameter	Value	Units	normal values		Clinical assessment[1]
			Lower	Higher	0 1 2 3
Fasting glucose					
Total cholesterol					
HDL cholesterol					
LDL cholesterol					
Triglycerides					
Uric Acid					
Creatinine					
Creatinine/albumin ratio					
Glycohemoglobin (Hb_{AIC}) [2]					

[1] normal value: 0
abnormal value without clinical significance: 1
abnormal value with clinical significance: 2
not performed: 3

[2] Glycohemoglobin (Hb_{AIC}) only for those whose fasting glucose is above normal value during Visit #1.

6. EXCLUSION CRITERIA (for Visit >1)

Type 1 diabetes or gestational diabetes	NO [ ]	YES [ ]
Advanced liver disease and/or cirrhosis	NO [ ]	YES [ ]
Cancer	NO [ ]	YES [ ]
Uncontrolled thyroid disorders	NO [ ]	YES [ ]
Exacerbated chronic inflammatory disorders rheumatoid arthritis	NO [ ]	YES [ ]
Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)	NO [ ]	YES [ ]
Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis);	NO [ ]	YES [ ]
Pregnancy	NO [ ]	YES [ ]
Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data	NO [ ]	YES [ ]
if all of the above are NO [ ]		PROCEED
if at least one of the above is YES [ ]		STOP

4. Clinical data collection form for heart failure patients

CLINICAL DATA COLLECTION FORM FOR GROUP 2 – Chronic Heart Failure

Visit:

Patient ID: **Date:**

Investigator:

1. CHRONIC HEART FAILURE DIAGNOSIS

1.1. CHF diagnosed during this study ☐

1.2. CHF diagnosed earlier ☐

- Less than 1 years ago ☐
- Between 1 to 2 years ☐
- Between 2 to 5 years ☐
- More than 5 years ago ☐

1.3. Current HF stage according to NYHA Stage:

- II ☐
- III ☐

1.4. Cause of chronic heart failure

- Coronary artery disease ☐
- Hypertension ☐
- Rhythm disorders ☐
- Valvular heart disease ☐ (type_____)
- Cardiomyopathy ☐ (type_____)
- Other disorders of the heart ☐ (periacardial disease, endocardial disease) (type_____)

2. METABOLIC SYNDROME COMPONENTS

Criteria	Current patient value
Waist circumference ≥ 94 cm in males; ≥ 80 cm in females	cm
Triglycerides ≥ 150 mg/dL (1.7 mol/L) OR drug treatment for elevated triglycerides	mmol/l ☐
HDL-C < 40 mg/dL (1.0 mmol/L) in males; < 50 mg/dL (1.3 mmol/L) in females) OR drug treatment for reduced HDL-C	mmol/l ☐
Blood pressure, systolic ≥ 130 and/or diastolic ≥ 85 mm Hg OR antihypertensive drug treatment	systolic: mmHg diastolic: mmHg ☐
Fasting glucose ≥ 100 mg/dL (≥ 5.6 mmol/L) OR drug treatment of elevated glucose	mmol/l ☐

3. OTHER BIOMETRIC MEASUREMENTS

Weight: Kg	Fat mass: %	Fat mass measurement method:
Height: cm	BMI:	
Pulse rate: beats/min		

4. DRUG TREATMENT

HF		**Dosage**
☐	ACE inhibitors (e.g., ramipril)	
☐	Beta-blockers (e.g., metoprolol)	
☐	Combined alfa and beta blockers (e.g., carvedilol)	
☐	Aldosterone receptor antagonist (e.g., spironolactone)	
☐	Nitrates (e.g. ISDN)	
☐	Angiotensin II receptor blockers (e.g., losartan)	
☐	Ivabradine	
☐	Digoxin	
☐	Loop diuretics (e.g., torasemide)	
☐	Thiazides(e.g. hydrochlorthiazide)	
☐	Other diuretic	
☐	Omega-3 polyunsaturated fatty acids	
Other medications (hypertension, CAD)		
☐	Alpha blockers (e.g., doxazosin mesylate)	
☐	Calcium channel blockers (e.g., amlodipine)	
☐	Central alpha agonists(e.g., moxonidine)	
☐	Renin inhibitors(e.g., aliskiren)	
☐	Aspirin	
☐	Other	
Antidiabetic agents		
☐	Biguanides (e.g., metformin)	
☐	Sulfonylureas (e.g., glimepiride)	
☐	Meglitinides (e.g., repaglinide)	
☐	Thiazolidinediones (e.g., pioglitazone)	
☐	dipeptidyl peptidase IV inhibitors (e.g., sitagliptin),	
☐	α-glucosidase inhibitors (e.g., acarbose)	
☐	Insulin	
☐	Other	
Cholesterol medications		
☐	Statins (e.g., atorvastatin,simvastatin)	
☐	Fibrates (e.g., fenofibrate)	
☐	Niacin	
☐	Bile acid binding resins (e.g., cholestipol, cholestyramine)	
☐	Cholesterol absorption inhibitor (e.g., ezetimibe)	
☐	Combination cholesterol absorption inhibitor and statin	
☐	Omega-3 fatty acids	
☐	Other	

5. LABORATORY TESTS

Parameter	Value	Units	normal values		Clinical assessment[1]
			Lower	Higher	0 1 2 3
Fasting glucose					
Total cholesterol					
HDL cholesterol					
LDL cholesterol					
Triglycerides					
Uric Acid					
Creatinine					
Creatinine/albumin ratio					
Glycohemoglobin (Hb_{AIC}) [2]					

[1] normal value: 0; abnormal value without clinical significance: 1; abnormal value with clinical significance: 2; not performed: 3

[2] Glycohemoglobin (Hb_{AIC}) only for those whose fasting glucose is above normal value during Visit #1.

6. ECHOCARDIOGRAPHY

(a) 6.1. Ejection Fraction (biplane *Simpson's* method): _____ %

(b) End systolic volume: _____ ml

(c) End diastolic volume: _____ ml

6.2. Left ventricular diastolic function

		Patient`s values	Normal	Impaired relaxation (Grade 1)	Pseudo-normal (Grade 2)	Reversible restrictive (Grade 3)	Irreversible restrictive (Grade 4)
Transmitral inflow	E/A		1.0-2.0	< 1.0	1.0-2.0	>1.0	> 2.0
	DecT	ms	150-240 ms	> 240 ms	150-240 ms	< 150 ms	< 150 ms
IVRT		ms	70-90 ms	>90 ms	<90 ms	<70 ms	<70 ms
Medial annulus	Em	cm/s	> 10 cm/s	> 7 cm/s	< 7 cm/s	5 cm/s	5 cm/s
	E/Em		<8	<8	> 15	> 15	> 15
Lateral annulus	Em	cm/s	> 12 cm/s	< 10 cm/s	< 10 cm/s	5 cm/s	5 cm/s
	E/Em		<10	< 10	> 10	>10	>10
LA size			Normal	Normal	↑↑	↑↑↑	↑↑↑

7. SIX MIN WALK TEST (m):

8. EXCLUSION CRITERIA (for Visit >1)

Type 1 diabetes or gestational diabetes	NO [ ]	YES [ ]
Advanced liver disease and/or cirrhosis	NO [ ]	YES [ ]
Cancer	NO [ ]	YES [ ]
Uncontrolled thyroid disorders	NO [ ]	YES [ ]
Exacerbated chronic inflammatory disorders rheumatoid arthritis	NO [ ]	YES [ ]
Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)	NO [ ]	YES [ ]
Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis);	NO [ ]	YES [ ]
Pregnancy	NO [ ]	YES [ ]
Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data	NO [ ]	YES [ ]
if all of the above are	NO [ ]	PROCEED
if at least one of the above is	YES [ ]	STOP

5. Clinical data collection form for chronic kidney disease patients

CLINICAL DATA COLLECTION FORM FOR GROUP 2 – Chronic Kidney Disease

Visit:

Patient ID: **Date:**

Investigator:

1. CHRONIC KIDNEY DISEASE DIAGNOSIS

1.1. CKD diagnosed during this study ☐

1.2. CKD diagnosed earlier ☐

- Less than 1 years ago ☐
- Between 1 to 2 years ☐
- Between 2 to 5 years ☐
- More than 5 years ago ☐

1.3. Current CKD stage : _____

1.4. Cause of CKD

- Diabetic nephropathy ☐
- Hypertensive nephropathy ☐
- Chronic glomerulopathy ☐
- Adult polycystic kidney disease ☐
- Obstructive uropathy ☐
- Tubulointerstitial nephritis ☐
- Other disorders of the kidney ☐

2. METABOLIC SYNDROME COMPONENTS

Criteria	Current patient value
Waist circumference ≥ 94 cm in males; ≥ 80 cm in females	cm
Triglycerides ≥ 150 mg/dL (1.7 mol/L) OR drug treatment for elevated triglycerides	mmol/l ☐
HDL-C < 40 mg/dL (1.0 mmol/L) in males; < 50 mg/dL (1.3 mmol/L) in females) OR drug treatment for reduced HDL-C	mmol/l ☐
Blood pressure, systolic ≥ 130 and/or diastolic ≥ 85 mm Hg OR antihypertensive drug treatment	systolic: mmHg diastolic: mmHg ☐
Fasting glucose ≥ 100 mg/dL (≥ 5.6 mmol/L) OR drug treatment of elevated glucose	mmol/l ☐

3. OTHER BIOMETRIC MEASUREMENTS

Weight: Kg	Fat mass: %	Fat mass measurement method:
Height: cm	BMI:	
Pulse rate: beats/min		

4. DRUG TREATMENT

CKD		**Dosage**
☐	ACE inhibitors (e.g., ramipril)	
☐	Aldosterone receptor antagonist (e.g., spironolactone)	
☐	Nitrates (e.g. ISDN)	
☐	Angiotensin II receptor blockers (e.g., losartan)	
☐	Ivabradine	
☐	Digoxin	
☐	Loop diuretics (e.g.,torasemide)	
☐	Thiazides(e.g. hydrochlorthiazide)	
☐	Other diuretic	
☐	Omega-3 polyunsaturated fatty acids	
Other medications (hypertension, CAD)		
☐	Alpha blockers (e.g., doxazosin mesylate)	
☐	Beta blockers (e.g. metoprololi)	
☐	Calcium channel blockers (e.g., amlodipine)	
☐	Central alpha agonists(e.g., moxonidine)	
☐	Renin inhibitors(e.g., aliskiren)	
☐	Aspirin	
	Other	
Antidiabetic agents		
☐	Biguanides (e.g., metformin)	
☐	Sulfonylureas (e.g., glimepiride)	
☐	Meglitinides (e.g., repaglinide)	
☐	Thiazolidinediones (e.g., pioglitazone)	
☐	dipeptidyl peptidase IV inhibitors (e.g., sitagliptin),	
☐	α-glucosidase inhibitors (e.g., acarbose)	
☐	Insulin	
☐	Other	
Cholesterol medications		
☐	Statins (e.g., atorvastatin,simvastatin)	
☐	Fibrates (e.g., fenofibrate)	
☐	Niacin	
☐	Bile acid binding resins **(**e.g., cholestipol, cholestyramine)	
☐	Cholesterol absorption inhibitor (e.g., ezetimibe)	
☐	Combination cholesterol absorption inhibitor and statin	
☐	Omega-3 fatty acids	
☐	Other	

5. LABORATORY TESTS

Parameter	Value	Units	normal values		Clinical assessment[1]
			Lower	Higher	0 1 2 3
Fasting glucose					
Total cholesterol					
HDL cholesterol					
LDL cholesterol					
Triglycerides					
Uric Acid					
Creatinine					
Creatinine/albumin ratio					
Glycohemoglobin (Hb_{AIC}) [2]					

[1] normal value: 0; abnormal value without clinical significance: 1; abnormal value with clinical significance: 2; not performed: 3

[2] Glycohemoglobin (Hb_{AIC}) only for those whose fasting glucose is above normal value during Visit #1.

6. ECHOCARDIOGRAPHY

6.1. Ejection Fraction (biplane *Simpson's* method): _____ %

End systolic volume: _____ ml

End diastolic volume: _____ ml

6.2. Left ventricular diastolic function

		Patient`s values	Normal	Impaired relaxation (Grade 1)	Pseudo-normal (Grade 2)	Reversible restrictive (Grade 3)	Irreversible restrictive (Grade 4)
Transmitral inflow	E/A		1.0-2.0	< 1.0	1.0-2.0	>1.0	> 2.0
	DecT	ms	150-240 ms	> 240 ms	150-240 ms	< 150 ms	< 150 ms
IVRT		ms	70-90 ms	>90 ms	<90 ms	<70 ms	<70 ms
Medial annulus	Em	cm/s	> 10 cm/s	> 7 cm/s	< 7 cm/s	5 cm/s	5 cm/s
	E/Em		<8	<8	> 15	> 15	> 15
Lateral annulus	Em	cm/s	> 12 cm/s	< 10 cm/s	< 10 cm/s	5 cm/s	5 cm/s
	E/Em		<10	< 10	> 10	>10	>10
LA size			Normal	Normal	↑↑	↑↑↑	↑↑↑

7. SIX MIN WALK TEST (m):

8. EXCLUSION CRITERIA (for Visit >1)

Type 1 diabetes or gestational diabetes	NO [ ]	YES [ ]
Advanced liver disease and/or cirrhosis	NO [ ]	YES [ ]
Cancer	NO [ ]	YES [ ]
Uncontrolled thyroid disorders	NO [ ]	YES [ ]
Exacerbated chronic inflammatory disorders rheumatoid arthritis	NO [ ]	YES [ ]
Concomitant use of drugs known to affect metabolism (e.g. corticosteroids, immunotherapy, nonsteroidal anti-inflammatory drugs etc.)	NO [ ]	YES [ ]
Chronic infectious diseases (e.g. HIV/AIDS, tuberculosis);	NO [ ]	YES [ ]
Pregnancy	NO [ ]	YES [ ]
Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data	NO [ ]	YES [ ]
if all of the above are	NO [ ]	PROCEED
if at least one of the above is	YES [ ]	STOP

6. Drop out report form

DROP OUT REPORT FORM

Patient ID:

Date:

Investigator:

1. GROUP ASSIGNED

Control group

Group 1 ☐

Group 2 ☐

CARRE intervention group

Group 1	☐	Physical activity tracker ID_____	☐
Group 2	☐	Blood pressure monitor ID _____	☐
		Weight scales ID _____	☐

2. DATE OF DISCONTINUATION OF THE STUDY:

3. CAUSE OF DROP OUT

5.1. Subject withdrawal of consent (or assent) ☐

5.2. Subject is not compliant with study procedures ☐

5.2.1. Technical problems, if yes provide a short description

_____

5.2.2. Patient dissatisfaction, if yes provide a short description

_____

5.3. Newly established diagnosis that resp. exclusion criteria ☐

Diagnosis _____

5.4. Protocol violation requiring discontinuation of the study ☐

5.5. Lost to follow-up ☐

5.6. Death ☐

Date of death:

Cause of death_____

5.7. Other ☐

Provide a short description_____

4. CURRENT DIAGNOSIS OF PATIENT DISCONTINUATING THE STUDY

_____

_____

_____

7. Patient informed consent form in Greek

ΕΓΓΡΑΦΟ ΠΛΗΡΟΦΟΡΗΣΗΣ ΑΣΘΕΝΟΥΣ

ΤΙΤΛΟΣ ΜΕΛΕΤΗΣ

CARRE: Εξατομικευμένη ενδυνάμωση ασθενών και υποστήριξη λήψης αποφάσεων στην καρδιονεφρική νόσο και συνασθένειες.

Αγαπητέ Κύριε ή Κυρία

Καλείστε να λάβετε μέρος σε μια επιστημονική μελέτη που πραγματοποιείται από τη **Σχολή Ιατρικής, Δημοκρίτειο Πανεπιστήμιο Θράκης, Π.Γ.Ν.Α..**

Παρακαλούμε αφιερώστε κάποιο χρόνο για να διαβάσετε το παρακάτω κείμενο. Μπορείτε να κάνετε όσες ερωτήσεις θέλετε προκειμένου να σχηματίσετε πλήρη εικόνα αυτής της μελέτης πριν αποφασίσετε αν επιθυμείτε να πάρετε μέρος ή όχι σε αυτήν.

ΠΟΙΟΣ ΕΙΝΑΙ Ο ΣΚΟΠΟΣ ΑΥΤΗΣ ΤΗΣ ΜΕΛΕΤΗΣ

Το έργο CARRE στοχεύει σε διεπιστημονική έρευνα για την ανάπτυξη τεχνολογιών για την κατανόηση της συνασθένειας και την ανάπτυξη υπηρεσιών για ενδυνάμωση των ασθενών και την υποστήριξη λήψης απόφασης από τους ασθενείς και το ιατρικό προσωπικό. Σκοπός της μελέτης είναι διερευνήσει αν η διαδικτυακή εφαρμογή που έχει αναπτυχθεί είναι χρήσιμη στους πολίτες, μπορεί να βελτιώσει την ποιότητα ζωής τους και να τους υποστηρίξει σε εκείνες τις καθημερινές επιλογές που μπορούν να βελτιώσουν (ή να μην επιδεινώσουν) την κατάσταση της υγείας τους.

Εάν αποφασίσετε να λάβετε μέρος στη μελέτη θα σας παραδοθεί σχετικός εξοπλισμός προσωπικών συσκευών εμπορίου ώστε να μπορείτε να καταγράφετε στο σπίτι σας την ημερήσια δραστηριότητα σας, το βάρος σας, την αρτηριακή σας πίεση και κατά περίπτωση το σάκχαρο αίματος καθόλη τη χρονική διάρκεια της μελέτης. Στη συνέχεια θα μπορείτε να χρησιμοποιείτε την διαδικτυακή εφαρμογή CARRE (http://visual.carre-project.eu/) για να βλέπετε τις προσωπικές σας μετρήσεις και την αντίστοιχη εξέλιξη των προσωπικών σας παραγόντων κινδύνου.

Στην αρχή, στο τέλος και σε τακτικές εξαμηνιαίες συναντήσεις κατά τη διάρκεια της μελέτης θα αξιολογηθούν τα παρακάτω:

1. ποιότητα ζωής, με βάση το ερωτηματολόγιο SF-36,
2. κατάρτιση και κατανόηση πληροφορίας για την προσωπική υγεία, με βάση συνδυασμό των ερωτηματολογίων HSQ47 και Lipkus,
3. ενδυνάμωση σε θέματα προσωπικής υγείας, με βάση το ερωτηματολόγιο SUSTAINS,
4. βελτίωση κλινικής εικόνας, με βάση στοιχεία του ιατρικού φακέλου σας.

ΧΡΕΙΑΖΕΤΑΙ ΝΑ ΠΑΡΩ ΜΕΡΟΣ;

Η συμμετοχή σας σε αυτήν την μελέτη είναι εντελώς εθελοντική. Η θεραπευτική σας αγωγή και η σχέση σας με τον γιατρό σας δεν θα επηρεαστεί σε καμία περίπτωση, όποια και να είναι η απόφασή σας σχετικά με τη συμμετοχή σας σε αυτή τη μελέτη.

Αν αποφασίσετε να πάρετε μέρος θα χρειαστεί να υπογράψετε το έγγραφο ενημερωμένης συγκατάθεσης για να βεβαιώσετε ότι ο σκοπός, η διάρκεια και οι προβλεπόμενες συνέπειες της μελέτης σας έχουν εξηγηθεί και ότι έχετε δώσει τη συγκατάθεσή σας να συμμετάσχετε.

Παρέχοντας την άδειά σας, δίνετε την άδεια να χρησιμοποιηθούν συγκεκριμένες πληροφορίες από το ιατρικό σας ιστορικό με ανώνυμο και εμπιστευτικό τρόπο και να αναλυθούν για ερευνητικούς σκοπούς.

ΤΙ ΘΑ ΣΥΜΒΕΙ ΣΕ ΕΜΕΝΑ ΑΝ ΠΑΡΩ ΜΕΡΟΣ;

Αν συμφωνήσετε να πάρετε μέρος σε αυτή τη μελέτη εσείς δεν θα χρειαστεί να κάνετε κάτι. Δεν θα γίνει τίποτα περισσότερο ή λιγότερο από ότι χρειάζεται για τη θεραπεία που κάνετε. Τα αποτελέσματα από τις εξετάσεις που χρειάζεται να κάνετε για τη θεραπεία σας θα χρησιμοποιηθούν για τη μελέτη αυτή. Δεν θα χρειαστεί καμία παραπάνω εξέταση.

Η συμμετοχή σας στη μελέτη αυτή δεν αλλάζει σε τίποτα την θεραπευτική αγωγή την οποία θα ακολουθήσετε. Δεν θα απαιτηθεί από εσάς να πάρετε πειραματικά φάρμακα ή να κάνετε οποιεσδήποτε άλλες εξετάσεις που να συνδέονται με την παρούσα μελέτη.

Η συμμετοχή σας στην παρούσα μελέτη δεν θα έχει κανένα αντίκτυπο στις αποφάσεις ως προς την θεραπευτική αγωγή, που έχουν ληφθεί από τον γιατρό σας.

ΠΟΙΟΙ ΕΙΝΑΙ ΟΙ ΚΙΝΔΥΝΟΙ ΤΗΣ ΜΕΛΕΤΗΣ

Δεν υπάρχει κανένας παραπάνω κίνδυνος αν δεχθείτε να συμμετάσχετε σε αυτή τη μελέτη.

ΤΙ ΓΙΝΕΤΑΙ ΜΕ ΤΗΝ ΕΜΠΙΣΤΕΥΤΙΚΟΤΗΤΑ

Η επεξεργασία προσωπικών δεδομένων θα γίνει σύμφωνα με την Οδηγία της ΕΕ σχετικά με την Εμπιστευτικότητα Δεδομένων (95/46/EC) και την αντίστοιχη εθνική νομοθεσία. Έχετε δικαίωμα να τροποποιήσετε ή/και να ακυρώσετε την πρόσβαση στα δεδομένα σας οποιαδήποτε στιγμή, σύμφωνα με την εθνική νομοθεσία και κανονισμούς.

ΠΡΟΣΒΑΣΗ ΚΑΙ ΑΝΩΝΥΜΙΑ

Οι συμμετέχοντες στη μελέτη ερευνητές και το Θεσμικό Συμβούλιο/Επιτροπή Δεοντολογίας έχουν καθήκον τήρησης εμπιστευτικότητας απέναντί σας και δεν θα αποκαλύπτεται τίποτε σχετικά με την ταυτότητά σας εκτός του νοσοκομείου και ερευνητών της μελέτης. Η προσωπική σας ταυτότητα (το όνομά σας, η διεύθυνσή σας και άλλα αναγνωριστικά στοιχεία) δεν πρόκειται να συγκεντρωθούν και θα παραμείνουν εμπιστευτικά.

ΑΠΟΤΕΛΕΣΜΑΤΑ

Ανώνυμα δεδομένα που θα συγκεντρωθούν στη μελέτη αυτή, ακόμη και μετά την ολοκλήρωση της μελέτης θα χρησιμοποιηθούν για συμπληρωματική ανάλυση.

ΤΙ ΓΙΝΕΤΑΙ ΣΧΕΤΙΚΑ ΜΕ ΤΑ ΕΞΟΔΑ

Δεν πρόκειται να επιβαρυνθείτε με κάποια δαπάνη και ούτε να πάρετε κάποια αποζημίωση για τη συμμετοχή σας στην μελέτη. Στο τέλος της μελέτης θα πρέπει να παραδώσετε τον εξοπλισμό που θα σας χορηγηθεί για τη μελέτη.

ΤΙ ΓΙΝΕΤΑΙ ΜΕ ΤΗΝ ΑΣΦΑΛΙΣΤΙΚΗ ΚΑΛΥΨΗ

Καθώς πρόκειται για μη επεμβατική μελέτη οι θεραπευτικές σας αγωγές καθορίζονται αποκλειστικά και μόνον από τον γιατρό σας, πράγμα που εμπίπτει στο πεδίο ασφαλιστικής κάλυψης γενικής ευθύνης του θεράποντος ιατρού.

ΕΓΓΡΑΦΟ ΕΝΗΜΕΡΩΜΕΝΗΣ ΣΥΓΚΑΤΑΘΕΣΗΣ

Ημερομηνία:

Αριθμός Ασθενούς:

Τίτλος της μελέτης

CARRE: Εξατομικευμένη ενδυνάμωση ασθενών και υποστήριξη λήψης αποφάσεων στην καρδιονεφρική νόσο και συνασθένειες.

Σκοπός της μελέτης

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1. Διάβασα το έντυπο ενημερωμένης συγκατάθεσης για αυτή τη μελέτη. Έλαβα μια εξήγηση για το σκοπό, τη διάρκεια και το πιθανό όφελος της μελέτης και το τι θα αναμένεται να κάνω. Οι απορίες μου απαντήθηκαν ικανοποιητικά.
2. Συμφωνώ να πάρω μέρος σε αυτή την μελέτη.
3. Κατανοώ ότι η συμμετοχή μου στη μελέτη είναι **εθελοντική** και ότι είμαι ελεύθερος/η να αποσυρθώ οποιαδήποτε στιγμή χωρίς να δώσω οποιαδήποτε δικαιολογία, χωρίς να επηρεαστεί η ιατρική μου φροντίδα ή τα νόμιμα δικαιώματα μου.
4. Η Ανεξάρτητη Επιτροπή Δεοντολογίας/Συμβούλιο Θεσμικής Επιθεώρησης ή τοπικές ρυθμιστικές αρχές σύμφωνα με τους τοπικούς κανονισμούς μπορεί να θελήσουν να εξετάσουν το ιατρικό μου φάκελο για να επαληθεύσουν τις πληροφορίες που έχουν συγκεντρωθεί. Υπογράφοντας το παρόν έγγραφο, παρέχω την άδεια για αυτή την εξέταση του φακέλου μου.
5. Κατανοώ την περιγραφή στο παρόν έγγραφο που αφορά στο μέτρο στο οποίο οι προστατευμένες πληροφορίες σχετικά με την υγεία μου θα χρησιμοποιηθούν ή θα αποκαλυφθούν για μελέτη σε σχέση με έρευνα. Επίσης κατανοώ την περιγραφή στο παρόν έγγραφο που αναφέρεται στο βαθμό στον οποίο οι προστατευμένες πληροφορίες σχετικές με την υγεία μου θα χρησιμοποιηθούν ή θα αποκαλυφθούν.

Επώνυμο:_____ Όνομα:_____

(κεφαλαία γράμματα) (κεφαλαία γράμματα)

Υπογραφή: _____ Ημερομηνία: _____

(να συμπληρωθεί από τον/την ασθενή τη στιγμή της συγκατάθεσης)

Θεράπων ιατρός ή άτομο που πραγματοποίησε τη συζήτηση για την παροχή συγκατάθεσης.

Βεβαιώνω ότι έχω προσωπικά εξηγήσει τη φύση, το σκοπό, τη διάρκεια, και τις προβλεπόμενες επιδράσεις και τους κινδύνους της μελέτης στο άτομο που αναφέρεται πιο πάνω.

Επώνυμο: _____ Όνομα: _____

Υπογραφή: _____ Ημερομηνία: _____

8. Patient informed consent form in Lithuanian

Protokolo Nr.: 20

Versija: 02

Data 2016-05-04

INFORMUOTO ASMENS SUTIKIMO DALYVAUTI BIOMEDICININIAME TYRIME

„CARRE PASLAUGŲ ĮVERTINIMO TYRIMAS“

IR INFORMACIJOS APIE BIOMEDICININĮ TYRIMĄ FORMA

PACIENTUI SERGANČIAM LĖTINE INKSTŲ LIGA

VUL Santariškių klinikos, kartu su kitais 5 partneriais iš Graikijos, Didžiosios Britanijos, Lietuvos ir Lenkijos dalyvauja Europos Sąjungos FP7-ICT projekte *„CARRE“ - kardiorenaliniu sindromu sergančių pacientų įgalinimas bei bendra sprendimų palaikymo sistema“*. Lietuvoje šį projektą atstovauja VUL Santariškių klinikos ir Kauno technologijos universitetas. Pagrindinis projekto tikslas yra sukurti inovatyvią informacinių technologijų sistemą tarp paciento bei sveikatos priežiūros specialisto, kuri kardiovaskulinėmis bei inkstų ligomis sergančius pacientus *(„CARRE“ – trumpinys, sudarytas iš anglų kalbos žodžių - kardiovaskulinės ir inkstų ligos)* skatintų savarankiškai rūpintis savo sveikata, labiau domėtis liga bei aktyviai dalyvauti ją gydant.

Šioje informuoto asmens sutikimo ir informacijos apie biomedicininį tyrimą formoje Jums bus pateikta informacija apie biomedicininį tyrimą *„CARRE paslaugų įvertinimo tyrimas“,* (toliau – tyrimas) bei Jūsų sutikimo dalyvauti tyrime tvarka.

Prašome Jūsų atidžiai perskaityti žemiau pateiktą informaciją apie šį tyrimą ir jei sutinkate jame dalyvauti, pasirašyti šią informuoto asmens sutikimo formą. Neskubėkite ir atidžiai perskaitykite šį dokumentą. Jei nesupratote kokio nors žodžio ar teiginio, būtinai užduokite visus iškilusius klausimus tyrimą atliekančiam gydytojui. Neprivalote apsispręsti iš karto - prieš priimdami sprendimą galite pasitarti su šeimos nariais ar draugais.

Tyrimo tikslas - įvertinti širdies ir/ar inkstų ligomis sergantiems pacientams sukurtos savistabos sistemos naudą bei patikrinti ar ši sistema skatina aktyviau dalyvauti savo ligos gydyme.

Tyrimo uždaviniai - įvertinti sukurtos „CARRE“ sistemos teikiamas paslaugas ja besinaudojantiems pacientams, t. y.:

- Įvertinti jos įtaką pacientų įgalinimui ir jų gebėjimui aktyviau dalyvauti savo ligos gydyme;
- Įvertinti įtaką pacientų sveikatos raštingumui;
- Įvertinti įtaką pacientų gyvenimo kokybei bei sveikatai

Tyrimo užsakovas ir vieta. Šį tyrimą užsakė Europos komisija (FP7-ICT programa). Jis bus atliekamas dviejuose centruose – Vilniaus universiteto ligoninės Santariškių klinikose (Santariškių g. 2, 08661 Vilnius, įmonės kodas: 124364561) bei Aleksandropolio universitetinėje ligoninėje (Graikija).

Asmenų pakvietimas dalyvauti tyrime. Jūs esate kviečiamas (-a) dalyvauti šiame tyrime, nes Jums yra diagnozuota inkstų liga, sukėlusi inkstų nepakankamumą. Šis tyrimas neturės jokios įtakos Jums jau paskirtam medikamentiniam gydymui, kurį ir toliau tęs Jūsų šeimos gydytojas.

Jei sutiksite dalyvauti šiame tyrime, Jūs atsitiktine tvarka būsite priskirtas vienai iš grupių - kontrolinei arba CARRE grupei. Nepriklausomai nuo to į kurią grupę pateksite, šeimos gydytojo ar gydytojo specialisto paskirtas gydymas nebus keičiamas.

Nauda Jums – išmoksite geriau kontroliuoti savo ligą, gausite daugiau informacijos apie savo sveikatą ir Jums naudingą gyvenseną, būsite papildomai konsultuojami gydytojo specialisto.

Tiriamųjų skaičius. Tyrimo metu numatoma ištirti 160 asmenų, po 80 kiekviename tyrimo centre.

Tyrimo trukmė. Tyrimas truks nuo Jūsų pasirašyto informuoto asmens sutikimo iki 2016 m. spalio mėnesio.

Tyrimo eiga. Jūsų bus prašoma be šio vizito dar kartą papildomai apsilankyti VULSK, konsultacinėje poliklinikoje, gydytojo nefrologo konsultacijai (pradedant tyrimą bei baigiant tyrimą). Kiekvieno apsilankymo VULSK trukmė neturėtų viršyti 2 valandų.

Pirmojo vizito pas nefrologą metu be Jums įprastinės priežiūros, ištyrimo ir gydymo, nepriklausomai nuo to kurioje grupėje būsite, papildomai Jūsų bus prašoma užpildyti 3 klausimynus ir bus atliekami papildomi laboratoriniai tyrimai (glikuotas hemoglobinas (sergantiems cukriniu diabetu), bendras cholesterolis, DTL – cholesterolis, MTL – cholesterolis, trigliceridai, šlapimo rūgšties tyrimas iš veninio kraujo), kardioechoskopija, 6 minučių ėjimo testas. Antrojo vizito metu, numatomo 2016 m. spalio mėn., Jus papildomai konsultuos gydytojas nefrologas, Jūsų bus prašoma pakartotinai užpildyti 3 klausimynus bei bus atliekamas detalus laboratorinių rodiklių tyrimas (gliukozės kiekis kraujyje, glikuotas hemoglobinas (sergantiems cukriniu diabetu), bendras cholesterolis, DTL – cholesterolis, MTL – cholesterolis, trigliceridai, šlapimo rūgštis, kreatininas, albumino ir kreatinino santykis šlapime), kardioechoskopija, 6 minučių ėjimo testas, jei nebūsite buvęs tirtas šiame centre paskutinių 30 dienų laikotarpyje. Visi minėti tyrimai Jums bus atliekami nemokamai.

Galima rizika ir nepatogumai - Jums reikės dar vieną kartą papildomai atvykti į VULSK savu transportu ir lėšomis. Dalyvaudami tyrime vieno apsilankymo metu sugaišite iki 2 valandų (be kelionės į/iš klinikos) savo laiko. Tyrimo metu per apsilankymus Jums bus taikomas intervencinis tyrimo metodas - kraujo ėminio paėmimas iš periferinės venos, kuris gali sukelti nedidelį nepageidaujamą laikiną poveikį sveikatai (pirmojo vizito metu - kaip pacientui, atvykusiam į apsilankymą ligų prevencijos kabinete bei antrojo – papildomai, kaip tyrime dalyvaujančiam tiriamajam). Dažniausios neigiamos reakcijos susijusios su šia procedūra: psichologinis diskomfortas (baimė) dėl dūrio sukeliamo skausmo, kraujavimas iš dūrio vietos, rečiau - hematoma dūrio vietoje, infekcijos patekimas, paraudimas, paburkimas). Tyrime dalyvaujančių pacientų patirtos išlaidos nebus kompensuojamos ir kompensacija už laiką, sugaištą dalyvaujant tyrime, nebus mokama.

Vilniaus universiteto ligoninės Santariškių klinikos turi sudarytą Pagrindinių tyrėjų ir biomedicininių tyrimų užsakovų civilinės atsakomybės privalomojo draudimo sutartį. Dėl žalos, įvykusios biomedicininio tyrimo metu arba atsiradusios kaip biomedicininio tyrimo pasekmė, atlyginimo, prašome kreiptis į Vyr. juristę Renatą Ivanauskaitę (Santariškių 2, Vilnius, tel. 2365006).

Tiriamojo teisės:

- Gauti įprastinę sveikatos priežiūrą, jei Jūs atsisakytumėte dalyvauti biomedicininiame tyrime arba atšauktumėte sutikimą dalyvauti biomedicininiame tyrime.
- Gauti informaciją apie galimus gydymo būdus, jei Jūs nesutiktumėte ar atšauktumėte sutikimą dalyvauti tyrime (alternatyvas dalyvavimui tyrime).

- Atsisakyti dalyvauti tyrime bei atšaukti sutikimą dalyvauti tyrime bet kuriuo metu, nenurodant priežasčių ir motyvų.

  Norint atšaukti sutikimą Jums reiks, kaip galima anksčiau, telefonu informuoti Jus įtraukusį tyrėją, gyd. L. Rimševičių (tel.: 864545485). Jūs būsite pakviestas atvykti tyrimo nutraukimo vizitui į VULSK konsultacinę polikliniką ir tyrėjui arba kitam jo įgaliotam biomedicininį tyrimą atliekančiam asmeniui pateikti prašymą raštu. Apsilankymo metu, jei buvote priskirtas „CARRE“ grupei, taip pat turėsite perduoti Jums išduotas tyrimo priemones, jei Jums buvo tokios išduotos. Tyrėjas, gavęs Jūsų rašytinį prašymą atšaukti sutikimą, nedelsiant nutraukia informacijos apie Jus rinkimą ir atlieka kitus su Jūsų dalyvavimo biomedicininiame tyrime nutraukimu susijusius veiksmus, numatytus biomedicininio tyrimo protokole. Jei prašymas atšaukti sutikimą dalyvauti biomedicininiame tyrime siunčiamas paštu ar per kurjerį, tyrėjas arba jo įgaliotas asmuo per 3 darbo dienas raštu patvirtina prašymo gavimą. Asmeniniai užkoduoti duomenys, surinkti iki tiriamojo pasitraukimo iš tyrimo, nenaikinami.

Konfidencialumas. Biomedicininio tyrimo metu surinktų duomenų valdytojai yra tyrimą vykdantys centrai Lietuvoje (VšĮ Vilniaus universiteto ligoninės Santariškių klinikos, Santariškių g. 2, 08661 Vilnius, įmonės kodas: 124364561) ir Graikijoje (Medicinos mokykla, Trakijos Demokrito universitetas ir Aleksandropolio universitetinė ligoninė, University Campus, Dragana, 68100 Alexandroupoli, Graikija).

Siekiant užtikrinti Jūsų duomenų konfidencialumą, Jūsų vardas ir pavardė tyrimo metu, pasirašius informuoto asmens sutikimo formą, bus pakeisti specialiu skaitmenų kodu, kurį sudarys triženklė skaičių kombinacija (užkoduoti duomenys). Koduota informacija apie Jūsų sveikatą, neleidžianti nustatyti Jūsų tapatybės, bus prieinama FP7-ICT programos projekto „CARRE: kardiorenaliniu sindromu sergančių pacientų įgalinimas bei bendra sprendimų palaikymo sistema“ konsorciumo partneriams pasirašiusiems Konsorciumo sutartį. Su konfidencialiais duomenimis, leidžiančiais tiesiogiai nustatyti Jūsų tapatybę, galės susipažinti tik tyrėjas ir tyrimo personalas įprastinio vizito pas kardiologą metu.

Duomenys tyrimui bus renkami iš Jūsų ir iš Jūsų ambulatorinės kortelės:

- Iš Jūsų bus renkami šie duomenys: lytis, amžius, svoris, liemens apimtis, kūno masės indeksas (KMI), sistolinis kraujo spaudimas, diastolinis kraujo spaudimas, pulsas.
- Jei laboratoriniai tyrimai ar kardioechoskopija būtų atlikti tyrime dalyvaujančiame centre (dėl kitų priežasčių) paskutinių 30 dienų laikotarpyje, pirmojo ir antrojo apsilankymų metu iš Jūsų ambulatorinės kortelės bus renkami šie duomenys: alkio glikemija, glikozilintas hemoglobinas (Hb_{AIC}), lipidograma, trigliceridai, šlapimo rūgštis, kreatininas, albumino ir kreatinino santykis šlapime, kardioechoskopijos duomenys (E/A, deceleracijos laikas, IVRT, mitralinio vožtuvo medialinio ir lateralinio žiedų judesio greitis, kairiojo prieširdžio dydis). Jei 30 dienų laikotarpyje tyrimai nebuvo atlikti, minėti duomenys bus renkami iš apsilankymų metu atliktų laboratorinių tyrimų, kardioechoskopijos, 6 minučių ėjimo testo rezultatų.

Pagrindinis tyrėjas yra atsakingas už tai, kad tyrimo metu surinkti tiriamųjų duomenys būtų saugomi pagal galiojančius įstatymus. Visi tyrimo dokumentai bus laikomi bylų segtuvuose rakinamoje spintoje atskirai nuo dokumentų, susijusių su pacientų kodavimu ir identifikavimu. Surinkti duomenys bus saugomi, laikantis griežto konfidencialumo, 15 metų nuo tyrimo pabaigos tyrimo centro archyve.

Jūs turite teisę susipažinti su savo asmens duomenimis ir teisę reikalauti ištaisyti neteisingus, neišsamius, netikslius savo asmens duomenis.

Yra atlikta Valstybinės asmens duomenų apsaugos inspekcijos (A. Juozapavičiaus g. 6, 09310 Vilnius, tel. 8 5 2127532) išankstinė patikra.

Šis tyrimas yra gavęs Vilniaus regioninio bioetikos komiteto leidimą atlikti biomedicininį tyrimą

Kontaktiniai duomenys

Tyrimo centras

Vilniaus universiteto ligoninės

Santariškių klinikos

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El. paštas: info@santa.lt

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Tyrimo užsakovo atstovas

Gyd. Domantas Stundys

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Santariškių g. 2, Vilnius

Tyrėjas

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Vilniaus regioninis bioetikos komitetas

Tel. Nr.: 852686998

El. paštas: rbtek@mf.vu.lt

M. K. Čiurlionio g. 21/27 (231 kab.), Vilnius

SUTIKIMAS DALYVAUTI TYRIME

Savo noru sutinku dalyvauti šiame tyrime. Supratau man pateiktą informaciją. Man buvo atsakyta į visus mano visus pateiktus klausimus. Turėjau pakankamai laiko apsvarstyti man suteiktą informaciją apie biomedicininį tyrimą. Suprantu, kad mano dalyvavimas tyrime yra savanoriškas. Supratau, kad duodamas (-a) sutikimą, galiu bet kada pasitraukti iš tyrimo nenurodydamas (-a) priežasčių. Supratau, kad norėdamas (-a) atšaukti sutikimą dalyvauti biomedicinininiame tyrime, turiu apie tai raštu informuoti tyrėją ar kitą jo įgaliotą biomedicininį tyrimą atliekantį asmenį.

Pasirašydamas šią sutikimo formą, leidžiu naudoti savo duomenis ta apimtimi ir būdu, kaip nurodyta Informuoto asmens sutikimo formoje.

Patvirtinu, kad gavau Informuoto asmens sutikimo formos egzempliorių, pasirašytą tyrėjo ar kito jo įgalioto biomedicininį tyrimą atliekančio asmens.

_____

Asmens vardas, pavardė, parašas

_____

Data, laikas

Annex 2

Instruments for CARRE Impact Assessment

This annex presents the 4 survey instruments used in the assessment of the impact of CARRE service. In particular:

(1) Quality of life SF-36 questionnaire s

(2) Health literacy questionnaire

(3) Patient empowerment measurement SUSTAINS questionnaire

(4) System Usability Scale (SUS) questionnaire

1. Quality of life SF-36 questionnaire

This survey asks for your views about your health, how you feel and how well you are able to do your usual activities. Answer every question by checking the appropriate response. There are no right or wrong answers. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. Compared to one year ago, how would you rate your health in general now?

Much better	Somewhat better	About the same	Somewhat worse	Much worse
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

		Yes, limited a lot	Yes, limited a little	No, not limited at all
		☐	☐	☐
a	Vigorous activities, such as running, lifting heavy objects, participating in strenuous activities	☐ 1	☐ 2	☐ 3
b	Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c	Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d	Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e	Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f	Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g	Walking more than a kilometer	☐ 1	☐ 2	☐ 3
h	Walking several hundred meters	☐ 1	☐ 2	☐ 3
i	Walking one hundred meters	☐ 1	☐ 2	☐ 3
j	Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would have liked	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Had difficulty performing the work or other activities (eg, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Did your work or activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks …

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. How TRUE or FALSE is each of the following statements for you?

	Definitely True	Mostly True	Don't know	Mostly False	Definitely False
a I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. Health literacy questionnaire

Health Literacy Questionnaire

HLA	*On a scale from very easy to very difficult, how easy would you*	1 Very difficult	2 Difficult	3 Easy	4 Very easy
1	find information about symptoms of illnesses that concern you?				
2	understand the leaflets that come with your medicine?				
3	judge the advantages and disadvantages of different treatment options?				
4	judge if the information about illness in the media is reliable?				
5	use information the doctor gives you to make decisions about your illness?				
6	follow instructions from your doctor or pharmacist?				
7	find information about how to manage unhealthy behaviour such as smoking, low physical activity and drinking too much?				
8	find information on how to prevent or manage conditions like being overweight, high blood pressure or high cholesterol?				
9	understand health warnings about behaviour such as smoking, low physical activity and drinking too much?				
10	judge how reliable health warnings are, such as smoking, low physical activity and drinking too much?				
11	judge if the information on health risks in the media is reliable?				
12	decide how you can protect yourself from illness based on information in the media?				
13	find information on healthy activities such as exercise, healthy food and nutrition?				
14	understand information in the media on how to get healthier?				
15	judge where your life affects your health and well- being?				
16	judge which everyday behaviour is related to your health?				
17	make decisions to improve your health?				

18	influence your living conditions that affect your health and wellbeing?				
19	take part in activities that improve health and well-being in your community?				
HLB Answer the following questions					
20	Imagine that we rolled a fair, six-sided die 1,000 times. Out of 1,000 rolls,how many times do you think the die would come up even (2, 4, or 6)?				
21	In the BIG BUCKS LOTTERY, the chances of winning a $10.00 prize is 1%. What is your best guess about how many people would win a $10.00 prizeif 1,000 people each buy a single ticket to BIG BUCKS?				
22	In the ACME PUBLISHIN SWEEPSTAKES, the chance of winning a caris 1 in 1,000. What percent of tickets to ACME PUBLISHINGSWEEPSTAKES win a car?				
23	Which of the following numbers represents the biggest risk of getting a disease?	1 in 100	1 in 1000	1 in 10	
24	Which of the following numbers represents the biggest risk of getting a disease	1%	10%	5%	
25	If Person A's chance of getting a disease is 1 in 100 in ten years, and person B's risk is double that of A's, what is B's risk?				
26	If Person A's risk of getting a disease is 1% in ten years, and person B's risk is double that of A's, what is B's risk?				
27	If the chance of getting a disease is 10%, how many people would be expected to get the disease: Out of 100?				
28	If the chance of getting a disease is 20 out of 100, this would be the same as having a ____% chance of getting the disease.				
29	The chance of getting a viral infection is .0005. Out of 10,000 people, about how many of them are expected to get infected?				

3. Patient empowerment measurement SUSTAINS questionnaire

1. How much of the health information that you receive from healthcare professionals **during face-to-face visits** do you understand?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

2. How much of the health information from test results and medical reports you receive **electronically or on paper** do you understand?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

3. How much of the health information from **other health-related sources** such as websites, books, etc. do you understand?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

4. How much are you aware of the **warning signs/symptoms** related to your health?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

5. How much do you understand the **impact** of your disease in terms of **life-style adaptations**?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

6. How much do you think you are aware of the possible **progression of your disease**?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

7. How **well-informed** do you think you are about the **treatment options** regarding your disease?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

8. How often do you check your general health **when you are feeling alright**?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

9. How promptly do you **follow up on any warning signs** about your health?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

10. How much of the **life-style related advice** you receive from healthcare professionals do you follow?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

11. Do you take your **medication** exactly as prescribed?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

12. How often do you record data of **health monitoring activities** suggested to you by healthcare professionals?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

13. How often do you read your available test results or medical reports **before going to face-to-face consultations** with your doctor?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

14. Do you **think of questions in advance** that you want to ask your doctor during face-to-face consultations?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

15. Do you look for **additional information** regarding your health?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

16. How much say do you think you have in making **decisions regarding your treatment**?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

17. To what extent do you feel **able to draw your healthcare professionals' attention** to the issues that are a priority for you?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

18. How much does your treatment plan reflect **your preferences and choices**?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

19. How satisfied are you with **your relationship with the healthcare professionals** you regularly interact?

1 (none)	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 (all)**	**Unable to respond**

20. In general, how frequently do you visit a doctor (GP or specialist) for **any type of consultations**?

- □ Once a week or more
- □ Once every two weeks
- □ Once every three weeks
- □ Once every month
- □ Three or four times a year
- □ One or two times a year
- □ Less than once a year
- □ Never

21. How long does it take you to reach to the **closest primary care centre**?

- □ 15 minutes or less
- □ Between 15 to 30 minutes
- □ Between 30 minutes and one hour

□ Between one and two hours
□ More than two hours
□ Don’t know

22. How long does it take you to reach to your **general practitioner**?

□ 15 minutes or less
□ Between 15 to 30 minutes
□ Between 30 minutes and one hour
□ Between one and two hours
□ More than two hours
□ Don’t know

23. How long does it take you to reach to the **closest hospital**?

□ 15 minutes or less
□ Between 15 to 30 minutes
□ Between 30 minutes and one hour
□ Between one and two hours
□ More than two hours
□ Don’t know

4. System Usability Scale (SUS) questionnaire

	Strongly disagree				Strongly agree
1. I think that I would like to use this system frequently	1	2	3	4	5
2. I found the system unnecessarily complex	1	2	3	4	5
3. I thought the system was easy to use	1	2	3	4	5
4. I think that I would need the support of a technical person to be able to use this system	1	2	3	4	5
5. I found the various functions in this system were well integrated	1	2	3	4	5
6. I thought there was too much inconsistency in this system	1	2	3	4	5
7. I would imagine that most people would learn to use this system very quickly	1	2	3	4	5
8. I found the system very cumbersome to use	1	2	3	4	5
9. I felt very confident using the system	1	2	3	4	5
10. I needed to learn a lot of things before I could get going with this system	1	2	3	4	5