Integrating the home and the professional care environments through standards: a prototype for tDCS home monitoring

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ABSTRACT

Current electronic health record (EHR) systems mainly manage and store health data and document related to the time the patient is in the hospital. The main objective of this PhD project is to include into the patient’s EHR data generated and acquired in the domestic environment, thus allowing the safe and reliable exchange of such data among clinicians, caregivers, and patients, according to a newly developed protocol for mobile applications.

Currently, the “Healthcare Information Exchange” (HIE) movement promotes the integration among different enterprises allowing document exchange by the adoption of established standards like HL7 and HL7-CDA Rel. 2.0 (Clinical Document Architecture of Health Level 7). Even though the HIE and the priorities published by the AMA (American Medical Association) envisage the communication between patient’s systems and professional EHR systems, available standards are not ready to support such functionalities. To achieve such integration, it is necessary to (1) investigate to what extent the existing protocols suffice for the needs of the patients; (2) design a specific architecture for the data exchange between patient’s mobile applications and professional EHR systems; (3) provide a proof-of-concept of such integration. This work addresses all these issues by: (1) studying how the HL7-CDA 2 protocol needs to be amended in order to map all the attributes needed from the patient side, taking into deep consideration also security aspects; (2) defining an architecture and setting up an information protocol for an innovative integrated system to exchange information between the home care and the professional environments, in accordance to international standards and recommendations; (3) developing a use-case based proof-of-concept of this architecture in order to manage the patient treated with transcranial direct current stimulation (tDCS) at home.

The main scientific output of this thesis is to propose an adjustment of the current HL7 protocol, to include the cases in which the patient is involved into the integrated health care process through a mobile application, taking into consideration not only the technical point of view but also issues regarding access to health personal records. To do so, the thesis describes a prototype of EHR/mobile app integration devoted to the monitoring of patients affected by depression or chronic pain treated at home with transcranial direct current stimulation (tDCS). The innovative aspect of this integrated system is the use of a new template of HL7 document that is used to exchange information between the EHR (clinician side) and the mobile app (patient’s side).
The results of this project provide the basis for a new integrated care communication protocol that currently does not exist but is needed to prompt integrated health. The current thesis describes a trial use of the protocol that can be considered an example to guide standard initiatives, like HL7, in including use cases where the empowered patient and caregiver are involved into integrated health care process. This research activity cannot be carried out by other stakeholders, like vendors, because their corporate aims cannot guarantee the necessary national and international interoperability level.
LIST OF ABBREVIATIONS

AMA: American Medical Association
App: mobile Application
CCD: Continuity of Care Document
CDA2: HL7 Clinical Document Architecture Release 2
CFR: Care Report Form
DPA: Data Protection Authority
EHR system: system or platform for the management of EHR in hospital by professional user
EHR: Electronic Health Record
EMR: Electronic Medical Record
FDA: U.S. Food and Drug Administration
HIE: Health Information Exchange
HL7: Health Level Seven International
ICT: Information and Communication Technology
IDBAC: unique identifiers associated with patients in WebBioBank (equivalent to master patient index, MPI)
IHE: Integrating the Healthcare Enterprise
MDD: Major Depression Disorder
MDDS: Medical Device Data Systems
MPI: Master Patient Index
mPHMR: mHealth Personal Healthcare Monitoring Report
OIDs: ISO Object Identifiers
ONC: The Office of the National Coordinator
OU: Operative Unit
sOU: super Operative Unit
PHMR: Personal Healthcare Monitoring Report
PHR: Personal Health Record
POMR: problem-oriented medical record
rEHR: research Electronic Health Record
RMIM: Refined Message Information Model
tDCS: transcranial Direct Current Stimulation
UML: Unified Modeling Language
SUMMARY

Mobile Health applications (mHealth apps) are opening the way to patient’s responsible and active involvement in their own healthcare management. However, apart from apps allowing patients to access their Electronic Health Records (EHRs), mHealth apps are currently simply developed as dedicated “island systems”. In the last few years, the diffusion of smartphones among health professionals and inside the home environment has become more and more relevant. For example, in hospitals, doctors frequently use mobile apps to share clinical images among different wards and the EHR of a patient. As this application requires a secure Wi-Fi and it implies the selection of a specific patient, it has to be used only by doctors inside the hospital. At home, citizens use mobile apps to obtain information related to their health or to their wellness maintenance. The bi-directional health information exchange between mHealth apps and EHR systems is a recent challenge both from the technological and the regulatory point of view. Many examples of such integration can be found in the literature, but all of them differ from the system described in the present work, because they have been developed either for hospitals or to let patients check their clinical documents but without contributing to data collection.

The aim of the present study is to extend clinical data collection outside the hospital, during patient’s home treatments. The proposed system is not a simple Personal Health Record (PHR) allowing patients and caregivers to view health-related data and documents, but it provides educational and operative instructions for safe treatment at home and collects data regarding evaluation scales of patients for the optimization of the care planned by professionals. The developed prototype presents the following major innovative aspects: (1) the integration of the role of caregivers with the clinical pathway of the patient, by sharing information and instructions and; (2) the possibility of configuring the contents of the app (exercises, evaluating scale or instructions) according to the results of monitoring. In this way, it is possible to configure the mobile application according to the patient’s health status and rehabilitation progress. From the scientific point of view, the topic of this study concerns the definition of an architecture and the set up of a protocol for an innovative interface to exchange information among the home care process, the electronic medical record, and the professional environment, in accordance to international standards and recommendations.
CHAPTER 1: INTRODUCTION

This chapter provides the reader with a brief description of the issues introduced by the exponential diffusion of mobile health applications (mHealth apps). The first FDA regulatory guidance trying to define the difference between mobile apps, mobile medical apps and medical devices can be considered as a milestone in the definition of the regulatory requirements for mHealth apps. In the literature, there are some examples of connecting a mobile app to an EHR system, but all the described solutions maintain two independent datasets, and are not intended to implement an integrated monitoring system for chronic patients at home. Therefore, the chapter introduces the innovative aspects of the technological solution proposed in this study, in order to carry out a standard based bi-directional health information exchange between mHealth apps and EHR systems. The new system guarantees a real time integration of data and a personalization of the mobile app contents according to the care plan prescribed by healthcare professionals.

CHAPTER 2: BACKGROUND AND RELATED WORK

The first paragraph of the chapter deals with regulatory guidance and health IT ecosystems. It refers to the limitations of the technological and of the regulatory solutions available for the combined use of EHR systems and mobile applications. According to the American Medical Association (AMA), an improvement of Electronic Health Record usability has to be urgently addressed, in order to reduce the dissatisfaction reported by clinicians during the use of modern technologies for the management of charts. According to the association, a well-designed EHR system, integrated with mobile technologies, is essential for the coordination of team-based care, for the improvement of physicians’ experience with technology, and for the reduction of administrative costs. Moreover, improving EHR usability and finding its proper place in the overall health information technology (health IT) ecosystem is an important goal to be achieved as soon as possible. In “Improving Care: Priorities to Improve Electronic Health Record Usability” published in 2014, the association declares that: “Aside from these eight EHR usability priorities, the AMA believes that additional research is needed to determine how EHR use promotes or inhibits high quality care. It is essential to better understand the cognitive needs of physicians and how EHR products can meet them, identify evidence that outlines the benefit tools that support decision-making and explore how EHRs influence the patient encounter. All are opportunities for research that would benefit the advancement of EHR technology. Finding evidence of what works and what doesn’t work will be critical to improving EHRs.”
The future health IT landscape includes not only EHRs as the centrepiece of the health IT ecosystem, but also mobile technologies which are viewed as one of the most spread tools allowing both data collection into open source platforms dedicated to clinical research and the personalization of the care plan based on continuous health status monitoring. However, the AMA recognizes that not all the EHR usability issues are directly related to software design as some may be related to regulatory requirements or to suboptimal practice workflow processes incorporated into the EHRs. For this reason, the chapter deals with the current FDA guidance, with European guidelines for mobile medical applications and provides the reader with some examples of process modelling in health care. The chapter includes a presentation of current policies regarding health information exchange (HIE), integrating healthcare enterprise (IHE), and analysis of the integrated care system described in literature.

The second part of the chapter covers materials and methods used to model the system architecture and to develop the integrated care system “tDCS integrating home monitoring system”. UML is the standard visual modelling language widely used in IT context to specify, visualize, construct and document artefacts of a software system. UML is independent from both the software lifecycle and the used technologies, and thus it is the de-facto standard to build object-oriented software. A UML model can be rendered from different points of view, using different types of UML diagrams. The UML language describes both the static structure and the dynamic behaviour of a system.

A standard review reveals that the HL7 draft standard PHMR (Personal Healthcare Monitoring Record) is a kind of clinical document that can be used for the definition of reports for home monitoring systems. In fact, PHMR carries personal healthcare monitoring information from PHM systems to different type of health records (EHR, PHR or EMR). So in the integrated care process proposed in this thesis, message exchanges between mobile apps and EHR systems have to comply with PHMR, even if some adjustments are needed for the generation of such reports from mobile app in an anonymous format.

To deploy an integrated system, a dedicated mobile app is developed for data exchange with the EHR system named WebBioBank. This is a web-based platform used in research for anonymous data collection during clinical trials. This technical specification fulfills the requirement of the new communication protocol based on the exchange of anonymous messages. The validation methodology is also described in this chapter, in order to define the testing procedure dedicated to the first prototype of integrated home monitoring system based on mobile app.
The last paragraph of the chapter describes the use case for the first implementation of an integrated system between mobile apps and EHR systems. Chronic illnesses or neurodegenerative diseases are among the most common scenarios for home telehealth systems. The choice of the use case is based on the type of pathology, the complexity of treatment, and the active role of the caregiver. Transcranial Direct Current Stimulation (tDCS) meets these requirements because it is a non-invasive technique that can be used at home for the treatment of different diseases. However, for a safe home treatment, an active role of the caregiver is mandatory. An integrated home monitoring system for patients undergoing tDCS allows one to design a system configurable according to the caregiver’s level of education and to the pathology or disease progression. This system introduces the possibility for a physician to access not only the tDCS prescriptions but also the results of the patient’s evaluations performed at home. This solution allows the physician to monitor the efficacy of the daily home treatment and, possibly, to adjust the stimulation parameters during the following visit according to the patient’s home evaluations.

CHAPTER 3: DESIGN CONSIDERATIONS

Nowadays both in the USA and in Europe different policies and projects aim at encouraging electronic health information exchange, improving EHR systems according to medical associations’ priorities, integrating healthcare enterprises and regulating mHealth apps. Considering this context and the vision of a future “health IT ecosystem”, the integration between mHealth app and EHR system, where patient and caregiver are empowered and actively involved into care processes, is a predicted consequence.

The third chapter clarifies that the objective of the present study is not to develop an integrated home monitoring system, but to verify if the existing standard regarding electronic health data exchange can be applied also when the clinical document is generated by a mobile app. The thesis aims at including into the EHR data acquired in a domestic environment, and at allowing the exchange of such data between clinicians, caregivers, patients according to a newly developed protocol for mobile applications. Through the study of a use case, it is possible to define the requirements of the integrated system and then model the communication protocol and the system architecture. During the implementation of a prototype of this use case, the maximum attention is given to the application and/or adaptation of standards on messages shared between mobile apps and EHR systems.
The current study concerns the definition of an architecture and the set up of an information protocol for an innovative interface to exchange information between the home care process, the electronic medical record, and the professional environment, in accordance to international standards and recommendations. The main scientific output will guide the decision to confirm or to adjust the current HL7 protocol, and to involve the patient into the integrated health care process through a mobile application, taking into consideration not only technical aspects but also issues regarding access to health personal records.

The second paragraph of the chapter defines the requirements of the new integrated home monitoring system, the system architecture and the functionalities, by using UML use case diagrams, activity diagrams, and sequence diagrams. These diagrams show the home monitoring process in details from both sides: EHR system and mobile app. A three-tier architecture characterizes the integrated home care system based on the clinical document exchange between the EHR system and the mobile app. The client tier includes three different user interfaces and the local registry that is used only by physicians to manage the identified data. The middle tier implements the interface between the mobile app and the EHR system in order to share the database. The data tier is entirely located in a cloud-hosted virtual machine and contains the unique database, the framework manager of the EHR system, and the IIS (Internet Information Services) where the dedicated web service is installed.

CHAPTER 4: SYSTEM DESCRIPTION

The innovative feature of this integrated home monitoring system is the interface between the mobile app and the EHR system in order to share the database. The XML snippets, used to code and to decode data, comply with mHealth Personal Healthcare Monitoring Report (mPHMR), a new anonymous standard for clinical documents exchange between mobile apps and EHR systems with an architecture which permits a good system scalability, flexibility and reliability.

The new communication protocol between the mobile app and the EHR system is document-centred. The anonymous messages exchange is the innovative aspect of the integrated monitoring system. For this reason, the main result is the definition of the mPHMR. This is an XML-based standard intended to specify the encoding, the structure, and the semantics of clinical documents produced by the mHealth app to exchange data with the EHR system.
The chapter defines in detail the differences between the mPHMR and the HL7 draft standard PHMR that has to be adjusted in order to allow the generation of such reports by mobile apps as well as by monitoring devices.

Next, the chapter describes the integrated monitoring system (composed by: the EHR system, the mobile app and the dedicated web service) and the results of validation tests. An Operative Unit dedicated to tDCS patient is created in the EHR system and a module is developed for the app content customization. In this way, the doctor can add, to the EHR system, a prescription based on the information provided by the app according to the pathology, disease progression or caregivers’ education level. A web service implements the integration between the app and the EHR system using a unique database to manage the mPHMR exchange and data storage. Finally, the chapter refers to the results of tests for the validation of the integrated system.

CHAPTER 5: DISCUSSION AND CONCLUSION

The chapter deals with the major innovative technological and clinical aspects of the integrated monitoring system developed in this study. The lack of specific standards dedicated to mHealth apps and the low usability of EHR systems, which do not favour the electronic health information exchange, make it crucial to adopt standards for the regulation of clinical data exchange between mobile apps and EHR systems. The new communication protocol proposed and tested in this study is based on anonymous messages. The development of a proof-of-concept of such integration demonstrates that the adoption of the HL7 standard is not sufficient to guarantee safety and privacy issues arising from the use of mobile apps. The new architecture allows a good system scalability, flexibility, and reliability even if the first prototype has some limitations in terms of controls on phone numbers and encryption of messages. In the future prospective of a national interoperability between mobile apps and EHR systems, the implementation of regional registries for mPHMR messages can be evaluated. In this case, it is necessary to define a common minimum set of metadata to be included into the Header of mPHMR. In conclusion, the main scientific output of the present study is to guide the decision to confirm or to adjust the current HL7 protocol, to include cases where patients and caregivers are actively involved into the integrated health care process through a mobile application, taking into consideration not only the technical point of view but also the issues regarding access to health personal records.
1. INTRODUCTION

In the last few years, the widespread diffusion of mobile technologies has favoured an exponential growth of mobile applications which can be compared to the diffusion of HTML web pages after the introduction of the “world wide web” communication system in the ‘90s. Mobile applications implement more and more complex activities and functionalities thanks to the continuous innovation of technologies used for the realization of smartphones which can undoubtedly be regarded as a combination of a cell phone and a handheld computer. This tech revolution has launched a challenge among developers to design innovative mobile applications which can be used in different fields and contexts. In just a few years the diffusion of this new type of software, easily available either for free or for a small fee on well-established online app stores, reaches hundreds of thousands applications used in very different context and fields.

The introduction of mobile “apps” (a diminutive of “applications”) into the health context, accessible in stores under the headings “medicine” “health” and “wellness”, is opening new ways to improve health and health care delivery [Marceglia et al. 2012]. Apps can be used by citizens to adopt a healthier lifestyle or to access to useful information, by caregivers to receive relevant information about pathologies and assistance guidelines, by patients to check their chart content and by healthcare professionals to access the EHR systems in the hospital instead of using unmovable workstation such as computers. However, as mobile apps are widely used and easy to download, issues regarding their quality, the reliability of the services and the fact that the information provided is accessible to anybody, no matter their level of education or specialization, are becoming more and more crucial.

In 2014 “research2guidance”, a consultancy and market research company, conducted a study on mHealth apps publishing. The report shows that today mHealth apps publishers predominantly target chronically ill patients (31%) and health and fitness-interested people (28%). As primary users, physicians are targeted by 14% of app developers. The “Other” category includes nurses (2%) and health insurers (2%) as well as still different, but significantly smaller target groups (Figure 1-1).
Figure 1-1: mHealth: consumers. Source research2guidance mHealth app Developer Economics survey 2014, n=2032.

Figure 1-2 shows the result of the study related to mHealth apps categories shared: the biggest group of mHealth apps could be categorized as fitness apps. More than 30% of all apps listed in the Health & fitness and Medical app sections of Apple App Store, Google Play, BlackBerry Appworld and WindowsPhone Store. These applications are fitness trackers or exercise guides. The second and third largest groups are Medical reference (16.6%) and Wellness apps (15.5%). Medical reference apps provide information about drugs, diseases, symptoms and give advice on how to take drugs or what to do in case of experiencing pain. They also show locations of pharmacies and medical centres. Wellness apps summarize all kinds of relaxation solutions, yoga instructions and beauty tips.

Figure 1-2: mHealth: mHealth app categories shared. A total of 808 apps from Apple App Store, GoolgePlay, BlackBerry App World and Windows Phone Store were analysed (March 2014). Source: research2guidance mHealth App Developer Economics survey 2014.
The new “Global Mobile Health Trends and Figures Market Report 2013-2017” estimates that about 500 million smartphone users worldwide will be using a health care application by 2015, and by 2018, 50 percent of the more than 3.4 billion smartphone and tablet users will have downloaded mobile health applications. In this scenario, FDA “encourages the development of mobile medical apps that improve health care and provide consumers and health care professionals with valuable health information” [FDA Mobile Medical Applications]. On 25 September 2013, FDA issued the “Mobile Medical Applications Guidance for Industry and Food and Drug Administration Staff” in which the difference between mobile apps and mobile medical apps, the condition when a mobile application can be considered a medical device and the relative regulatory requirements are defined.

The implementation of a direct connection between mobile medical apps and EHR systems certainly guarantees the safety and reliability of the information exchanged between clinicians and patients. Until now, there are few examples of such as integration. Moreover, communication protocols or standardized formats for reporting have been developed or adjusted in order to share clinical documents between mobile phones and EHR systems. The present study deals with the definition of a new system architecture for a home integrated monitoring system, where the clinical documents shared between home and hospital environments comply with a new format of monitoring report based on international standards and adapted to mobile applications.

1.1. Brief description of the issue

Health care systems and social care systems use different technologies to control health and wellbeing of the patient at home, to monitor vital signs or other biophysical data, to give advice or care [Valdez et al. 2014]. Mobile personal health applications (mHealth apps) are becoming part of everyday behaviour of patients and citizens as a support for care management, health information, wellness maintenance, and personal monitoring. mHealth apps provide information that are potentially relevant for patient’s assessment, progression, monitoring and for early detection of diseases, and track healthy behaviour. Nonetheless, communication and data sharing between these software programs and ICTs used by health professionals are not subject to specific protocols or regulations. International standards and protocols for data sharing and EHR (Electronic Health Record) management between health professionals systems do exist. There is still the need to examine if these standards and protocols are also relevant for data sharing between home and professional environments, or if, on the other side, some dedicated protocols are needed.
Nowadays, eHealth data exchange complies with the following standards: HL7 (Health Level Seven) and HL7-CDA Rel. 2.0 (Clinical Document Architecture of Health Level 7) [Health Level 7 web site]. These standards do not consider a direct communication between health professionals inside hospitals and patients at home. Over the last few years, the technological progress in mHealth (mobile Health) has made patients and citizens more active and informed (empowered, Bell et al. 2004): it is necessary to investigate if the existing protocols suffice for the needs of the patients. For example, according to the HL7-CDA release 2 protocol, the Header of each message has to include the elements regarding the identification of the health professional who wrote the shared clinical document. In case of a message sent from a mHealth app at home to the EHR system inside a medical centre, fields in the Header are not adequate and need to be completed adding information about the user of the mobile app. In this case, the author of the message is different from the doctor and his identification number has to be stored with the data collected at home into the database. In this way, when the clinician opens the EHR, he can now view data collected at home and the author of the relative message (the user of the mobile app). All of these aspects must be deeply taken into consideration during the design of both the architecture for the new ICT system and the protocol enabling the direct communication and data sharing between medical centres and home.

1.2. Relevance of the topic

From the social and clinical point of view, daily management of a patient at home is one of the most striking scenarios and this makes an integrated health care system for the continuous assistance to the patient essential. Furthermore, dealing with some kinds of pathologies requires high qualification of the caregivers, continuous training and the acquisition of practical skills and operational instructions for the daily management of diseases. Safety of home treatment traditionally depends on frequency of medical visits or phone contact between clinicians/nurse and patient and the regularity in compilation of patient-held diaries [Oakley et al. 2010]. Telephone interview during the follow–up period has been used for many years but it has been revealed as time consuming and non-specific. Mobile personal health applications (mHealth apps) can enhance direct communication between patients and health professionals. Moreover, patients' empowerment plays a crucial role in daily management of home treatment.

As for the technical aspect, an integrated home monitoring system has to be developed in accordance with dedicated communication protocols and system architecture. Reports exchange between hospital and home environment must comply with international standards already used for
the EHR management (such as HL7, CDA2, PHMR) but taking into consideration that at home a patient and/or a caregiver can use a mobile application for the generation of such messages. The new integrated system has to manage user authentication both in the two environments in order to avoid access to the health information by unauthorized people, especially through the mobile. The main risk could be the insertion of clinical data (for example patient evaluating scale) from the mobile app into the EHR system by users who are not the patient and or the caregiver enrolled into the monitoring system.

Sharing data between mobile apps and EHR systems generates issues in terms of regulations and interoperability. The management of de-identified data from the professional side (EHR system in hospital) and of anonymized messages from the non-professional side (mobile medical app used at home) represents an important technological challenge.

1.3. Innovative aspects of the proposed solution

Current management systems of digital medical records mainly manage and store data only about activities performed inside hospitals. The current study deals with data acquired in a domestic environment and with the exchange of such data among clinicians, caregivers and patients according to new standards. Moreover, as the study shows, data acquired from the two environments (hospital and home) are stored in the same database in a way that the messages include all the necessary information for the data archiving into the correct tables corresponding to the EHR of the patient. Manual data entry is not necessary because data transmission and archiving process is automatically performed.

The main difference with the previous studies is the use of one unique database: until now mHealth apps have been developed as stand-alone systems that can communicate with healthcare professionals through dedicated channels (e.g., ad-hoc developed web platforms) or e-mails. Patient’s information can be stored either on the personal mobile device or on the web platform but it cannot be integrated with EHR systems.

The complete records of a patient’s health pathway can be reconstructed by retrieving data and information from different databases. Beside this, manually data entry is necessary to re-enter patient’s clinical information into dedicated Web platforms, thus replicating existing digital data. As a solution, other systems allowing healthcare professionals to view and evaluate the data collected at
home have been developed, but these technological solutions can only create independent set of data and their integration is a loss of time.

The idea of this study is to create a support system for patients and caregivers through ICT, according to the international standards such as HL7, in order to guarantee the compatibility with the existing information system of hospitals. Figure 1-3 depicts the research scenario composed of two independent environments: the first one includes ICTs dedicated to healthcare professionals (for example: Electronic Health Records, Biobanks, Data mining); the second one includes technologies such as devices and mobile applications dedicated to home monitoring and support to citizen, caregivers and patients.

So far, most of the issues originated from the communication between these two environments are still unsolved. In particular, this study identifies three main gaps:

- Safety gap: only authorized users can participate and interact with the integrated health care system personalized for the patient. Whereas, on the patient’s side, the quality of the tools is not always guaranteed;
- Communication gap: mapping of the specialist medical terminology on familiar medical lexicon to improve doctor-patient communication and knowledge sharing is lacking [Koh et al. 2013, McDonald et al. 2013];
- Interoperability gap: patients and caregivers at home need proper operative instructions and information in order to give useful feedbacks to healthcare professionals.

The current research project has two proposals:

- to model a direct communication channel between clinicians and patients at home. Starting from existing use cases, it is possible to define the requirements of the communication between patients and their doctors and adjust the existing protocols for the integrated health care;
- to verify if the present eHealth International Standards of data sharing and communication are applicable to this model by the implementation of the protocol in a prototype for as single use-case, using available technology and newly implemented integration infrastructures.

The main scientific output of this study is the definition of a new template for anonymized home monitoring report, named “mHealth Personal Healthcare Monitoring Report“, dedicated to the exchange of clinical documents between mobile applications and EHR systems. Based on this template of messages, this study proposes a standards-based architecture that may be adopted by
mHealth apps developers and EHR providers to facilitate the bi-directional exchange of information between these two IT systems which represent the everyday practice for patients (mHealth apps) and for healthcare professionals (EHRs).

Results can be a guide for the decision to confirm or to adjust the current HL7 protocol, to include cases where the patient is involved into the integrated health care process. This project takes into consideration not only the technical point of view but also issues regarding access to health personal records. In the USA a similar experience was conducted during the project “Blue Button” [Medicare's Blue Button site], an open source software which IT providers of EHR systems can integrate in order to allow patients to access to their health personal data (EHRs) and download clinical documents [Ackerman 2013].

1.4. Thesis Outline

Chapter 2 provides the reader with a description of the state of the art regarding regulatory requirements and public consultation for mHealth apps. Particular attention is posed on a recent AMA’s recommendation that suggests an improvement of EHR usability based on patient’s mobile technology. This chapter also refers to present policies for health information exchange (HIE) and integrating healthcare enterprise (IHE) and includes an analysis of the integrated care system described in literature. The second part of the chapter describes methods used to model the system architecture and to develop the integrated care system “tDCS integrating home monitoring system”: a proof-of-concept of this new integration system between EHR and mHealth app. A standard review reveals that HL7 draft standard PHMR is a kind of clinical document that can be used for the definition of reports for this home monitoring system. Chapter 3 clarifies the objective of the present study: the thesis aims at including into an electronic health record (EHR) data acquired in a domestic environment and allowing the exchange of such data between clinicians, caregivers, patients according to a newly developed protocol for mobile applications. The chapter describes the system architecture and functioning using UML diagrams. Chapter 4 demonstrates that adjustments on this standard are necessary in order to regulate clinical reports generated from mobile app used by patient or caregiver at home. The modified standard is called mHealth Personal Health Monitoring Report (mPHMR). The chapter includes description of components developed on both EHR side and mobile app side and results of the final validation test of the integrated system. Chapter 5 sketches out some conclusions and discussion of limitations and future improvements of such kind of integration.
2. BACKGROUND AND RELATED WORK

This chapter deals with the state of the art and related work. The chapter first considers regulatory guidance and health IT ecosystem: priorities defined by the American Medical Association (AMA) when developing an health record and the guidance from the FDA and European public consultation regarding mHealth apps. Then the chapter refers to policies for electronically health data exchange (HIE and IHE) and includes an analysis of the integrated care system described in literature. In the second part, the chapter describes materials and methods necessary to model the system architecture and to develop the integrated care process “tDCS integrating home monitoring system”. This chapter includes the following paragraphs:

- Unified Modeling Language: UML diagrams are used both to design the home monitoring process and to model the structure and the behaviour of the new integrated system.
- HL7 – CDA2 templates: the exchange of documents between mobile app and EHR system follows a standard format that describes constraints on the CDA Header and Body elements in Personal Healthcare Monitoring Report (PHMR). PHMR is a HL7 draft standard normally used to carry personal healthcare monitoring information from PHM systems to different type of health records (EHR, PHR or EMR).
- WebBioBank: is the EHR system used to realize the desired integrated system in order to fulfil the requirements “Anonymous data transmission from/to mobile app” and “De-identified data stored inside the EHR system”. It is a web-based platform used in research because it does not store personal data: it allows doctors to manage de-identification data and researchers to process anonymized data [Rossi et al. 2014].
- mHealth app development tools: the first prototype of the desired integrated system is implemented using Windows Phone mobile app because the EHR system is a Windows-based solution. Even if, this is not a constraints of compatibility between EHR system and mobile app thanks to the innovative system architecture (described in chapter 3). The aim of this work is to analyse the applicability of available standards for the exchange of clinical documents between EHR system and mobile app, so the development of different mobile apps (such as: Android and iOS) goes beyond the scope of this thesis.
- System validation: this paragraph describes validation test used to verify the correct data exchange between mobile app and EHR and to analyze if the mobile app runs well in different smartphones and fulfills quality requirements.

- Case study: The case study described in the present chapter can be considered a home telehealth system where the connected monitoring device is the mobile app. Using a common smartphone patient and caregiver can read operative instruction or educative information about the treatment otherwise they can fill modules dedicated to the home monitoring of the patient. On the other side, health professional can access to the EHR of the patient and view data collected at home. The software on the server side does not interpret or process data collected at home: it just receives the messages from the mobile app and stores data into the corresponding EHR. The interpretation of data is always performed by clinicians.

2.1. Regulatory guidance and health IT ecosystem

2.1.1. AMA’s priorities

Since the nineteenth century, the American Medical Association (AMA) has promoted scientific advancement, improved public health, and invested in the doctor/patient relationship [AMA site]. With the recent introduction of modern technologies, such as EHR systems and mHealth apps, into daily care management, the AMA has become an important source of feedbacks coming from the final users of these technologies. Regarding EHR systems, the association recognizes their importance for the improvement of care services and for the reduction of their cost. At the same time, it underlines the fact that the present EHR systems are not adequate to provide health professionals with efficient and effective clinical work.

Although EHR systems have been increasingly adopted over the past decade, thanks to market and governmental incentives, their effective use is still limited due to usability issues. This kind of problem frequently originates from the level of alignment between the design and implementation of EHRs and the workflow requirements or preferences of doctors within and across specialties and settings. Leaders in health information technology usability [Middleton et al. 2013] have also identified the need to improve EHRs by defining their proper role within the “health IT ecosystem”. In this scenario, the AMA is suggesting the desired future capabilities of EHR systems: clinical care improvements must be the primary focus. With this aim, permanent research is necessary in order to improve the EHR usability starting from a better understanding and measuring its effectiveness not
only for health care professionals but also for final users (patients and caregivers) who increasingly rely on this technology. In addition, EHR vendors should upgrade their products taking into consideration the feedbacks coming from final users; e.g. their level of satisfaction and the integration of EHRs during the daily health management. To sum up improving EHR usability requires significant effort from all stakeholders: vendors, health care professionals, institutions, patients and researchers.

In 2013 in six states a qualitative and quantitative study sponsored by the AMA named RAND was conducted [Freidberg et al. 2013]. The report “Factors affecting physician professional satisfaction and their implications for patient care, health systems and health policy,” identified a number of issues related to EHRs that, according to the physicians, limited their professional satisfaction and the potentiality to improve patients’ care. The issues included in many EHRs are: “poor usability, time-consuming data entry, interference with face-to-face patient care, regulatory requirements, insufficient health information exchange and degradation of clinical documentation quality.”

On September 16 2014, the AMA published eight priorities in order to improve EHR systems for the final benefit of patients [AMA, 2014]:

I. Enhance Physicians’ Ability to Provide High-Quality Patient Care: “Effective communication and engagement between patients and physicians should be of central importance in EHR design. The EHR should fit seamlessly into the practice and not distract physicians from patients.” This means that EHR systems should not reduce the time dedicated to interaction with patients, as reported by many clinicians using poorly designed EHRs. The document retrieved by the EHR ought to be immediately available during the visit and the doctor should not need to replicate data or to perform manual data entry. EHRs should fulfil the workflow needs of clinicians: EHR vendors should focus more on user interface and workflow design in the development of their products, conducting analysis to better understand how physicians perform their daily work.

II. Support Team-Based Care: “EHR design and configuration must: (1) facilitate clinical staff to perform work as necessary and to the extent their licensure and privileges permit and (2) allow physicians to dynamically allocate and delegate work to appropriate members of the care team as permitted by institutional policies.” Present EHR systems do not facilitate team-based care: for example, physicians have to enter data or perform tasks that other team members should do. Instead, EHR systems ought to differentiate user
accounts according to the role inside the care team and should implement the workflow where activities are conducted by the corresponding role. In this way EHR systems can coordinate the team during the entire assistance to the patient or caregiver.

III. Promote Care Coordination: "EHRs should have enhanced ability to automatically track referrals and consultations as well as ensure that the referring physician is able to follow the patient’s progress/activity throughout the continuum of care.” The patient’s movements between different care settings are an example of a situation in which the EHR system has to ensure that the referring physician is easily able to follow the patient’s progress/activity throughout the care. EHRs have to guarantee interoperability with other forms of health IT in order to facilitate the flow of relevant information across care transitions.

IV. Offer Product Modularity and Configurability: “Modularity of technology will result in EHRs that offer flexibility to meet individual practice requirements. Application program interfaces (APIs) can be an important contributor to this modularity.” The same EHR product can be used in different units, hospitals or specialties so it has to implement different workflow. The best technological solution is a system easily configurable by the health professionals themselves, who know well the workflows inside their care team.

V. Reduce Cognitive Workload: "EHRs should support medical-decision making by providing concise, context sensitive and real-time data uncluttered by extraneous information. EHRs should manage information flow and adjust for context, environment and user preferences.” An improvement of EHR systems could be the real time data acquisition and automatic transmission of alert from other external systems in order to facilitate prompt medical decisions.

VI. Promote Data Liquidity: “EHRs should facilitate connected health care—interoperability across different venues such as hospitals, ambulatory care settings, laboratories, pharmacies and post-acute and long-term care settings. This means not only being able to export data but also to properly incorporate external data from other systems into the longitudinal patient record. Data sharing and open architecture must address EHR data ‘lock in’.” Patients’ care can be improved only by interoperability and data transmission based on a reliable method of identity management. This means that EHRs have to be able to export data and to incorporate external data from other systems maintaining the unique identification of the patient. EHRs must always include the identity of physicians, patients and organizations.
VII. Facilitate Digital and Mobile Patient Engagement: “Whether for health and wellness and/or the management of chronic illnesses, interoperability between a patient’s mobile technology and the EHR will be an asset.” Another possible improvement of EHR systems is the support of digital patient engagement and the capability to download and synthesize data from wearable sensor technologies for real-time monitoring and tracking of important medical information. Moreover, the increasing diffusion of smartphones among patients and health professionals suggests that mHealth apps can play a fundamental role in new models of care delivery. Considering such integration, interoperability requirements must be included during design of new EHR systems.

VIII. Expedite User Input into Product Design and Post-Implementation Feedback: “An essential step to user-centered design is incorporating end-user feedback into the design and improvement of a product. EHR technology should facilitate this feedback.” The sensation of frustration reported by users of present EHR systems should be reduced including, into the development life-cycles of products, the analysis of feedbacks coming from final users.

The design of new integrated home monitoring systems has to consider all the priorities published by the AMA. These warnings highlight the necessity to extend interoperability beyond EHRs and to support other health IT systems. In particular, the integration of EHRs with emerging mobile health applications is an outstanding asset. This innovative solution can contribute to the automatic population of open platforms used in clinical research where “big data” analysis is crucial for the result significance during clinical trials. The integration of EHRs with mHealth apps can also facilitate individual patient encounters through the use of “small data.”

The AMA also recognizes that not all EHR usability issues are directly related to software design but some may be related to regulatory requirements. Current standards provide the specifications for EHR/EHR communication [ISO 13606-1:2008] and policies suggest cross-institutional EHR interoperability to allow data sharing [Blumenthal et al. 2010, Barbarito et al 2012]. The EU commission has issued a mandate [EU commission, 2007] to enforce the adoption of EHR systems. Moreover, considering the possible integration between mHealth apps and EHR systems into “health IT ecosystem”, it is mandatory to consider the regulations regarding both EHR systems and mobile medical apps.
2.1.2. Mobile Medical Applications Guidance from FDA

In the context of a widespread diffusion of mobile health applications (mHealth apps) and in the perspective to integrate these new tools into health IT systems, the FDA issued the “Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff” [FDA, February 2015]. In this document, the agency establishes the differences between Mobile Medical Application (Mobile Medical App) and the common mobile apps. A “mobile medical app” is a device intended to be used as an accessory to a regulated medical device or to transform a mobile platform into a regulated medical device. The classification of a mobile app as a device depends on its intended use: whether it is used for the diagnosis of a disease, for the cure, mitigation, treatment, or prevention of a disease, or whether it is intended to affect the structure of the human body, the mobile app is a mere device. In addition, if a mobile app is intended for use in performing a medical function (i.e. for diagnosis of a disease or the cure, mitigation, treatment, or prevention of a disease) it is a medical device, regardless of the platform it runs on.

Appendix A of the guideline provides examples of mobile apps that the FDA does not consider to meet the definition of medical device and, therefore, are not mobile medical apps. In this list it is possible to find: mobile apps that are intended to provide access to electronic “copies” of medical books, educational tools intended to increase patients’ awareness, education, and empowerment or mobile apps that automate general office operations in a hospital.

This guideline explains the agency’s oversight of mobile medical apps as devices. It only focuses on the apps that present a greater risk to patients if they do not work as intended and on the apps that cause smartphones or other mobile platforms to impact the functionality or performance of traditional medical devices. The FDA believes that this subset of mobile medical apps (Appendix C of the guideline) poses the same or similar potential risks to public health as currently regulated devices if they fail to function as intended. The following are mobile apps that the FDA considers as “mobile medical apps” subject to regulatory oversight:

- “Mobile apps that are an extension of one or more medical devices by connecting to such device(s) for purposes of controlling the device(s) or for use in active patient monitoring or analyzing medical device data”. For example, they include a mobile application displaying patient-specific images from a server and remotely displayed data from bedside monitors, or an application controlling the delivery of insulin on an insulin pump by transmitting control signals to the pumps from the mobile platform. These kinds of mobile application have to
comply to the regulations applicable to the connected medical device in order to address any associated risks.

- “Mobile apps that use attachments, display screens, sensors or other such similar components to transform a mobile platform into a regulated medical device are required to comply with the device classification associated with the transformed platform”. An example of this kind of application is a mobile app that uses the built-in accelerometer on a mobile platform to collect motion information for monitoring sleep apnoea. Another example can be a mobile app that monitors a patient’s heart rate variability from a signal produced by an electrocardiograph, vectorcardiograph, or blood pressure monitor. In this case the mobile app has to be classified as cardiac monitoring software under 21 CFR 870.2300 (Cardiac monitor).

- “Mobile apps that become a regulated medical device (software) by performing patient-specific analysis and providing patient-specific diagnosis, or treatment recommendations. These types of mobile medical apps are similar to or perform the same function as those types of software devices that have been previously cleared or approved.“ When a mobile app uses patient-specific parameters and calculates dosage or creates a dosage plan for therapy: this type of software presents the same level of risk to patients regardless the platform they run on.

Meanwhile the FDA intends to exercise enforcement discretion. In other words, the FDA does not intend to enforce requirements under the FD&C Act for the kinds of mobile apps that:

- Help patients to self-manage their disease or conditions without providing specific treatment or treatment suggestions;
- Provide patients with simple tools to organize and track their health information;
- Provide easy access to information related to patients’ health conditions or treatments;
- Help patients to document, show, communicate potential medical conditions to health care providers;
- Automate simple tasks for health care providers
- Enable patients or providers to interact with Personal Health Record (PHR) or Electronic Health Record (EHR) systems; or
- Are intended to transfer, store, convert format, and display medical device data in its original format from a medical device.

Some mobile apps in the above categories and listed below may be considered mobile medical apps, and others might not. For those mobile apps listed below that are devices, the FDA intends to exercise enforcement discretion because they pose a low risk to patients:
• “Mobile apps that provide or facilitate supplemental clinical care, by coaching or prompting, to help patients manage their health in their daily environment”. For example apps that coach patients with their conditions and promote strategies for maintaining a healthy lifestyle.

• “Mobile apps that provide patients with simple tools to organize and track their health information”. Tools allowing patients to organize and track health information without altering or changing a previously prescribed treatment or therapy and to share this information with their health care provider as part of a disease-management plan.

• “Mobile apps that provide easy access to information related to patients’ health conditions or treatments”. For example apps that are drug-drug interaction or drug-allergy look-up tools.

• “Mobile apps that are specifically marketed to help patients document, show, or communicate to providers potential medical conditions”. They Include apps that serve as videoconferencing portals to enhance communications between patients, healthcare providers, and caregivers or apps specifically intended for medical uses that employ the mobile device’s built-in camera or a connected camera for purposes of documenting or transmitting pictures.

• “Mobile apps that perform simple calculations routinely used in clinical practice” such as BMI calculators.

• “Mobile apps that enable individuals to interact with PHR systems or EHR systems” providing patient and provider with a mobile access to electronic health record.

• “Mobile apps that meet the definition of Medical Device Data Systems”. These apps are intended to transfer, store, convert format, and display medical device data without controlling or altering the functions or parameters of any connected medical device (MDDS).

Mobile medical apps manufacturers must meet the requirements associated with the applicable device classification. If the mobile medical app falls within a medical device classification, its manufacturer is subject to the requirements associated with that classification. A mobile medical app, according to the FDA regulation, may be classified as class I (general controls), class II (special controls in addition to general controls), or class III (premarket approval). This classification depends on the risk the device poses to the patient and/or the user. On January 20, 2015, the FDA issued a draft guidance in order to regulate the low risk general wellness products [FDA, General Wellness: Policy for Low Risk Devices]. Examples of mobile applications considered low risk general wellness products are:

• a mobile app that monitors and records food consumption to “manage dietary activity for weight management and alert the user, healthcare provider, or family member of unhealthy dietary activity”,

a mobile application that solely monitors and records daily energy expenditure and cardiovascular workout activities to “allow awareness of one’s exercise activities to improve or maintain good cardiovascular health.” or

a mobile application that plays music to “soothe and relax” an individual and to “manage stress.”

This guidance reflects the FDA’s growing understanding of mHealth and the need of a balanced regulatory policy. Even in European projects, the creation of new standards, based on a transactional analysis of the impact of mobile technologies onto the healthcare context, is one of the main aims.

In 2012 the European Commission published the “eHealth Action Plan 2012-2020” where benefits and associated risks of mobile health apps are recognized. It indicates that the rise of mHealth is blurring the distinction between the traditional provision of clinical care and self-administration of care due to the empowerment of patient. In this new scenario, roles and responsibilities of different actors are not clearly defined inside care processes. Furthermore, this document underlines the potential of mobile health and wellbeing apps for patients and the need to have a clear legal framework to ensure their development and safe adoption.

Stakeholders, such as mobile app developers and mobile platform manufacturers, are seeking guidance and applicable rules. A description, even if non-exhaustive, of the EU legislation applicable to lifestyle and wellbeing apps is summarized in the report “Commission staff working document on the existing EU legal framework applicable to lifestyle and wellbeing apps” [European Commission, 2014]. In Europe, if an mHealth app falls under the definition of a medical device or of an in-vitro diagnostic medical device, this application has to comply with the safety and performance requirements of Directive 93/42/EEC or Directive 98/79/EC respectively. On 26 September 2012, the European Commission adopted two proposals, one for a regulation on medical devices and the other for a regulation on in-vitro diagnostic medical devices. When these pending revisions are approved, they will be applicable to all medical devices in the Union, including mobile applications that are intended to be used as medical devices. Moreover, today there are no binding rules in the UE for a clear distinction between health apps, medical apps and medical devices. So, when the medical devices directives do not apply to apps, clarity is required to identify the rules they must comply with.

In January 2012, in order to help software developers and manufacturers to identify whether their products fall or not under the two Directives, the Commission’s services published a guidance on this issue which is continuously updated [Guidelines on the qualification and classification of stand-alone software used in healthcare within the regulatory framework of medical devices, MEDDEV 2.1/6]
January 2012]. According to this guidance, depending on its intended purpose, software may or not fall under the definition of a medical device or of an in vitro diagnostic medical device. Certainly, there is the need to assess the legal issues arising from the use of lifestyle and wellbeing apps, considering the potential safety risks they may pose to citizens' lives.

In the eHealth Action Plan 2012-2020 project the European Commission announced the necessity of a broad stakeholders’ consultation on existing barriers and issues related to mHealth deployment. The results can help the EU identify the right way to regulate mobile applications without blocking mHealth potentials. On April 10, 2014, the European Commission launched a public consultation on mHealth in the form of a Green Paper which considered the potential of mobile health, its technological aspects and which presented the issues where stakeholders’ input is necessary. The public consultation also analysed mHealth potentials to maintain and improve patients’ health and well-being and encourage their empowerment. The stakeholders were given 13 weeks to answer some questions on a wide range of themes: data protection, legal framework, patients’ safety and transparency of information, mHealth role in healthcare systems and equal access, interoperability, research & innovation and international cooperation. On the basis of the responses to the Green Paper, the Commission will take steps at EU level to support mHealth deployment [GREEN PAPER on mobile Health 2014]. The results of the public consultation were published on 12 January 2015. A total of 211 responses from a wide range of stakeholders were received: industry, national and regional authorities, health professionals, research community, non-governmental organisations, patients’ associations. Most answers agreed on the fact that safety and performance requirements are not adequately covered by the current EU legal framework [E.C. Summary report on the public consultation on the green paper on mobile health 2015]. This result highlights the necessity to improve a regulatory framework about mobile apps in Europe.

Although in Europe there are directives for the regulation of medical devices (Dir. 93/42/CEE and Dir. 98/79/CEE) and for the guidance of manufacturers to establish when new software can be classified as medical device (MEDDEV 2.1./6), there is no standard or regulation for mHealth apps that do not fall into the definition of medical device. Future EU directives will come from the pending revision of medical device directives and from the results of the Green Paper. However, any mobile app has to comply with the European legislations regarding the protection of personal data (Dir. 95/46/CEE, Dir. 2002/58/CEE and D.Lgs. 30 giugno 2003 n. 196) and the consumers’ protection.

The findings of a survey, started in May 2014 by the Italian Data Protection Authority (DPA) to check the compliance of medical apps with Italian legislation, show that users are not protected
adequately. Out of a total of 1,200 apps surveyed, barely 15% provide really meaningful privacy notices and in 59% of the cases the DPAs found it hard to locate pre-installation privacy notices [“App mediche: garante privacy, serve più trasparenza nell'uso dei dati”, 2014]. The national registry of mHealth apps managed by the Health Ministry should be a useful solution for the control of medical applications.

Finally, it is possible to generalize the regulatory process of a mobile app into the following steps:

1. choice of the qualification of the mobile app: it is necessary to define if the software is a medical device or not based on its functionality and its intended use. This decision can be different for each module included into the same application: it depends on the functionality implemented into the module.

2. implementation and monitoring: the contract with the customer/patient has to include the manufacturer’s responsibilities regarding the medical device and the consensus of the patient to data collection and processing into the EHR, or the CRF in case of clinical trials. The manufacturer also has to clarify the procedure for software update and bugs resolution.

Even if different medical device classification rules are contained in the EU directives and in the FDA guidelines both regulations are dealt with in the present work due to the lack of specific standards dedicated to mHealth apps.

Based on MEDDEV 2.1/6 the mobile app included into the integration home monitoring system proposed in this study is a medical device and it cannot be considered stand-alone software. The software is not enclosed into a medical device but it has to be considered an accessory of a medical device (in our use-case a transcranial DC stimulator) because the application includes operative instructions that can influence the use of the medical device at home.

The FDA guidelines are useful for developers in determining if a product can be considered a mobile medical app and list the FDA’s expectations for that product depending on the classification. The integration home monitoring system proposed in this study includes a webservice that connects a smartphone to the EHR system transforming them into class I medical devices (according to MDDS classification regulation 21 CFR 880.6310). In this use case, it is not necessary to apply this oversight authority because the mobile app functionality cannot pose a risk to patient’s safety if the system does not function as intended. The mobile app developed in this study instructs patients and caregivers about the correct use of tDCS device at home, but it does not communicate with the stimulator for the stimulation parameter adjustment. This tool does not enable the patient to access the EHR as its
aim is to transfer data like operative instructions and results of daily patient evaluation scales between
the mobile app and the EHR system.

2.1.3. Health Information Exchange (HIE)

Nowadays, little health record is shared electronically, leaving doctors without the information
they need to provide the best care in time. The study of Williams et al. reveals that in the USA critical
information is not routinely shared across transitions of care and in most cases it is delivered using
emails or fax but not electronically [Williams et al. 2012]. This can bring about a delay in data
transmission between hospitals and the points of care where the clinician has to take prompt decisions
about the care. Furthermore, the lack of readily available clinical information (such as medication
lists, radiology images, and lab results) leads to additional costs for the repetition of testing, imaging,
and visits. In 2010, only 19 percent of hospitals reported that they exchanged patients’ clinical record
information electronically with providers outside their system [American Hospital Association,2010].
Customized coding is frequently needed to connect health information technology systems for the
information exchange: this is due to the lack of standards or to the flexibility adopted during their
implementation. The standardization of health information exchange would reduce the cost and the
complexity for providers, vendors, and health information exchange organization, which is the aim
of the HIE (Health Information Exchange). In this scenario, the Office of the National Coordinator
for Health Information Technology, Department of Health and Human Services, has led the process
of establishing the essential building blocks that will support the health information exchange. The
aim of this office is to develop additional policies and standards that will make information exchange
easier and cheaper and will facilitate its use on a broader scale [Williams et al. 2012].

Most privately built HIEs are owned and managed by hospitals or hospital systems owing to
capital requirements and the necessary policy development. The benefits of an HIE include:
implementation of use cases according to provider’s needs, storage control, data sharing within the
network, setting privacy and security control. In the USA, most states are building a statewide
infrastructure for information exchange offering a wide range of capabilities such as: secure
messaging and exchange of electronic lab results, communication with participating regional
affiliates, access to statewide provider directories and often low-cost exchange options [HIE toolkit].
However, as they follow different emerging models and business approaches to support electronic
health information exchange, the advancement of each HIE is not the same all over the country.
Moreover, only some vendors incorporate the functionality of electronic health information exchange into their Electronic Health Record (EHR) system.

Figure 2-1: An example of HIE model: secure and efficient transmission of patients' medical information between citizen, hospital, pharmacy, laboratory, primary care and health specialists. Share medical information electronically reduces medical errors, improves appropriateness of treatments delivered and creates a more cost-effective health care system with less waste. [Available from: http://www.healthit.gov/sites/default/files/nlc_whathie.docx]

According to the site [www.healthit.gov](http://www.healthit.gov) the Health Information Exchange (HIE) “allows doctors, nurses, pharmacists and other health care providers to securely share a patient’s vital medical information electronically reducing the need for the patient to transport or relay their medical history, lab results, images or prescriptions between health professionals. Instead, this information is shared between health care providers before the patient arrives for an appointment or goes to the pharmacy to pick up a medication”. Figure 2-1 depicts an example of HIE model.

The HIE suggests the creation of a “health IT ecosystem” in which data are securely exchanged among providers, patients can access their healthcare documents, and clinical research benefits from the aggregated data collected in the clinical setting [The Office of the National Coordinator for Health Information Technology, 2014]. “A 10-Year Vision to Achieve an Interoperable Health IT Infrastructure” is an invitation to health IT stakeholders (clinicians, hospitals, public health, technology developers, payers, researchers and policymakers) to join ONC in figuring out how they can collectively achieve interoperability across the “health IT ecosystem” (Figure 2-2).
Before starting with the implementation of the future “health IT ecosystem” it is necessary to:

- increase interoperability of the existing health IT infrastructure;
- improve technical and policy conformance among networks, technical systems and their components with the aim to support interoperability;
- empower individuals with new tools: health information from the care delivery system should be easily accessible to individuals so they can become more active partners in their health;
- create an interoperable infrastructure enabling patients and caregivers to find, send, receive, and use their own health information both within and outside the care delivery system;
- protect privacy and security in all aspects of interoperability.

It is clear that the realization of such vision improves both health and health care systems through the optimization of services and the reduction of costs. However, EHR providers, national and international regulatory agencies, health professionals and patients are required to foster a close collaboration and to make a big effort. The health information exchange (HIE) environment, characterized by a mix of public and privately funded exchanges, cannot support true interoperability without commitments from EHR vendors and the ONC. Both EHR vendors and the ONC need to support current and future data exchange standards ensuring that the data exchanged between EHRs is accurate, timely and resistant to errors.
Moreover, in a “health IT ecosystem”, it is mandatory to consider how it is possible to regulate the integration between different types of health records available nowadays and shared electronically: electronic health records (EHRs), personal health records (PHRs) and case report forms (CRFs). The PHR represents the life-long collection of health-related documents managed by the patients themselves [Kaelber et al., 2008] and the CRF includes de-identified data for clinical trials. Following previous suggestions of patient’s accessible EHRs [Wiljer et al., 2008], the Patient Care Coordination (PCC) Technical Framework of IHE now includes the XPHR profile describing the integration scenario for the PHR/EHR exchange of content [IHE, 2013].

Figure 2-3: Integration profiles and exchange standards between Electronic Health Record (EHR), Personal Health Record (PHR) and Case Report Form (CRF) [Marceglia et al. 2015b].

Marceglia et al. have recently identified [Marceglia et al. 2015b] four health information exchange categories: the EHR-EHR data exchange within the same institution, the EHR-EHR data cross-institutional exchange, the EHR-PHR exchange, and the EHR-CRF exchange. The study reveals that nowadays the EHR-EHR communication is regulated by the standard ISO 13606 while the exchange of structured documents between PHRs (PHR-PHR exchange) and between CRFs (CRF-CRF exchange) is based on standard messages (HL7-based) or using structured documents (HL7 Clinical Document Architecture, release 2, CDA-2). So far no standards are available for the interoperability between EHR, PHR and CRF (Figure 2-3). However, the review by Marceglia et al. shows that the standard information exchange between health documental systems is always mediated by structured standard clinical documents. In the context of the “health IT ecosystem”, the inclusion of mHealth apps in the HIE perspective would facilitate the individual’s contribution to their own
health record. A two-way exchange from professional health information systems to patient-managed
digital health systems, based on structured standard clinical documents, can be a considered a turning
point.

2.1.4. Integrating the Healthcare Enterprise (IHE) and Cross Enterprise
Document Sharing (XDS) Profile

Integrating the Healthcare Enterprise (IHE) is an initiative designed to stimulate the integration
of the information systems between different healthcare institutions (hospitals, points of care, etc).
Its aim is to ensure that, during the care of patients, all required information for medical decisions is
both correct and available to healthcare professionals.

An EHR is a set of sensitive data written in a machine readable format (i.e., HL7’s CDA [HL7,
2009]) regarding the healthcare history of a patient. Without an explicit patient’s consent, the content
of an EHR may not be disclosed to unauthorized people. Moreover, an alteration of such data may
have a severe impact on the health status of the patient. For this reason, any application developed
for EHR management has always to guarantee a secure access and transmission: confidentiality,
authentication, and authorization are crucial aspects for the product success. As described in the
previous paragraph 2.1.3, the Health Information Exchange needs the transmission of the EHRs from
clinics to hospitals and from hospitals to points of care. Thus, initiatives like [HL7 2009, The IHE
Initiative 2009] have been promoted for the definition of standard methodologies for the secure and
interoperable EHR exchanges between hospitals. In particular, Integrating the Healthcare Enterprise
(IHE) has been developed for the definition of standard methodologies for secure and interoperable
exchanges of healthcare data and the management of the patient’s identifiers.

IHE is an initiative by healthcare professionals and industry: it “promotes the coordinated use of
established standards such as DICOM and HL7 to address specific clinical needs in support of optimal
patient care. Systems developed in accordance with IHE communicate with one another better, are
easier to implement, and enable care providers to use information more effectively” [The IHE
Initiative, 2009].

The most widely used setting for exchanging patients’ documents within healthcare organizations
is based on the IHE Cross Enterprise Document Sharing (XDS) profile depicted in Figure 2-4.
Figure 2-4: Cross-Enterprise Document Sharing (XDS): clinical documents are stored in the Repository of the corresponding Enterprise meanwhile the metadata of each document are allocated in a common Registry for the indexing of patient documents. The central Registry can be used for the retrieval of clinical document between enterprises [available at: http://www.slideshare.net/nzhug/ihe-crossenterprise-document-sharing-xds].

The XDS profile is composed of a central document registry that acts as a catalogue for one or more databases (document “repositories”) where the documents reporting healthcare data for a patient are stored. The repositories extract metadata from documents and update the registry that can be used by the document consumer in order to obtain the corresponding links to the repositories where the data can be downloaded. The actors involved in XDS workflow are:

- Document Source: the source of both documents and their metadata (e.g., medical device, EHR system)
- Document Repository: it stores documents and their digital signature document, requests indexing in the Document Registry and supports retrieval
- Document Registry: it indexes document and supports search
- Patient Identity Source: it feeds identity of patients known to the Document Registry
- Document Consumer: it initiates search and retrieves documents for consumers (e.g., a doctor’s workstation)
The communication between the actors is implemented with SOAP (Simple Object Access Protocol) messages and the IHE model defines the use of an authentication assertion, encoded using the Security Assertion Markup Language (SAML), containing the identity of the user.

Figure 2-5 represents the transaction diagram for the XDS model. Figure 2-6 shows the transaction diagram in a future new healthcare scenario where a mobile app shares data with enterprises.

Figure 2-5: Transaction diagram of XDS: clinical documents are generated by the Document Source and transmitted to the Repository. It registers metadata of the received document into the Registry that can be queried by the Consumer. The Registry retrieves patient identity and the link where the desired document is stored [available at: http://www.slideshare.net/nzhug/ihe-crossenterprise-document-sharing-xds].

Figure 2-6: Transaction diagram of XDS: in a future healthcare scenario also mobile app will be used in the HIE perspective to facilitate individual’s contribution to their own health record. In this case, clinical document stored in the Repository can be send from doctor’s workstation but also from patient of caregiver which use dedicated app at home. They can be also document consumer in order to retrieve operative instruction or education according to the care plane dedicated to the patient.[Rossi et al. 2015b]
This model fits very well with the Integrating Healthcare Enterprise (IHE) needs because it is:

- Distributed: Each care delivering organization (Document Source) can publish clinical information for others but the original document remains stored in the source database.
- Cross-Enterprises: there is a unique index (Document Registry) for published documents that can be queried in order to receive the link to the desired document.
- Document centric: published clinical data are organized into a “clinical document” using a standardized document type (HL7-CDA, CCD, DICOM..)
- Document content neutral: the content of the document is processed only by the source and the consumer so the infrastructure can be generic.
- Standardized Registry Attributes: the documents are described by a standardized set of attributes in order to allow query from different EHR products.
- Standard based: the standards used in IHE are Electronic Business Standard (ebXML, SOAP..), Internet Standard (HTML, HTTP, PDF, JPEG…) and Healthcare Content Standard (HL7 CDA, CCD, DICOM,..).

In 2012 Masi et al. proposed a communication protocol, based on the IHE specifications, to authenticate healthcare professionals and assure patients’ safety. The authors conducted a formal analysis on the protocol that reveals a security flaw. Their results demonstrate that the mere adoption of the international standards does not guarantee the absence of such type of flaws. In conclusion, the authors say: “an aspect that needs to be considered is mobility of healthcare professionals among clinics and hospitals. In fact, differently from patients, healthcare professionals need to authenticate themselves, possibly on different clinics. Since IHE does not provide any standard for regulating such mobility, to guarantee the coherence of ARR’s audit trails some commonly used solutions can be exploited, ranging from using different accounts for the same professional to adopting a synchronized directory structure” [Masi et al., 2012].

2.1.5. Examples of communication between mobile apps and EHR systems

In the literature, there are some examples of integration between a web-based platform and mobile technologies. In 2008, a two-year project was conducted in Thailand in order to increase accessibility to healthcare services in rural and remote areas [Kaewkungwal et al. 2010]. The project involved the integration of cell phones into the healthcare system in order to improve antenatal care and immunization service for the under-service population living in the border area. This integrated
module allows to schedule visits, it automatically generates a message reminder for mothers and it lets healthcare personnel during visits outside clinical centres to update the health status of patients using the mobile phone. Unlike standard paper-based methods, this solution makes monitoring health status more efficient and timely. In fact, data collected by health personnel with smartphones from remote area are synchronized into a unique database of the national healthcare system.

This study does not describe a particular communication protocol but it demonstrates how effective the use of mobile technologies in spreading healthcare services up to remote area can be and it shows to what extent a smartphone can make data collection and monitoring more timely efficient.

In the context of a highly integrated computerized system, another example of benefits introduced by mHealth is the Onco-TreC, a home monitoring system designed to improve the interaction between a cancer patient and a healthcare professional for the treatment adherence during oral therapies at home [Galligioni et al. 2015]. The system is divided into a mobile diary and a web dashboard. Using an Android app the patient at home can record the parameters related to his/her health status and the drug dose taken. The application also includes an alarm to alert, by email, the professional in case of a critical condition of the patient at home. The web-dashboard allows the health professional to access in real time to the data collected at home and to monitor adherence to prescriptions or side effects. The innovative aspect of Onco-TreC is the integration of such module into a local system (OncoSys) specially developed for the total management of cancer patients. The aim of this system is to give doctors better information about the toxicity and the compliance to the therapy. In particular, Onco-TreC automatically updates the electronic Oncological Patient Record (eOPR) into the local system so that data are available wherever a decision making support is necessary. This example of home monitoring system dedicated to cancer patients is based on the TreC platform for health services that allows patients to access to their clinical documents (medical reports, results of examination..) and to manage their personal diary (list of drugs, therapies, intolerances and allergies). In the last year, new services such as the possibility to access to the service from mobile technologies and a remote monitoring application for chronic pathologies (diabetes, asthma and hypertension) have been added to TreC. This platform is based on the concept of Personal Health Record and it can be adapted to specific pathologies [TreC].

The two studies mentioned above are examples of mobile technologies integrated with a local health system, but they do not describe a specific communication protocol or any technical details of messages shared between an mHealth app and the health system. In the following list of projects, there are studies that consider the application of a standard during data transmission between a mobile
app and the health system. The first example is the project “eCare/eCare Mobile” [Mayr et al. 2010] developed for the exchange of nursing care data among hospitals, nursing homes and home healthcare services. This project is based on the IHE guidelines and the standard HL7 CDA2. The system is accessible by health professionals, using a standard web browser in a hospital or nursing home and by home healthcare providers using mobile devices at home. The dedicated mobile application allows the digitalization of the home care documentation and the visualization of exchanged data between healthcare providers. This is a technical solution to solve all those problems to record the services offered to each patient at home, usually occurring when the paper-based method is used. The new system automatically generates the care summary on the date of an emergency to favour the patient’s transfer and compelling care. According to the authors’ experience, when a patient is admitted to an acute hospital service a paper summary is frequently lost.

The HL7 standard can be jointly used with ISO/IEEE 11073 in order to report observations on a medical device in a format readable by clinical applications. In this way, the patient’s and device data, mapped according to such format, can be easily exchanged so that they can be immediately available for clinical decision support. Instead of a bilaterally mapping of device data into a target format, Ingenerf et al. use a generic HL7v3 Refined Message Information Model (RMIM) that allows different output formats: HL7 CDA, HL7 PHMR or web services. The authors describe a new method for the migration of intensive care device data to a desired HL7 compliant output format: first the device output data is extracted into an intermediate “simple” XML based format, exported data instantiate the RMIM model (adapted to 11073 standard) and then the mapping to the target output format is made using XSL-transformation roles [Ingenerf et al. 2012]. In their use case “Enabling decision support by SmartCare based on Integrated Care Manager data”, the desired output format is PHMR, which is a HL7 format for the storing and processing of monitoring data. Their approach is flexible because it is possible to vary the type of medical devices at the schema level and to choose different standardized output formats. This solution enables different clinical applications to extract device data from a generic model (11073 RMIM) instead of a bilaterally mapping to different target standards. However, once the desired output format is chosen, it also has to be localized to national requirements for the semantic interoperability between clinical systems. For example, the research paper by Christensen describes how in Denmark a common data format for storing telemedical measurements through a localization process of PHMR (the international HL7 standard data format for encoding measurements) was used by device at home [Christensen 2014]. The Danish localization process demonstrates that there are several open issues to be handled before a PHMR document can
be unambiguously understood by two health IT systems in the same country. The issues they describe are related to:

- the management of a national list of OIDs (ISO/IEC Object Identifiers) for the identification of regional hospitals, registers or standards inside the PHMR. The root OID has to be registered at the international HL7’s OID registry and the definition of the descending identifiers has to be done in collaboration with national standard in order to avoid duplication of OIDs.

- the use of regional terminologies for the semantic definition of observations reported into the PHMR because international codes and vocabularies, such as LOINC, do not include a codification for specific or local terms.

- the validity and soundness of measurements made by patients at home. In PHMR, data can be registered through electronic transmission but the values can also by entered manually by the patient or the caregiver. No fields in a standard PHMR specify how data is provisioned and in which context. The Danish solution defines the branch OIDs for two dimensions of methodCodes: "One for author context (who was involved in making the measurement), and one for the data provision (which means were used to transfer the value to the document)". A code system is assigned to each dimension.

- The interpretation of the author field when a document contains medical measurements made at home. It may be a medical device, the patient, the caregiver or the physician involved in the prescription. The Danish solution identifies as the author the disease management professional, the one who finalizes the document in a telemedicine setting.

- The insufficient device information included in the standard PHMR for the correct interpretation of measures valued by clinicians. The Danish solution suggests that more information regarding the calibration of the device that generates the PHMR report should be introduced.

All the issues, rising from the Danish PHMR localization process, have to be considered whenever a PHMR is generated from a home monitoring system. Terminology mapping in general is the main barrier to interoperability as it appears in all health information exchange problems. The tools provided by the UMLS or mapping tools that extract terms from national and international ontologies can be considered during the definition of the communication protocol for the exchange of health records.
Interoperability issues in health IT depend not only on the communication protocol but also on the limits imposed by EHR vendors. EHR systems currently available on the market are formatted in such a way that modification or personalization for the specific hospital, ward or physician are quite difficult. In 2009, Mandl et al. proposed a EHR like platform with a selection of modular applications (apps) characterized by a functionally separation between the core system and substitutable apps. This solution can reduce healthcare technologies’ costs and support both standard compliance and adherence to specific care workflow [Mandl et al. 2009]. The principle of substitutability is the central aim of the SMART Platform project [Mandl et al. 2012]. The aim of this project is to reduce barriers for ‘app’ developers in the health IT systems and it is funded by the Office of the National Coordinator for Health Information Technology as a part of the Strategic Health IT Advanced Research Projects (SHARP) Program [Office of the National Coordinator for Health Information Technology]. Health IT systems (such as EHRs, PCHR and health information exchanges) that have implemented the SMART API or a portion of it, are defined ‘SMART containers’ and can be considered as data sources available on the SMART API. The substitutable ‘SMART applications’ consist in few lines of HTML and JavaScript code including reference to the external SMART JavaScript library for the access to desired data from ‘SMART containers’. Substitutability requires semantic interoperability between applications and containers. For this reason, SMART defines a highly normalized data model of a medical record and uses medical standards for coding (LOINC and SNOMED CT). SMART API provides read-only view of the patient record, that in the app’s code is represented as a resource with a URI specified according to the path of the respective container. SMART API can be used in several EHR apps developed by another team so this project is an example of how the lack of interoperability in health IT can be solved and it can be considered a step towards a universal exchange.

An example of an integration between an EHR and a PCHR (Personally Controlled Health Record) was implemented by updating the open source Indivo to support the SMART API [Franckle et al. 2013]. Indivo’s underlying data model was reconciled with those of the SMART project enabling the system to act as a patient-facing apps platform. Another example comes from the collaboration between two SHARP centres (SMART and NCCD) and NIH centre which resulted in the development of a patient summarization app using SMART platform [Klann et al. 2013]. This innovative application reduces the EHR complexity as it moves from a multipage disconnected data to a concise problem-oriented medical record (POMR). It displays a problem-oriented view of medications and graphs of laboratory results. It can be run in nearly any SMART-enabled EHR environment but also in SMART-enabled i2b2 instance. The clinical research data repository platform i2b2 (founded by NIH) is enabled to support SMART creating a new container named ‘SMART-
The result of such a collaboration is the starting point for the development of new applications that implement intuitive and problem-oriented views of a patient record: EHRs or clinical data extracted from EHRs and stored in i2b2 repository for the research purpose. To sum up with, the SMART application can be written for providers, patients or researchers because the platform has three containers developed for the following health IT platforms: an electronic health record system (OpenMRS), a personal health record system (Indivo) and a clinical research repository (Informatics for Integrating Biology and the Bedside, i2b2). This means that SMART might be an ideal platform for a quick dissemination of innovative tools.

All the studies mentioned in this paragraph deal with interoperability issues arising from electronically data exchange between different EHR systems and health applications. In most cases, the application creates a direct connection between a patient and the health professional with the aim to allow the patient to view his own personal medical report. In only one study [Galligioni et al 2015] the patient at home can insert data into a mobile application connected to a dedicated web-based platform (electronic Oncological Patient Record system, OncoSys) integrated to the local health system. In literature, this is the most similar integrated home monitor system to the use case analysed in the present study. The aim of this thesis is not the development of an integrated care system but to demonstrate that a dedicated standard for reports generated by a mobile app is necessary whenever a smartphone is used at home during integrated home care services.

2.2. Process modelling in health care

Process modelling in health care has to be periodically redefined due to the continuous innovation of the technologies used for the service delivered. In other fields, various types of process models have been developed and applied to define the actions within a complex process and to better understand how actors and resources interact to achieve the desired outcomes. In the healthcare scenario, the most used process model is the flowchart [De Rosier et al. 2002, Lyons et al. 2004] but during the planning of health care delivery particular attention must be paid on users involved (health care practitioners or patients). In 2009, Jun et al. advised that “Given the variation in health care processes, we argue that the sole use of flow diagrams limits the potential impact of process modelling on improving health care provision and there are additional methods that could be usefully applied”.

Nowadays, there is a large amount of different methods and tools to use for the process modelling in the IT domain. The choice of the best methodology to use in a specific context depends on the experience of the developer, particularly in the healthcare context where not all the process modelling
techniques fulfil care complexity and variability. For example, the same care workflow changes in case of daily management of the patient or in case of acute emergency: users involved and activity’s priority can be very different.

Jun et al. reviewed the literature on process modelling methods in order to identify distinctive characterization that should be useful in the health care scenario. Their search is driven by a combination of keywords such as modelling or mapping, process and system with additional criteria which only consider diagrammatic descriptions of systems and exclude purely mathematical or stochastic modelling. Through the comparison of what each method semantically represents, the authors identifies eight diagram types with distinctive differences:

- **Stakeholder diagrams**: they show how stakeholders are hierarchically structured. In general, a stakeholder is a person who has a role inside a software project: it can be classified as customer or developer. In the healthcare scenario stakeholders can be: hospitals, wards, pharmacies, laboratories, multidisciplinary teams, health professionals or common patients. This type of diagram is comparable to the UML Entity relation diagrams or UML Class diagrams [Maciaszek et al. 2002].

- **Information diagrams**: they show the hierarchical structure of documents or information. This type of diagrams can be useful for understanding documentation issues: degree of standardization of documents, level of usage of electronic documents and links between electronic and paper-based documents. In the healthcare scenario the documents can be a patient summary, a discharge summary, a prescription, etc. These diagrams are comparable to Entity relation diagrams, UML Class diagrams or Information modelling methods.

- **Process content diagrams**: they represent a hierarchical list of activities of the care process and are comparable to Hierarchical task analysis or Use case diagrams.

- **Flowcharts**: they describe the sequence of activities so they can be helpful in understanding the overall sequence of care processes. This type of diagrams is comparable to UML Activity diagrams or Process description diagrams.

- **Swim lane activity diagrams**: they show a sequence of activities with a clear role definition by arranging activities according to responsibilities. In the healthcare context, the role depends on the profession inside a multidisciplinary team (doctor, nurse, technician, welfare worker, etc.) or it depends on the environment (caregiver at home or health worker in a nursing home).

- **State transition diagrams**: they define the way in which a system’s behaviour changes over the time by showing the system’s states (nodes), transition conditions (underlined text
between nodes) and transition actions (text between nodes with no underline). In the context of care processes, system’s states can be defined as patient-related states. This type of diagrams is comparable to State machine diagrams, State transition network diagrams or Petri nets.

- **Communication diagrams:** they show information/material interactions between stakeholders. For example, an arrow means information flow and a dotted arrow can represent medicine flow.

- **Data flow diagrams:** they show how information is processed and where information is stored. In the healthcare scenario, a patient record can be an example of data stored and different type of arrows can represent information and medicine transmission between activities inside a care process. In general, they are considered limited in describing the care processes where there is much information processed and stored. This kind of diagrams is comparable to Function modelling method.

Each method is different from the other in the combination of nodes and links. In general, nodes mainly describe stakeholders, information, activities or states, whereas links (connecting lines between nodes) represent hierarchy, sequence or information/material interactions. Into the first three diagram types, links are hierarchical between stakeholders, information and activities, respectively. Into the second three diagram types, links are sequential links of activities or states.

The last two diagram types (communication diagrams and data flow diagrams) describe information inputs and outputs between stakeholders or activities respectively. After the literature review and the classification of diagram types, the authors applied the models to three health care scenarios and interviewed a group of clinical and non-clinical workers about their agreement to models.

Evaluation results show that flowcharts are the most used diagrams, whereas state transition diagrams, communication diagrams and data flow diagrams are the least ones. Around half of the participants had prior experience with the three hierarchical-link diagrams (stakeholder diagrams, information diagrams and process content diagrams). Flowcharts are the easiest to understand, while the three hierarchical-link diagrams do not provide sufficient information to be helpful in understanding how the care process works.

Many participants appreciated the fact that state transition diagrams can help them to see the process in a more patient-centred way by describing care processes using patient-related states. From the analysis of their results, authors suggest the use of stakeholder diagrams and information diagrams
during the initial phase of modelling in order to set the boundary of modelling, to identify the stakeholders and to understand the information structure. Process content diagrams can be functional in recognizing an overall process breakdown structure and in describing sub-processes to the different levels of detail. Swim lane activity diagrams can be used in modelling multidisciplinary teamwork for clear understanding of the roles in various tasks.

These results reveal that some kinds of diagrams can prove highly beneficial to the care process modelling even if they are not popular. The authors consider the state transition diagrams to have great potential utility in understanding care processes in a patient-centred way. Communication diagrams were considered to be very helpful in taking in interaction issues in terms of patient safety problems where well-timed interaction between people, teams and departments are crucial. Human–machine interactions in health care can be showed in Data flow diagrams where data interaction is the main driver. Considerations of Jun et al. suggest using more than one type of diagram in describing the complexity of healthcare processes so that issues coming from task, people and information/material exchange can be better understand.

To sum up, the choice of the type of diagram depends on the stage of the modelling, the presence in the care process of a multidisciplinary team and on the data interactions between medical devices and humans. State transition diagrams represent the unique model that can show the care processes from a patient-centred point of view. The idea to introduce mobile applications into health IT contributes to the development of an innovative system for the support of health care delivering and for the education of the patient and the caregiver at home. Empowered patients and caregivers is the most significant difference with the traditional care processes where citizens are passive and not informed. In this new patient-centred healthcare scenario, redesigning care workflows and electronic communication through different devices (mobile apps and EHR systems) but also taking in consideration security and privacy issues, is mandatory.

In general, the system architecture depends on the electronic health record standard for the communication of the patient’s record information and on the resolution of security and privacy issues. The introduction of mobile applications increases the risk of security and privacy violation because of the large size of population that would have access to electronically health records. In addition, users of a mobile app can be non-specialized personnel and, in the worst situation, they are not authorized by the patient to access to the home monitoring system.
Moreover, in case of data collection at home and data storage into the EHR system, health professionals are only responsible for the data inserted by them in the hospital, after having authenticated to the EHR system, and not for the data collected at home by the app users.

Separation of health data from the identifying data stored in form of registries can prevent compromising data by indirect access in case of multiple actors within the same network. Another solution could be separating encrypted data from the keys necessary to decrypt but unfortunately a mobile app used at home does not allow this separation when it shares data with a EHR system. Proper authentication of the app’s user at home can prevent unauthorized access to the home integrated system. For each healthcare process, all these solutions must be included into diagrams during the initial phase of modelling.

2.3. The Unified Modeling Language (UML)

Healthcare information systems can be modelled from the user's perspective using the “Unified Modelling Language” (UML), a non-proprietary object modelling standard. This visual modelling language is widely used in the IT context to specify, visualize, construct and document the artifacts of a software system. It is independent from both the software lifecycle and the technologies used, so it is the de-facto standard for building object-oriented software. In general, a diagram models the system as a collection of discrete objects that interact to perform tasks that are ultimately beneficial for an outside user. Modelling a system from several separate but related viewpoints permits it to be understood for different purposes. It is important to distinguish between the UML model and the set of diagrams of a system. A model can be rendered, from different points of view using different types of diagrams. A diagram is a partial graphic representation of a system's model. The UML captures information about the static structure and dynamic behaviour of a system representing them into two different views of a system model:

- **Static (or structural) view**: it emphasizes the static structure of the system using objects, attributes, operations and relationships. The static structure defines the kinds of objects necessary to a system implementation, as well as the relationships among these objects. For example, a class diagram is a structural view of the system model.

- **Dynamic (or behavioral) view**: it emphasizes the dynamic behaviour of the system by showing collaborations among objects and changes to the internal states of objects. The dynamic behaviour defines the history of objects over the time and the communications
among objects to accomplish goals. For example sequence diagrams, activity diagrams and interaction diagrams are dynamic views of the same system model.

Three types of UML diagrams are used for the modelling of the integrated home monitoring system described in this thesis:

- **UML use case diagram**: it describes the proposed functionality of a new system. Inside the diagram there are nodes and lines. Nodes can be Actors or Use Case, meanwhile lines represents different types of relationship.

**UML use case diagram**

<table>
<thead>
<tr>
<th>Component</th>
<th>Symbol</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actor</td>
<td>![Actor Symbol]</td>
<td>It is the role that a user (a person or a machine entities) plays during the interaction with the new system. The same user can have different roles: in this case in a diagram he is depicted with more than one symbols. Each actor performs a piece of the entire workflow that achieves the final goal.</td>
</tr>
</tbody>
</table>

*Figure 2-7: UML class diagrams. It represents the hierarchically categorization of different types of UML diagrams. The UML diagrams used to model the integrated home monitoring system are highlighted. [UML class diagram available from: https://en.wikipedia.org/wiki/Unified_Modeling_Language].*
Each Use Case describes a functionality to be built in the proposed system.

- **Association**: It represents the communication between a Use Case and an Actor. For example, it can mean that the user is involved in a functionality.

- **Include**: The Use Case A includes the Use Case B when the functionality of A requires some operations of B.

- **Extend**: The behaviour of Use Case B, in particular conditions, can be extended with the functionality of A.

- **Generalization**: This relationship can be applied between use cases or actors. It means that the second object is a particular case of the first one.

**Table 2-1: UML use case diagram: symbols specification.**

- **UML activity diagram**: it displays the sequence of activities. The diagram shows the workflow from the beginning to the end detailing the many decision paths that exist in the progression of events contained in the activity. The activity diagram includes the following elements: initial node, actions, control flow, decision node and the final node.

<table>
<thead>
<tr>
<th>Component</th>
<th>Symbol</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial node</td>
<td><img src="image" alt="Initial Node Symbol" /></td>
<td>It is a control node at which flow starts when the activity is invoked.</td>
</tr>
<tr>
<td>Action</td>
<td><img src="image" alt="Action Symbol" /></td>
<td>Actions are steps of an activity.</td>
</tr>
<tr>
<td>Control flow</td>
<td><img src="image" alt="Control Flow Symbol" /></td>
<td>Control flow, a lines with an arrowhead, regulates the flow from one action to the next</td>
</tr>
<tr>
<td>Decision node (branching)</td>
<td><img src="image" alt="Decision Node Symbol" /></td>
<td>It is a control node that accepts tokens on one or two incoming edges and selects one outgoing edge from one or more outgoing flows.</td>
</tr>
<tr>
<td>Fork</td>
<td><img src="image" alt="Fork Symbol" /></td>
<td>It splits a single control flow into two or more threads that are subsequently executed in parallel. Thus, a fork bar has one incoming transition and several outgoing transitions.</td>
</tr>
<tr>
<td>Join</td>
<td><img src="image" alt="Join Symbol" /></td>
<td>It merges several of parallel threads into a single thread again. Thus, a join barrier has several incoming transitions and only a single outgoing transition. It waits until all incoming threads have arrived at the barrier before proceeding with the single master flow.</td>
</tr>
</tbody>
</table>
Final node

It is a control final node that stops all flows in an activity.

Table 2-2: UML activity diagram: symbols specification.

- UML sequence diagram: it provides a graphical representation of objects’ interactions over time. It typically shows an actor and the objects or components he interacts with in the execution of a workflow or in a flow of events. This diagram drafts objects as lifelines running down the page and messages as arrows from the source lifeline to the target lifeline. It shows the flow of messages from one object to another.

<table>
<thead>
<tr>
<th>Component</th>
<th>Symbol</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifeline</td>
<td><img src="app_user.png" alt="Lifeline Diagram" /></td>
<td>It is a named element which represents an individual participant in the interaction.</td>
</tr>
<tr>
<td>Execution</td>
<td><img src="service.png" alt="Execution Diagram" /></td>
<td>It is an interaction fragment which represents a period in the participant's lifetime. The duration of an execution is represented by two execution occurrences: the start occurrence and the finish occurrence.</td>
</tr>
<tr>
<td>Synchronous call messages</td>
<td><img src="search.png" alt="Synchronous Call Diagram" /></td>
<td>Synchronous call typically represents operation call: send message and suspend execution while waiting for response. Synchronous call messages are shown with filled arrow head.</td>
</tr>
<tr>
<td>Asynchronous messages</td>
<td><img src="start.png" alt="Asynchronous Call Diagram" /></td>
<td>Asynchronous call send message and proceed immediately without waiting for return value. Asynchronous messages have an open arrow head.</td>
</tr>
</tbody>
</table>

Table 2-3: UML sequence diagram: symbols specification.
2.4. **HL7 – CDA2 templates: the Personal Healthcare Monitoring Report**

Health Level Seven International (HL7) is a “standards developing organization dedicated to providing a comprehensive framework and related standards for the exchange, integration, sharing, and retrieval of electronic health information that supports clinical practice and the management, delivery and evaluation of health services” [HL7 site].

The HL7 Clinical Document Architecture (CDA) is a XML-based standard intended to specify the encoding, structure and semantics of clinical documents for exchange. The content of the document (xml file format) consists of a textual part (which ensures human interpretation of the document contents) and of structured parts (for software processing relying on SNOMED and LOINC codifications). In general, a CDA document is made up of two main parts: Header and Body. The Header includes all the information regarding the identification of the document, the patient, the author and the hospital that is in charge of maintaining the clinical document. The Body includes different sections where data are coded: each sections is composed by a textual part and a structured part. This standard is used for the electronically data exchange of clinical documents whose author is always a health professional.

In 2010, HL7 issued the “Implementation Guide for CDA Release 2.0 Personal Healthcare Monitoring Report (PHMR)”, a draft standard for trial use. It describes the constraints on the CDA Header and Body elements for the generation of Personal Healthcare Monitoring Report (PHMR) documents. This kind of report includes personal healthcare monitoring information and it is produced automatically from Personal Healthcare Monitoring devices. For example, this international HL7 standard data format can be used to encode measurements made by devices at home [Christensen 2014]. The structure of the PHMR is based on a CDA-2 XML template: the Header identifies the clinical document and participants. The Body includes data regarding vital signs, results and medical equipment and optionally the sections purpose and medications. Here below there is a brief description of the XML-elements included in the Header of the PHMR:

- **ClinicalDocument**: this is the root element of the PHMR and it includes many descendant elements. The elements “id”, “setid” and “versionNumber” identify univocally the report. The element “typeId” is a technology-neutral reference to HL7 CDA2 standard and the element “templateId” identifies the template defining constraints on the content of the report. The value 2.16.840.1.113883.10.20.9 of its root attribute means a conformance of the report to the draft standard PHMR. The “code” element at the root level of the document specifies the particular kind of report; in case of the PHMR the value of its code attribute is 53576-5
according to LOINC codification. The “title” element, which specifies the local name used for the document, must be present. The “effectiveTime” refers to the document’s creation time and it must comply with the ISO 8601. The element “confidentialityCode” is a required contextual component of the CDA. It represents the level of confidentiality of the information. The “LanguageCode” refers to the language of the report taking in consideration that PHMRs must be readable by medical practitioners, caregivers, and patients.

- **recordTarget**: it represents the person whose document the chart belongs to. Typically, this is the patient who is also the subject of the report. This element includes the following information of patient: name, surname, address, telephone number, gender and date of birth.

- **author**: it corresponds to the people and/or machines that created the document. This element must include name, telephone number and address of the author of the document and it optionally can include the name of the person and the details of its organization like for instance the hospital where the doctor works.

- **dataEnterer**: represents the person who transferred the information from other sources into the clinical document. This element is optional.

- **informant**: it describes the source of the information in a medical document. It is optional.

- **custodian**: it stands for the organization that is in charge of maintaining the document. The custodian is the steward that is entrusted with the care of the document. Every CDA document has exactly one custodian.

- **informationRecipient**: it is the intended recipient of the information when the document is created. The intended recipient may also be the health chart of the patient: in this case its element “Received Organization” is the scoping organization of that chart.

- **legalAuthenticator**: identifies the legal authenticator of the document and must be present if the document has been legally authenticated.

- **Authenticator**: it distinguishes the participant who attested to the accuracy of the information in the document.

- **documentationOf/serviceEvent**: this element summarizes the moment when the patient was seen and it may include a code to describe the encounter as well as to identify the provider, the location and the date of the appointment.

In the PHMR, the Body has to include the following mandatory sections:

- **medical equipment**: mandatory section that refers to the device that measures the monitoring parameters and generates the PHMR.
- **vital signs**: mandatory section that refers to measurements of blood pressure, temperature, oxygen saturation, respiratory rate and pulse.
- **Results**: mandatory section that records all the other values different from vital signs. It can include numeric observation or waveform series observations as entry types.
- **Purpose**: optional section that specifies the reason why the report is created.
- **Medications**: optional section that includes the patient's medication currently taken and any pertinent previous treatment. This field might also include the patient's prescription and dispense history.

Each section includes a text element for the human-readable content and XML structured elements in order to be machine-readable. Figure 2-8 shows the Body structure of PHMR.

![Figure 2-8: mandatory sections of body structure in PHMR.](image)

This draft standard is taken in consideration during the design of the new communication protocol between a EHR system and a mobile app because it fulfils with the monitoring requirements. A
mobile app can be considered a personal health monitoring device. However, PHMR has to be adapted because it does not consider the patient or the caregiver as the author of the report.

2.5. WebBioBank

WebBioBank is a web-based platform used in research for the management of electronic records. It is based on a proprietary configurable framework [wHospital web site] for the EHR management which is currently used in many Italian and European hospitals. Unlike the wHospital basic framework, WebBioBank also includes dedicated functionalities such as the de-identification of patients and the anonymization of data to support multicenter clinical studies, as well as an innovative module for biosignal storage, management, and analysis (processing layer). WebBioBank is hence a new system completely separated from wHospital that allows to manage heterogeneous data in an anonymous way during multicenter studies which also include biosignal analysis and collection of rEHR (research Electronic Health Records).

The system is accessed through a standard web browser, allowing users to perform various tasks for data management in an anonymous mode according to shared protocols. This system represents a new tool for the real time interaction between researchers and clinicians in different research centres. Using WebBioBank, the clinicians are able to add and manage information regarding a patient’s history, physiological signs and symptoms, therapy, neuropsychological test and scales, surgery and follow-up. At the same time, the researchers can provide shared advanced algorithms for signal processing that can be combined in analysis chains, ensuring that the data processing and analysis are the same in all of the centres involved in the research study. The available analysis algorithms can be applied to the raw data to extract significant measurement that can be correlated to the patient’s clinical state. Moreover, the system is open to any additional algorithm uploaded by researchers which can then be shared among centres. The system also ensures the anonymity of the clinical data/biosignal collection, protecting the privacy of the patients during large studies by other clinical centres. Since WebBioBank integrates the functionalities of traditional EHRs with those of the research support systems, such as the clinical research management systems (CRMS), it implements a “research” EHR (rEHR). WebBioBank is an ideal tool for data management during research protocol because it fulfils the following requirements:

- A unique common template for data and biosignal collection shared between different centres guarantees the availability of comparable data to clinicians, researchers, and biosignal analysis specialists, while signals and data should be locatable, supporting a faster and more cost-effective protocol.
The integrated management of clinical data and biosignals in order to help study the correlations between the clinical data and physiological results to uncover the underlying mechanisms.

Uploading of the mathematical and statistical shared algorithms that can be combined on-line to create signal processing chains specifically dedicated to the specific protocol. This provides a set of tools to biosignal analysis experts ensuring that biosignal analysis is performed uniformly among centres and that the neurophysiological results are comparable.

Anonymous data processing and sharing between different centres ensuring patient’s privacy also when involved in multi-centre studies.

Users with different roles (Role-Based Access Control) will gain access according to their job function to the clinical centre during each specific research protocol. User access must be controlled in WebBioBank using authentication to avoid unauthorised access. Each user is authorised to access, according to the role assigned, to those web-applications implementing his or her corresponding job tasks.

A customisable database according to the research protocol applied for faster query performance during data extraction which facilitates data re-use from both the clinical and the neurophysiologic point of view.

The possibility to create ad-hoc Clinical Report Forms (CRFs) dedicated to multi-centre clinical studies using shared templates supports researchers involved in clinical trials requiring specific data collection according to current regulations.

Compliance with rules and requirements to allow its use in a clinical setting is required because increasing amounts of data are captured digitally during clinical routine care.

The underlying wHospital framework defines a two-level user architecture: at the first level, there is the single clinical centre (named Operative Unit, OU), while a network of OUs called the “Super Operative Unit” (sOU) is available at the second level. The sOU is created and managed by the system administrator. The access policies are based on the definition of the user roles. Each user is associated with a role that gives him/her specific rights on data views and functions. The pre-defined user roles include the administrator, the clinician, the nurse and the pharmacist. The system administrator can include additional roles according to the needs of the clinical centre or study. The sOU administrator can configure a unique rEHR template working in all of the OUs included in the sOU. This allows homogeneous patient data collection and sharing among OUs belonging to the same sOU.
To enable anonymous data collection, WebBioBank saves the patient’s registry (external file with .xml format) and its corresponding identifier code (IDBAC, equivalent to MPI) locally in the single OU information system; on the web-based platform, only the unique ID BAC of patients are saved and there are no records collecting both the data and the codes which correspond to the obscured personally identifiable information. The records composed of a patient’s personal information and the ID BAC are only stored in a local registry file containing the identifiers and the ID BAC exclusively managed by the authorized user during data collection. The identifiers are not loaded into the web-based platform but they are necessary to insert data and signal in the corresponding rEHR during follow-up visits. In WebBioBank there are merely records of the ID BAC and the clinical data stored. The ID BAC is the identification number of the single record which, if necessary, can be transferred to other OUs. Therefore, the system can be flexibly adapted to manage single and multi-centre data and signal collection. In a single-centre data collection, a research centre is an OU and it can define the rEHR and experimental protocols for data collection. In the multi-centre data collection, each participating centre is an OU, and the OUs are grouped in a sOU. Within the sOU, users can share data based on a common rEHR template defined for the specific multi-centre study.

WebBioBank is characterized by a three-layered architecture: a web application layer, a processing layer and an infrastructure layer (figure 2-9). The web-application layer allows the configuration of a unique common template for data sharing in multicentre studies. The processing layer satisfies the research needs and allows for configuring processing chains that are dedicated to biosignal analysis. The infrastructure layer implements patient’s privacy, user’s authentication, the customisable database and the rules to enable use in a clinical setting. The second layer was specifically developed for WebBioBank and it is not available in wHospital that includes only the web-application and the infrastructure layers.

- The web-application layer: is designed in ASP.NET, Silverlight and C# languages. It consists of applications that manage patient’s records (rEHRs) patient’s registries, and signal processing interface. The rEHR modules can be “vertical” if they fully work within a certain rEHR in a certain OU (e.g. patient’s medical history or therapies) or “horizontal” if they do not belong to a single rEHR (e.g. patients’ lists, or the experimental protocol for signal acquisition).

- The processing layer: consists of server side service operations that extract the original signals and metadata (previously uploaded by users in .txt format) from the database and elaborate them according to the specific processing chain, as requested by the user. The resulting signals and metadata are stored in the same database located on the server. Any other processing is
performed remotely. In WebBioBank, many processing chains can be created for different research protocols. In this way, users can upload mathematical and statistical algorithms (.dll extension) to create single analysis blocks that can be combined in appropriate sequences by researchers, creating dedicated processing chains. The collection of the mathematical and statistical algorithms (as a .dll extension) in the processing layer is not a pre-existing library implemented by the system developers; the library is built through the work of users/researchers in the field.

- The infrastructure layer: is provided by the wHospital framework [wHospital site], which uses a relational database management system. Data are stored in a subject-centric manner and are accessible via the web. The server database is managed with a Microsoft SQL Server 2008 R2, but the wHospital framework allows the administrators to access and configure the database (for example, create new tables, j-query, data views) through a dedicated web-page called the “Framework Manager”. The access to the Framework Manager is strictly regulated to prevent unauthorised database access.

![Diagram of the three-layered architecture of WebBioBank](image)

*Figure 2-9: the three-layered architecture of WebBioBank [Rossi et al. 2014].*

Using WebBioBank, each OU administrator can define the specific OU rEHR template, which is composed of modules (the Clinical Forms) that will be automatically translated into relational database tables according to the type of data collected. Any OU rEHR can be shared with other OUs included in the same sOU. Patients belonging to a single OU cannot be viewed by another OU unless specifically authorised. Consequently, homogeneous data collection is possible when sharing a defined OU rEHR among different OUs belonging to the same OU. The WebBioBank actors include
the following: the administrator of sOU, the data manager and a single operative user (clinician, researcher or administrator of the operative unit). The sOU administrator can create a sOU dedicated to a specific multicentres research protocol.

This use case includes the systematic addition of different operative units (research centres) that participate in the protocol and the creation of an account for the Data Manager. During the system configuration it is possible to define the type of measures, the signal classification, the database architecture, the type and roles of users, the section and modules of the clinical forms. All these definitions depend on the specific research protocol and are defined by the sOU administrator and by the Data Manager. The system configuration includes the creation of user accounts for each operative unit. The OU user can add new patients, new registry items and new clinical forms associated to a patient and analyse only those data regarding his/her patients. The personal details of the patients are managed locally as the Data Manager can only elaborate the anonymous data collection.

Before using WebBioBank is used for a new multi-centre study, the administrator of the sOU must perform the following tasks (figure 2-10):

1. Define the protocol of the trial (type of data, content of clinical forms, signal processing algorithms) in collaboration with all of the professionals involved in the study to standardise the data collection.

2. Create the sOU, including the OUs representing each research centre involved, and give the Data Manager the password to access to the sOU and access to all anonymous data collected from all of the clinical centres.

3. Configure the system and the database according to the protocol in collaboration with the Data Manager and check the configuration according to the research protocol.

4. Give the password to single OUs for their administrator and users (clinicians and researcher).

Consequently, each OU belonging to the sOU will have the same clinical form template, signal processing application and user's roles according to the protocol defined. All the data will be automatically sent to the sOU without any personal information to ensure anonymous data sharing. Once the system is configured, data collection can begin: users can insert clinical data and bio-signals through a user-friendly interface inside each OU. In other words, clinicians can complete medical records during outpatient visits or hospitalisation for surgery while researchers can upload, classify, and preprocess biosignals.
During data collection, the OU users can extract data regarding the OU patients in Excel format. The file will not include registry data from patients as the patient’s ID BAC is used. This file may be useful for local periodic monitoring. At the end of data collection, the Data Manager of the sOU will be able to manage all the data collected from the different OUs.

In the literature, there are some examples where WebBioBank was used for the anonymous data collection and processing during multicentre studies regarding Deep Brain Stimulation [Marceglia et al. 2015a], Parkinson's Disease [Rossi et al. 2014] and nutrigenomic research [Conti et al 2015a, Conti et al 2015b].
Figure 2-10: UML activity diagram of a multicentre study using WebBioBank: from the configuration of the Super Operative unit (sOU) and the relative Operative Unit (OU) according to the common research protocol, to the anonymous data collection and analysis.[from: Rossi et al. 2014].
2.6 mHealth app development tools: the Windows Phone platform

In this study, the Windows phone mobile app is developed using Visual Studio and its components: Windows Phone SDK and Windows Phone Emulators. Emulators are used to debug the app: running the app on the emulator the developer can see how it looks on a Windows Phone. It is possible to choose among emulators for devices with different memory and display configurations. In addition, Visual Studio provides options for deploying and debugging the app on a physical mobile device connected to the computer. The smartphone has to be registered using the Windows Phone Developer Registration tool which after unlocking the phone, it allows to debug and test apps. In order to use this tool the developer has to have a current developer account on Windows Dev Center. At the end of the debug, the mobile app can be published.

Windows Dev Center dashboard lets developers to publish and manage their apps for Windows Phone devices. The first step is to login into the personal dashboard using the developer account and to create a submission. During the submission, the developer has to insert the following information regarding the new App: pricing, availability, App properties, description and the path to the new app's finished packages for the upload. After the developer successfully uploads the app's packages and submits them for certification, the packages are queued for testing. The system displays a message if it detects any errors during the preprocessing. At the end of the app submission there is the certification step. During this phase, the system conducts several tests:

- Security tests: This first test checks the app's packages for viruses and malware. If the app fails this test, the developer has to check his developing system running the latest antivirus software and then he is required to rebuild the app's package on a clean system.
- Technical compliance tests: Technical compliance is tested by the Windows App Certification Kit. The developer should always make sure to test the new app with the Windows App Certification Kit before the submission. He has to install and run the Windows App Certification Kit in order to validate and test the app locally before the submission and certification steps.
- Content compliance: The amount of time this phase takes varies depending on the complexity of the new app, on how much visual content it has and on how many apps the same developer has submitted recently. The developer has to provide any info that testers should be aware of in the Notes for certification page.

When the certification process is complete, the developer gets a certification report telling him whether or not the new mobile app passes certification. If this doesn’t occur, the report indicates
which test failed or which policy was not met. After the developer fixes the problem, he can create a new submission for the same app to start the certification process again. Once the app is certificated, it is ready to move to the publishing process. If the developer, in the previous steps, has indicated that the new mobile app should be published as soon as possible, this happens at the end of this phase. On the other hand, if he has specified that the new mobile app should not be released until a certain date, the system waits until that date to publish the app. During the publishing process, the app's packages are digitally signed to protect them against tampering after their release. After successfully going through the steps above, the new app is available in the Windows Store for customers to download.

In this work, the mobile app is developed using Extensible Application Markup Language (XAML) and C# language. Each page of the mobile app is designed using xaml and the c# code behind. The manifest file contains details about the app, such as the app ID and the capabilities that the app uses. The primary purposes of the manifest file are the following:

- to filter the app correctly in the Store, and to deploy and run the app on the device during its submission to the store.
- to store as metadata the information collected in the app database.

For the realization of the integrated monitoring system, within a single project in Microsoft Visual Studio both a mobile app and a web service are built. The web service is dedicated to the PHMR-compliant message exchange between the mobile app and the EHR system. Once developed, it is necessary to publish and install it as an application on the IIS of the virtual machine where there is the unique database of the integrated care system.

### 2.7 System validation

The Validation test of the system consisted into two different experiments: the first test checks the correct app configuration and data storage, the second test verifies if the mobile app runs well in different smartphones and fulfils quality requirements. Table 2-4 shows the test protocol of the first experiment. Possible errors during the implementation of a single action are detected when test result is different from the expected result: further app code examination or database check are necessary to search the cause of an unexpected behaviour of the system and to correct the relative code. Each action and the relative debug has to be repeated until the expected result is achieved.
EXPERIMENT 1

<table>
<thead>
<tr>
<th>Action</th>
<th>Expected result</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>The doctor creates a new EHR in WebBioBank and fills in the module for the configuration of app content according to the pathology of the patient. Then he creates a second EHR for another patient and configures the app for a different pathology.</td>
<td>Inside each EHR, the module for the configuration of the app content is filled. The item includes the configuration of app menu and two user accounts: one for patient and one for caregiver.</td>
<td></td>
</tr>
<tr>
<td>Log in the mobile app with the patient’s and the caregiver’s accounts.</td>
<td>The user can access to the application and the menu is in compliance with the pathology of the patient and the role of user.</td>
<td></td>
</tr>
<tr>
<td>In the mobile app patient fills in the McGill questionnaire and clicks on the save button.</td>
<td>The mobile app sends to the web service the mPHMR.</td>
<td></td>
</tr>
<tr>
<td>In the mobile app the caregiver fills in the Hamilton scale and click save button.</td>
<td>The mobile app sends to the web service the mPHMR.</td>
<td></td>
</tr>
</tbody>
</table>

Table 2-4: validation test protocol of the first experiment: the first column describes the action and the second column the expected result.

The first experiment is performed using the same smartphone emulator as during the debug. Once verified the correct app configuration and data storage, it is possible to proceed with the second experiment where quality of the mobile app is verified. During the debug of the mobile App, the tester can choose among emulators for devices with different memory and display configurations. At the end, the mobile app is tested on a physical mobile device connected to the computer. In this study, the smartphone registered for the final validation of the integrated system is a Microsoft Lumia 640:

- Model: RM-1072
- Storage: 8GB
- LCD display: 5"

A brief test is performed to verify the effect of different display configurations. In Visual Studio, the debug of the application is repeated using different emulators (Windows Phone SDK). For each debug the tester selects one of the following emulators characterized by different screen resolution:

- WVGA (800 × 480)
- WXGA (1280 × 768)
- 720p (1280 x 720)
- 1080p (1920 x 1080)
A final experiment regarding the maximum memory used by the mobile app is necessary considering the exchange and management of clinical documents between smartphone and EHR system. The default emulator in Visual Studio is WVGA 512MB Emulator, which emulates a memory-constrained Windows Phone. This default selection encourages to target the largest possible market for your Windows Phone app. For this reason, this kind of emulator is used in the second experiment. This test (table 2-5) consists in repeating the same operation with emulator or the registered smartphone for the performance analysis. During the debug of the mobile app the Windows Performance Analysis Tool is used to view memory use and performance parameters: startup time, total data uploaded, total data downloaded, max memory used and average memory used.

<table>
<thead>
<tr>
<th>EXPERIMENT 2</th>
<th>Action</th>
<th>Result</th>
</tr>
</thead>
</table>
| Run the app using the emulator: WVGA 512 MB | Log in the mobile app and navigate to the menu page. Select and fill in the Hamilton scale. | Startup time:  
Total data uploaded:  
Total data downloaded:  
Max memory used:  
Average memory used: |
| Run the app using the emulator: WVGA 512 MB | Log in the mobile app and navigate to the menu page. Select the McGill questionnaire and fill in the first session. | Startup time:  
Total data uploaded:  
Total data downloaded:  
Max memory used:  
Average memory used: |
| Run the app using a physical mobile device connected to the computer | Log in the mobile app and navigate to the menu page. Select and fill in the Hamilton scale. | Startup time:  
Max memory used:  
Average memory used: |
| Run the app using a physical mobile device connected to the computer | Log in the mobile app and navigate to the menu page. Select the McGill questionnaire and fill the first session. | Startup time:  
Max memory used:  
Average memory used: |
| Run the app using a physical mobile device connected to the computer | The mobile app generates a report where the Section Medical Equipment includes technical details corresponding to the device connected to the PC | Manufacturer:  
Model:  
Phone ID:  
Mobile app name:  
Mobile app revision: |

Table 2-5: validation test protocol for the experiment 2. The first column describes which devices to use during the debug, the second column shows which actions to perform and the third column is the result of the test.
2.8 Case study

The daily management of neurodegenerative diseases is one of the most striking scenarios where an integrated health care system is essential for the continuous assistance to the patient and requires caregivers’ qualification and training. In particular, patients affected by depression or chronic pain can be treated at home with non-invasive electrical neuromodulation (transcranial Direct Current Stimulation, tDCS) in order to reduce daily travel expenses between home and the hospital. However these patients need extensive monitoring and support aimed at both helping them managing the treatment and the possible problematic situations occurring (e.g., electrode drying or misplacement) and monitoring the clinical outcomes after treatment.

2.8.1 transcranial Direct Current Stimulation (tDCS)

Transcranial Direct Current Stimulation (tDCS) consists into the induction of a relatively weak constant current flow through the cerebral cortex using scalp electrodes. Usually, the electrode montage consists into two electrodes: the anode has a positive polarity and the cathode has a negative polarity. Both the electrodes can be either active or return electrode depending on the pathology and the target area of the stimulation. The electrodes are placed over the scalp according to the International 10-20 System. Depite being an ancient technique, with origins dated back to the Hellenistic period, tDCS was abandoned until the experiments of Volta in the very beginning of the XIX century. The technique was then re-discovered in the 1950s and 1960s primarily in animals. These early studies showed that subthreshold DC stimulation increases spontaneous neuronal activity if the anode is placed above or within the cortex, while exposure to cathodal polarity results in a reduced activity. This is caused by a subthreshold membrane depolarization by anodal and a hyperpolarization by cathodal stimulation [Purpura and McMurtry, 1965]. Like in animal experiments, the primary mechanism of tDCS in the human cerebral cortex is a subthreshold modulation of the neuronal resting membrane potential. Indeed, blocking voltage-dependent ion channels pharmacologically abolishes any effect of depolarizing anodal tDCS on cortical excitability. Although neuronal membrane polarization shifts sufficiently explain the primary effects on neuronal excitability during stimulation, these cannot fully explain the after-effects of the tDCS. Many studies in literature demonstrate that tDCS effects persist also after the end of the electrical stimulation. It was demonstrated in humans that the after-effects of tDCS depend on the modifications of the N-methyl-D-aspartate (NMDA) receptor-efficacy: the after-effects of tDCS are blocked by the NMDA receptor antagonist dextrometorphan and prolonged by the partial NMDA receptor-agonist D-
cycloserine [Liebetanz et al., 2002]. Objective evidence of tDCS effects in cerebral tissues are described with imaging modalities, including positron emission tomography [Lang et al. 2005], functional magnetic resonance imaging [Baudewig et al. 2001] and magnetic resonance spectroscopy [Arul-Anandam et al. 2008, Rango et al. 2008]. They suggest changes in regional blood flow, glutamatergic neurotransmission and membrane function after tDCS, even in brain regions distal to the site of stimulation due to neuronal networks. tDCS is hence able to alter spontaneous neuronal firing rates without producing action potentials during stimulation. This is because the current density produced by tDCS in the cortex is below the action potential threshold for cortical neurons. Even if tDCS is a very simple and non-invasive treatment, the effects of the stimulation in humans can be very different: they depend on the stimulation protocol (electrode montage, current intensity and polarity, etc.) and the population of neurons stimulated due to the complexity of neuronal network and the size of the electrode (about 35 cm$^2$). For this reason, the effect of different electrode montages and protocols is investigated by a lot of studies many of which demonstrate the positive effect of the neuro-modulation in different diseases. This technique does not substitute the common therapies but can enhance their effects. For example, during the post-stroke rehabilitation the use of tDCS can enhance the mobility and reduce the fatigue of patients. Safety of stimulation protocols (typically 1 – 2 mA intensity, electrode size between 25 and 35 cm$^2$, stimulation for up to 30 min per session) has been widely demonstrated in the last decade according to behavioral analyses, EEG and diffusion-weighted or contrast-enhanced MRI measures [Nitsche and Paulus 2000, 2001; Nitsche et al. 2003, 2004, 2008; Utz et al. 2010]. Within these limits, no major adverse events have been reported so far for about 2000–3000 subjects in laboratories worldwide apart from some slight tingling under the electrodes, headache and nausea which might occur in some cases but which are transient side effects [Poreisz et al., 2007]. Paying attention to stimulation technique and electrode preparation can prevent skin irritation under the electrodes. Depending on the brain target area, tDCS can be used for the treatment of different neurological pathologies. Whilst different uses of the tDCS are constantly being researched and expanded, the following pathologies can be treated safely and effectively using the tDCS: chronic pain, depression and stroke [Arul-Anandam et al. 2009, Nitsche et al. 2008]. tDCS could also be easily integrated in a rehabilitation program because devices are safe, simple and cheap [Thibaut et al. 2013].

The use-case analyzed in the present thesis considers only those pathologies that can be easily evaluated at home using simple rating scales: depression and chronic pain. The effects of tDCS treatment in these two pathologies are:
- **Chronic pain**: electrical stimulation of the brain attempts to reduce chronic pain by directly altering brain activity in the areas involved in pain processing: cortical and subcortical regions. Recent clinical studies prove that tDCS is more effective than sham stimulation in reducing pain in both fibromyalgia and spinal cord injury related pain. A sham-controlled trial with anodal stimulation to the primary motor cortex (2 mA, 20 minutes, five sessions) demonstrates the efficacy of tDCS for the treatment of chronic pain due to spinal cord injury [Fregni et al. 2006a]. Interestingly, the analgesic effect is cumulative: the greatest overall pain reduction is measured after five sessions of treatment. Differences in pain scores between the active and sham group persist up to a 2-week follow-up. The same protocol alleviates also pain in fibromyalgia [Fregni et al. 2006b]. The study conducted by Antal confirms that five daily sessions of tDCS over the hand area of the M1 can produce long-lasting pain relief in patients with chronic pain [Antal et al. 2010]. Ten daily sessions of tDCS in patients with chronic and medically refractory fibromyalgia can improve both pain scores (VAS) and the quality of life (FIQ) at the end of the treatment protocol. In addition, long-lasting clinical benefits can be assessed at 30 and 60 days after the end of the treatment [Valle et al. 2009]. A recent study [Villamar et al. 2013] demonstrates the effect of both anodal and cathodal tDCS over left primary motor cortex in 18 patients with fibromyalgia. In 2011, Zaghi et al. reviewed the clinical efficacy of tDCS for the treatment of pain through an updated systematic meta-analysis on the effects of primary motor cortex stimulation on pain. Their meta-analysis includes 18 studies that together show the effect of tDCS on a standardized pain evaluation scale.

- **Depression**: alterations of cortical activity and excitability, especially in prefrontal areas, characterize Major Depression Disorder (MDD). Early studies from the 1960s suggested some efficacy of DC stimulation to reduce symptoms in depression, but mixed results and development of psychotropic drugs resulted in an early abandonment of this technique. More recently, tDCS protocol for the treatment of depression has been optimized [Nitsche et al. 2009] and it has revealed to have antidepressant effects. The stimulation of the left prefrontal area (1 and 2 mA, 20 minutes per day for up to 10 days) reduces depressive symptoms [Fregni et al. 2006c, Boggio et al. 2008]. The first trial reported 69% improvement in mean Hamilton Depression Rating Scale (HDRS) scores after five sessions of active tDCS over 1.5 weeks, compared with 30% improvement in the sham group [Fregni et al. 2006c]. The second trial also reported positive findings: an improvement in the active group on HDRS of 40.5%, compared to 10.4% in the sham group, after 10 consecutive weekdays of treatment [Boggio et al. 2008]. Moreover, these differences in outcome between active and sham groups persist
at 1-month follow-up. A more recent non-placebo controlled clinical trial, involving hospitalized patients with drug-resistant depression at high risk of suicide, reports an improvement greater than 30% in depression rating scores [HDRS and Beck Depression Inventory] after anodal stimulation to the left dorsolateral prefrontal cortex (2 mA, twice-daily, for 5 days) [Ferrucci et al. 2009]. tDCS has some interesting, unique aspects such as noninvasiveness and low rate of adverse effects, being a putative substitutive/augmentative agent for antidepressant drugs, and low-cost and portability, which makes it suitable for use in clinical practice [Brunoni et al. 2012].

Table 2-6 summarizes the most widely adopted tDCS protocols described in literature for the treatment of these two pathologies.

<table>
<thead>
<tr>
<th>POLARITY</th>
<th>ACTIVE ELECTRODE POSITION</th>
<th>RETURN ELECTRODE POSITION</th>
<th>ELECTRODE SIZE (CM²)</th>
<th>CURRENT INTENSITY (mA)</th>
<th>DURATION (min)</th>
<th>NUMBER OF SESSIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>tDCS treatment for DEPRESSION</td>
<td>Anodal F3 (DLPFC)</td>
<td>F4</td>
<td>25-35 cm²</td>
<td>1-2 mA</td>
<td>20-30 min</td>
<td>10-15 sessions over consecutive days for once/twice weeks</td>
</tr>
<tr>
<td></td>
<td>Contralateral supraorbital area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tDCS treatment for CHRONIC PAIN</td>
<td>Anodal Left/Right primary motor cortex (C3 or C4)</td>
<td>Contralateral supraorbital area (FP1 or FP2)</td>
<td>25-35 cm²</td>
<td>1-2 mA</td>
<td>5-20 min</td>
<td>2-10 sessions over 10 days (two weeks)</td>
</tr>
</tbody>
</table>

Table 2-6: tDCS treatments of depression and chronic pain. The most common protocols and electrode montages from the literature. The electrode position refers to the International 10-20 System. The active electrode is placed over the target area and the return electrode is placed over the contralateral area or contralateral supraorbital area.

### 2.8.2 Home monitoring system dedicated to tDCS

In order to reduce daily travel expenses between home and the hospital, daily tDCS treatments can be performed at home after adequate training of patients and caregivers. Indeed tDCS devices are very simple, low-cost, portable and user-friendly. In general, home-tDCS kits are composed of a programmer, a DC stimulator and a pre-configured cap with electrodes. Once the device has been programmed by the physician, the stimulator can be used at home by the patient according to the tDCS prescription: a maximum of N stimulations with a fixed time interval between two consecutive sessions (for example: 24 hours). The administration of the treatment at home requires no difficult procedures, but particular attention has to be paid during the preparation of the correct electrode montage. At the end of the first treatment, the clinician has to confirm or adjust the tDCS prescription according to the effects perceived by the patient. During long lasting or repeated tDCS treatments, the efficacy of the stimulation depends on the disease progression, on the duration of after-effects, on the cumulative effect or combination with other therapies.
In this scenario, an integrated home monitoring system for patient undergoing tDCS daily treatment is essential to:

(1) guarantee safe home treatments: it is necessary to educate the caregiver with images and operative instructions for the correct preparation and placement of electrodes over the scalp before each stimulation. Many studies in literature highlight the importance of the correct hydration of electrode in order to reduce the risk of skin irritation under the electrode. At home, the major risk is to stimulate the patient with the wrong electrode montage: to modulate the activity of different cortical areas can induce undesired effects or make the treatment inefficient. This risk is reduced using a preconfigured cap that guarantees the correct reproduction at home of the montage prescribed by the clinician. However, before each home treatment it is necessary to verify the sponge hydration and the position of electrodes over the scalp. The mobile app can be a useful tool to support caregiver during the patient’s preparation before each stimulation.

(2) optimize stimulation parameters according to the current health status and to the stimulation outcomes: the same stimulation parameters can induce effects of different intensity or duration depending on to the patient’s quantity of hair or on the daily health status. For these reasons, usually the first tDCS treatment includes a few stimulations and at the end of the cycle, the patient has to return to the neuro-modulation centre in order to reprogram the stimulation unit. During the visit the patient can only describe to the physician the treatment effects perceived. The implementation of an integrated home monitoring system allows clinicians to visualize inside the EHR of the patient not only the stimulation parameters of the last tDCS prescription but also the results of the patient’s daily evaluation using a standardized rating scale. These measurements can be very useful during the optimization of stimulation parameters dedicated to the single patient.

(3) assess the disease progression: the tDCS is a non-invasive technique of neuro-modulation that can last, with different time intervals, up to years for the treatment of chronic diseases. Keeping both stimulation parameters (such as: current intensity, duration, etc.) and the number of sessions constant does not guarantee the same efficacy in time. A periodical measurement of the disease progression at home can contribute to improve the efficacy of the treatment.
2.8.3 Case-Study high-level process modeling

The information exchange between the EHR system and the mHealth app in the case study are defined using UML diagrams to represent the integrated care process named “tDCS integrating home monitoring”.

Figure 2-11 shows the UML activity diagram of the integrated care process that includes tDCS prescription, care plane definition, home monitoring and care plan optimization. The process starts with the patient’s admission: the physician creates a new EHR (Electronic Health Record) on the web-based platform. Personal data such as name, surname, fiscal code number, sex and date of birth are listed in a local registry stored in the workstation under the responsibility of the clinician. During the first visit the patient communicates to the doctor the name of the person to be enrolled in the integrated care process with the role of caregiver. The EHR system generates an identification number for the patient (equivalent to master patient index, MPI) and the caregiver (a string derived from MPI). At the same time, the doctor fills in the medical history inside the EHR and then proceeds with the patient’s management: from the diagnosis the clinician prescribes the first tDCS treatment. Within the EHR the doctor has to specify the stimulation parameters, the electrode montage and the care pathway definition. At the end of the EHR compilation and user identification, the doctor can access the patient’s EHR and fill in a module dedicated to the app configuration as app Admin. Before the patient’s discharge, a team of health professionals trains the patient and the caregiver on the tDCS, teaching them how to manage the tDCS device and which activities to perform at home.

The content of the mobile app depends on the role of the user and on the care pathway defined for the patient. The mobile app can include tDCS information, monitoring activities and operative instructions for the caregiver, to guarantee a safe home treatment. During the app configuration, the EHR system generates two user accounts: one for the patient and one for the caregiver. Using these accounts, both the patient and the caregiver can access the mobile app, read operative instructions about the correct electrode hydration and view images for the correct placement of the electrode over the scalp. In addition, the user of app has to perform planned activities such as filling in evaluating scales before and after each tDCS treatment. Permitted activities depend on the role of user (patient or caregiver). Once the activity is completed, the app automatically creates a report and sends it to the EHR system. Each report is created starting from the XML templates preconfigured by the EHR system: the model of the report depends on the pathology and it has to include the correct identification number of the EHR for the data storage. The mobile app inserts into the XML template additional data, such as the result of the evaluating scale and the identifying number of the author of
the clinical document (app user). A dedicated web service receives the reports from the mobile app and updates the database of the EHR system. The professional healthcare team can access the EHR and review data collected at home in real time. Monitoring data represent an objective measurement that can be useful for the evaluation of the efficacy of both the tDCS treatment and the care pathway.

At the end of the first cycle of treatment, the clinician can evaluate the adequacy of the treatment to the patient, depending on home monitoring data (branching B1). In case of low efficacy of tDCS, the clinician can contact the patient for a further visit, in order to improve the care pathway. For example, the doctor can change stimulation’s parameters (number of stimulations, time interval between stimulations, current intensity or stimulation duration). During the visit, the professional healthcare team can complete the training of the caregiver, in order to improve the patient’s preparation before each stimulation (such as: electrode hydration or montage) and consequently tDCS effects.

Once the optimal stimulation setting has been reached, the clinician can monitor the data collected at home through the EHR system, thus reducing daily travel expenses from home to the hospital and back (STOP phase of the UML activity diagram).

The data are exchanged between the EHR and the mobile app according to a standardized format normally used for clinical documents [HL7 2010], but adapted to fulfil the requirements of the mobile app generation. The details of this new model of clinical document are described in the chapter Result of the current thesis.
Figure 2-11: The UML activity diagram of the integrated care process named “tDCS integrating home monitoring”. The diagram has four swimlanes that identify actors: app administrator, clinical specialist, patient and caregiver. Clinical specialist and app admin use EHR system in order to define the care pathway and configure mobile app content. Patient and caregiver can use the configured mHealth app at home. The process starts with the patient admission. During the first visit the doctor can insert the tDCS prescription and the care pathway definition into the EHR of the patient. At the same time (fork F1), he/she can identify mHealth users and advise the app administrator to insert the identifiers for patient (pID) and caregiver (uID) into the database. The app administrator can configure App content according to the care pathway dedicated to the patient and user identifications (join J1). At home patient and caregiver can access to the mobile app using the credentials generates by the EHR system (fork F2). The mobile App includes information about tDCS, operative instructions and modules that the user has to fill during the execution of planned activities. It generates automatically report of planned activities and sends them to the EHR system (join J2). In hospital, clinician can access to the EHR and view in real time monitoring data collected at home. Using this information, doctor can evaluate the efficacy of the care pathway (branching B1). If tDCS is not adequate for the patient the doctor can contact the patient for a further visit in order to improve the tDCS prescription and care pathway. Reports exchanged between EHR system and mobile app are based on XML templates that are preconfigured by the EHR system (different types of report and ID of EHR) and completed by mobile app (insertion of results and user ID).
Figure 2-12 shows the UML use-case diagram of the integrated care process named “tDCS integrating home monitoring”. In order to create a new integrated monitoring system, the O.U. Admin and the mobile app Admin configure the EHR system and the mobile app, respectively. The mobile app Admin is a developer, who designs the mobile app and a dedicated web service for the exchange of messages between the EHR system and mobile app. The web service is hosted in the Internet Information Services (IIS) of the server where the EHR system is installed in order to share the same database. Instead, the O.U. Admin is the administrator of the Operative Unit on WebBioBank: the web-based platform for the management of EHRs. He can configure the EHR template and create new accounts for doctors and researchers enrolled into the Operative Unit. Both administrators are expected to share the same data model regarding the monitoring parameters that the mobile app collects at home and to send them to the EHR system.

In the UML model an <<extend>> relationship connects the two use cases “Communication of App content” and “Create mobile App”. This means that optional “Communication of App content” use case can be inserted into the behavior defined in the extended use case “Create mobile App”. In other words, this use case is complete and meaningful on its own and it could be extended with optional “Communication of App content” use case during the integration of a monitoring system. Doctors and Data Managers can access to the web site www.webbiobank.com to manage EHRs or to process data. In particular, researchers can view and download only anonymized data for data processing and analysis according to the clinical trial. The data stored on the platform are anonymous so that researchers cannot associate them to the patients’ registry, a local file managed only by doctors [Rossi et al. 2014]. For this reason, the only use case accessible by researcher in the UML diagram is “View anonymous data”. On the contrary, when accessing the Operative Unit, doctors can manage the patients’ list using the local registry for the identification of the EHR corresponding to the patient and for the enrollment of a new one in the Operative Unit. In the UML diagram the use cases “Manage local registry” and “Add new EHR” are extensions of the behavior “View patient list”. In WebBioBank, doctors can access the patient’s EHR in order to view data (including data collected at home) or to insert new clinical data into the EHR. They can find a module dedicated to the configuration of the mobile app content according to the pathology and the care pathway prescribed inside each HER.

During the configuration, the system generates new accounts for user of the mobile app (patient and caregiver at home). In the UML model, the use case “New App content prescription” is an extension of “Insert data into EHR” and includes the use case “new accounts for App user”. The use
case “Send of XML template and App content configuration” extends the use case “App content prescription” since when a user access to the mobile app the software call the web service that retrieves the app content configuration corresponding to the last prescription inserted into the EHR by the use case “App content prescription”. The patient and the caregiver can access the mobile app using their respective accounts at home: if the credentials are valid, the software retrieves the app content configuration according to the doctor’s last prescription and shows the corresponding items inside the main menu of the mobile app which can include information about the tDCS, operative instructions and evaluation scales according to the pathology. In the UML diagram the use case “mPHMR templates in isolate storage” includes the use case “Receive App content configuration” because during the loading of the menu content, the mobile app receives also templates of records corresponding to the item of the menu from the EHR system. These records are pre-configured with the identification number of the EHR and are stored in the isolated storage of the application. When the user fills an evaluation scale and touches the ‘save’ button the app automatically updates the corresponding template in the isolate storage and sends it to the EHR system for the data storage. In the UML model, the use case “mPHMR generation” includes the use case “Evaluation scale” and is included in the use case “Storage data”.

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Figure 2-12. The UML use case diagram of the integrated care process named “tDCS integrating home monitoring”. The WebBioBank FM is the framework manager site where the administrator of each Operative Unit (O.U.) can configure EHR template according to the pathology and create new accounts for doctors and researchers. The www.webbiobank.com is the web site where doctors and researchers in hospital can access to the EHR system. Researchers can only view anonymized data and export them into local files (such as excel) in order to analyse or process data for clinical trials. Meanwhile doctors can manage local file with the registry of patients (name, surname, sex, date of birth, social security number and the corresponding MPI) and create new EHR. Doctors can access to the EHR in order to read data or to insert new data. Inside the EHR doctor can configure the content of mobile app dedicated to the patient and create user accounts. At home, patient and caregiver can log in into the mobile App. If the credentials are valid, they can access to the main menu: items included into this list depends on the role and the app configuration performed by the clinician into the EHR. At the end of each patient evaluation at home, the mobile app automatically generates the report (mPHMR) and sends it to the EHR system.
3. DESIGN CONSIDERATIONS

The chapter defines the goals of the thesis, moving from the current scenario where an integrated care system based on mHealth apps is a promising solution. Next, the chapter lists requirements and constraints of the desired integrated system. The last paragraph of the chapter defines the system architecture and functioning: it describes the architecture of the integrated home monitoring system and UML models of the care process for the selected case study.

3.1. Major Goals

In the present health context, where thanks to the popularity of smartphones new mHealth apps have been introduced and where the reduction of costs and the improvement of prompt care are two priorities of national policies, the integration between mHealth apps and EHR systems is a predicted consequence. This can be considered as a new interpretation of the suggested scenario “health IT ecosystem” where patients’ medical information is shared among citizens, hospitals, pharmacies, laboratories, primary care and health specialists. Sharing medical information electronically reduces medical errors, improves the appropriateness of the treatments delivered and creates a more cost-effective health care system. Considering this scenario, the integration between mHealth apps and EHR systems can create a real home monitoring system characterized by the combination of the following advantages: mobility, velocity, immediacy, user-friendly and intuitive interface, compliance to the therapy, caregiver participation, patient empowerment and remote control by clinicians.

In the literature, there are some examples of direct connection between mobile applications and EHR or PHR systems but they do not describe a specific communication protocol or the technical details of the messages shared between a mHealth app and a health system. Many studies refer to the interoperability issue rising from regions or states. Up to now, in order to solve such problems, EHR vendors and national regulatory agencies have been required to make some efforts but mobile applications manufacturers have never been asked to discuss the issue. This is because the regulations for mobile apps are still incomplete. However, when a mobile application falls into the definition of “medical device” it is subject to the European directives and to the FDA guidelines. In addition to this, it has to comply with the legislations regarding the protection of personal data and the protection of consumers. Therefore, mHealth applications can be included into the “health IT ecosystem” scenario and this idea also fulfils the AMA priorities [AMA, 2014].
All the issues related to the generation of medical information from mHealth apps must be taken into consideration. It is clear that, when it comes to the integration between EHR systems and mHealth apps, a dedicated communication protocol is absolutely mandatory. In most studies in literature, the mobile application creates a direct connection between the patient and the health professional with the aim to visualize a personal medical report. Sometimes, mobile apps are only dedicated to health professionals and they must be used inside a secure Wi-Fi network such as the one in a hospital. In both cases, the risk of alteration of medical information by an unspecialized user through the mobile app is absent. In one study, the patient at home can insert data into a mobile application connected to a dedicated web-based platform integrated with the local health system [Galligioni et al. 2015]. This is the most similar integrated home monitor system described in literature to the use-case analysed in the present study.

The aim of this thesis is to demonstrate that a dedicated standard for reports generated by a mobile app is mandatory whenever a smartphone is used at home for the implementation of an integrated care system.

The topic of the present study concerns the definition of an architecture and the set up of an information protocol for an innovative integrated system to exchange information between the home care and the professional environments, in accordance with the international standards and recommendations. From the study of a use case, it is possible to design the general model for the integrated home monitoring system, from the requirements identification to the architecture definition. The thesis aims at including into an electronic health record (EHR) data acquired in a domestic environment and at allowing the exchange of such data among clinicians, caregivers and patients according to a new developed protocol for mobile applications. To achieve such integration, it is necessary to:

1. investigate to what extent the existing protocols suffice for the needs of patients at home;
2. design a specific architecture for the data exchange between patients’ mobile applications and professional EHR systems;
3. provide a proof-of-concept of such integration.

In this way, the study verifies the possibility to extend the use of recognized protocols to a direct data exchange between mHealth apps and EHR systems, in order to harmonize and to facilitate the cooperation among different users actively involved in this healthcare process (professionals, caregivers and empowered patient). The main scientific output can be to guide the decision to confirm or to adjust the current HL7 protocol, to include cases where the patient is involved into the integrated
health care process through a mobile application, taking into consideration not only the technical aspect but also issues regarding access to health personal records.

The case study analysed in this work is a home monitoring system dedicated to tDCS (transcranial Direct Current Stimulation) patients in order to reduce daily travel expenses between home and hospital. In this use case, the exchange of information between patient at home and the reference neurologist is crucial during tDCS treatments. Currently, the health IT scenario is composed of two independent environments, one dedicated to healthcare professionals (e.g., Electronic Health Records, EHRs), and one including mobile tools dedicated to citizens, caregivers and patients. Safety, communication and interoperability gaps prevented an effective data exchange between these two environments [Marceglia et al. 2012, Ackerman 2013]. The aim of this study is to implement an integrated home monitoring system for tDCS patients, in which a web-based platform for EHR management exchanges data with a mobile app used at home [Rossi et al. 2015a, Rossi et al. 2015 b].

3.2. Requirements

Considering the international standards for electronically health information exchange and the AMA priorities, the requirements of the new integrated system are:

- **Document-centric**: exchanged clinical data has to be organized into «clinical document», based on agreed standard document type (HL7-PHMR, Personal Health Monitoring Report). The present study has to define the mPHMR: mHealth Personal Healthcare Monitoring Report. This will be an XML-based standard intended to specify the encoding, structure and semantics of clinical documents produced by the mHealth app in order to exchange data with EHR system.

- **Interoperability**: the integrated system has to enable data exchange according to technological interoperability (e.g. standard communication architectures), and semantic interoperability (e.g. shared terminologies/ontologies).

- **Secure data transmission**: mHealth applications have to transmit data from home to hospitals ensuring security properties such as confidentiality (access protection), authentication (maintenance of data accuracy), and authorization (data accessible upon demand). Access to the system has not to be allowed to unauthorized people without an explicit patient’s consent.
- **Anonymous data transmission from/to mobile app:** mPHMR header has to mask personal data and address of patient, document’s author and the enterprise where the document is archived. All these pieces of information have to be replaced with identification numbers set up by the EHR system during the app content configuration according to the medical prescription. In this way, only authorized doctors to access the EHR can associate the clinical document to the patient.

- **De-identified data stored inside the EHR system:** the EHR system has to be organized into Operative Units (OUs), each of them, corresponding to a hospital or to a ward. Each OU can be configured according to EHR templates and users can access the corresponding OU with different roles (doctor, nurse, researcher, data manager) but only a clinician can access an OU and associate the personal data to the identifier number into the EHR list. In other words, the EHR system has to be a web-based platform where data are de-identified for clinicians and anonymous for users with other roles. This is possible only if the registry of patients is stored in a local file managed under the responsibility of the doctor while the data on the platform has only the identification number of the patient. In this way, if a user logs into the web-based platform with a different role (for example the one of data manager or researcher), he can only see an identification number but he cannot associate the registry because it is a local personal file assigned to the doctor.

- **App content configurable:** during the first visit the clinician has to create the EHR for the patient and from a particular module inside the EHR he/she can decide the content of the mobile application: information for user education, operative instruction and patient evaluating scale that the user has to fill at home. The content of mobile app depends on the pathology, the health state of the patient and the educational level of the caregiver. During this prescription the EHR system has to generate the account for the user of mobile app: the doctor has to communicate them to patient and/or caregiver. Each time the user logs into the mobile app at home, the software has to verify the validity of the account and retrieve from the database the last prescription dedicated to the patient. According to the data received the mobile app has to automatically: (1) configure its menu according to the prescription; (2) create the corresponding mPHMR templates into the isolated storage of the app; (3) initialize the Header of the mPHMR templates with the identification numbers of patient, user and operative unit where the corresponding EHR is archived.
- **No data storage inside the mobile app**: On the smartphone, no data has to be stored. mPHMR templates have to be generated at the user login and these files have to be stored in the isolated storage: a memory allocated inside this application. At the end of the compilation of the evaluating scale, the application has to insert the results into a new mPHMR and automatically send them to the web-based platform: any copy has to be stored on the mobile app. Each time the user logs off the application the software has to delete the content of isolated storage.

- **Unique database**: the data collected at home with the mobile app has to be archived inside the corresponding EHR. Using the same database avoids data replication and manual data entry is not necessary. Doctors can view in real time the data inside the EHR. This requirement fulfils the first AMA priority.

- **Team-based care**: both the EHR system and the mobile application have to be manageable by users with different roles, in order to facilitate team-based care of the patient at home. This requirement fulfils the second AMA priority.

- **Continuum of care**: integrating the mobile app with the EHR system allows the referring physician to be able to follow, from the EHR system, the patient’s progress/activity throughout the care. This requirement fulfils the third AMA priority.

- **Modularity and configurability of the integrated system**: both the mobile app and the EHR system must be configurable. EHR modulation can change according to the clinician’s needs and the content of the app can be personalized according to the pathology, the state of health and the level of education of the caregiver. This requirement fulfils the fourth AMA priority.

- **Data Liquidity**: EHR system has to import automatically data collected at home using the mobile App. This requirement fulfil the sixth AMA priority.

- **The exchange of faithful information**: As described in the ISO 13606:2008 standard regarding healthcare information exchange, this requirement implies preserving the original meaning intended by the author.

- **Patient and caregiver education**: the mobile app empowered both patient and caregiver so it is necessary that the app content includes also information and operative instructions for the education of user at home.
- **Traceability of author of shared messages**: when the clinician opens the EHR of the patient he has to view the data collected at home, the date of acquisition but also the identification number of author of the relative message generated by the mobile app. In this way, the doctor knows who and when the patient was evaluated at home.

In the list above, for each requirement there is a brief description of how the new integrated system can fulfil it. The system specification with further details is included into chapter 4 of the thesis. Constraints of the present project are limited to the compliance, where applicable, to the international standard (such as HL7 CDA2 or PHMR). Moreover, the standard information exchange between mHealth apps and EHR systems has to be always mediated by structured standard clinical documents. The prototype has to include the web-based platform named WebBioBank as EHR system because the data inside EHR are de-identified and this allows the desired anonymization of mPHMR.

### 3.3 System architecture and functioning

From a conceptual point of view, the integrated care system consists of two modules called "Care Pathway" and "Caregiver Support", both connected to a dedicated web-based platform for the management of EHRs [Rossi et al. 2015 a, Rossi et al. 2015 b].

"Care Pathway" means a process of defining, continuously monitoring and updating the home treatment plan, customized for every patient. The plan includes the following activities: follow-up, monitoring of the neurodegenerative course, adjustment of the treatment, care service and caregivers’ training. These activities are carried out by members of a multidisciplinary clinical team (composed of doctors, nurses, physiotherapists, speech therapists and psychologists) through an EHR of proven security and respectful of privacy. “Caregiver support” means the provision and use at home of the information necessary for the proper implementation of the Care Pathway. Using a user-friendly tool, for example a smartphone, mobile applications are available to caregivers and to patients for their training and information, i.e. a correct electrode hydration, patients’ preparation for the treatment and routine daily activities. Through these applications, caregivers and patients may receive information and send monitoring data to the clinical team of the reference hospital. The web-based platform is based on a platform (WebBiobank) currently used for the management of digital medical records [Marceglia et al. 2015a, Rossi et al. 2014]. A novelty of this work is the integration of the role of the caregiver with the care pathway of the patient, by sharing information and instructions. In particular, the platform for the management of digital medical records is integrated with a specific program (called “suite”) to configure the module "Caregiver support"; it allows to exchange data between the
multidisciplinary team of clinicians, caregivers and patients. The use of the suite is limited by security and confidentiality policies. The information stored in the database about one single patient is available to the respective caregiver through mobile applications. The mobile application records the parameters from home monitoring and sends them to the database. The access to the database through mobile applications is protected by identification and consent. Through the suite, clinicians can integrate the patient’s medical record with the dedicated “Care Pathway”. The care pathway also defines criteria for monitoring the patient’s care and coordinates the activities of clinicians and caregivers by providing them with the necessary operating instructions. Figure 3-1 depicts the XDS workflow for the integrated monitoring system. According to the XDS model document sources add (arrow 1 in figure) mPHMR to the repository that extracts metadata from the Header of mPHMR and send them to the registry (2). It indexes document and supports search (3). Retrieve data (4) are different between the two modules: mobile app retrieves mPHMR templates and menu personalization; meanwhile doctor can retrieve results of patient evaluation at home.

Figure 3-1: Cross-Enterprise Document sharing (XDS) profile for tDCS integrated care system composed by two modules: Caregiver Support and Care Pathway.

From a technological point of view, the integrated home care system developed in the present study is characterized by a Three-Tier architecture (figure 3-2). This kind of architecture allows in future to locate the middle tier in a different machine respect to the data tier in order to guarantee a
fast mPHMR exchange between hundreds of users and to reduce the computational cost on data tier. In WebBioBank, many processing chains can be created for different research protocols: users can upload mathematical and statistical algorithms (.dll extension) to create single analysis blocks that can be combined in appropriate sequences by researchers, creating dedicated processing chains. The collection of the mathematical and statistical algorithms (as a .dll extension) in the data tier is not a pre-existing library implemented by the system developers; the library is built through the work of users/researchers in the field. For this reason, it is preferable to keep the web service for mPHMR management and the data processing into two different tiers.

The client tier presents data to the user and allows data entry or optionally data manipulation. This tier includes three user interfaces and a local registry. The first user interface is the mobile app used by the patient and the caregiver at home for care support and data collection. The second interface is the web site of the EHR system dedicated to the administrator of the Operative Unit (ward) who creates accounts for health professionals and configures EHR templates depending on the pathology or the trial protocol. The third user interface is the web site of the EHR system used in hospital by health professional teams (doctors and researchers) for the management of EHRs. Doctors can select the EHR of the patient using the patient’s registry. This is a local file stored in the workstation of the hospital under the responsibility of the doctor. Meanwhile, researchers can extract anonymous data from the EHR system for the purpose defined in the clinical trial.

The middle tier implements the interface between the mobile app and the EHR system in order to use the same database. It consists of an innovative web service developed in the present study. In general, web services are a new type of web applications available for web-user or other web-connected programs. A more detailed definition can be: “A Web service is a software system designed to support interoperable machine-to-machine interaction over a network. It has an interface described in a machine-processable format (specifically WSDL). Other systems interact with the Web service in a manner prescribed by its description using SOAP messages, typically conveyed using HTTP with an XML serialization in conjunction with other Web-related standards” [W3C site]. The web service included in the middle tier of the tDCS home monitoring system is innovative because the XML used to code and to decode data complies with the mPHMR, a new anonymous standard for clinical document exchange between mobile apps and EHR systems.

The data tier includes data access components for resource sharing and for the configuration of the system. This layer is entirely located in the same cloud-hosted virtual machine. A unique database for the integrated system allows clinicians to view inside the EHR, also monitoring the parameters
collected at home. The general administrator of the EHR system uses the Framework Manager to create different Operative Units (O.U.). For each creation and configuration of O.U.s the Framework Manager updates the database consequently. The IIS of the virtual machine includes, as an application, the web service developed for the PHMR-compliant message exchange between the mobile app and the database (described in the middle tier).

As shown in Figure 3-3, the connection between the EHR side and the mobile app side is implemented by the exchange of mPHMR: XML-based PHMR structured documents optimized for the anonymous communication with mobile apps. The connector between the two systems is a dedicated web service that includes a generic function for credential verification and two specialized modules for the generation and the interpretation of the mPHMR. From the EHR side the output messages are the accounts for mobile app users, the configuration of the mobile app content according to the clinician’s prescription and the respective XML templates. From the “App configuration form” the EHR system stores in the database the app content configuration defined by the clinician.

Figure 3-2: Three-Tier architecture model of the integrated home care system. The client tier includes the mobile App, the web site where administrator of O.U. configures EHR and creates accounts, the web site where health professionals can manage EHR and the local registry of patients: a list managed exclusively by doctors. Middle tier consists in a dedicated web service for the management of messages exchange between mobile app and EHR system. The data tier includes the unique database, the framework manager for the configuration of the EHR system and the IIS where the web service is installed.
according to the pathology and the app user accounts generated automatically by the software. When the service “XML creator” is called by a client, it retrieves such information from the database and creates mPHMR templates. These documents have a preconfigured Header with the identification number of the EHR corresponding to the app user, who has called the service from the mobile app. The service replies to the client by sending these templates and the mobile app stores them in the isolate storage of the application in order to use them at the end of each patient’s evaluation. The connector retrieves from the database also the app user accounts generated by the EHR system, while the input messages received from the mobile app are the mPHMRs. When the service “mPHMR Interpreter” receives a message, it extracts the identification numbers of the corresponding EHR (IDEHR) and of the author (uID of app user) from the Header of the clinical document. The Body of the document includes the codified results of the patient’s evaluation performed at home. In this way, the service can find, inside each message, all the information required to store data in the EHR of the patient.

Figure 3-3: General Architecture of the information exchange between the personal mobile app and the EHR system: EHR system side.
From the mobile app side (figure 3-4) the messages shared through the connector are:

- Request, from the Login page, if the credentials keyed by the user are valid. The web service receives the credentials and checks in the database if the user can access the integrated care system. The Login page allows or denies the access to the application according to the data received from the web service.

- Request, from the Legend page, of the last app configuration defined by the clinician in the corresponding EHR. The web service replies with the content of the app dedicated to the specific pathology: this information is necessary for the Legend page to navigate the app menu page. At the same time, the “XML creator” stores in the isolate storage the corresponding mPHMR templates received from the EHR system.

- Send the real mPHMR created at the end of each patient’s evaluation at home. The mPHMR is made from the corresponding XML template by the insertion of codified evaluation results into the Body. The field Author is updated with the identification number of the user (uID) in the Header of the clinical document.

The mobile app is safe because the mPHMR is an anonymous document: it does not include personal data (detailed description is available in paragraph 4.1) but the identification numbers of user (uID), patient (pID), custodian (ID O.U.) that are used by the web service for the data storage into the correct EHR. The data inside the database are de-identified only for the doctor and anonymous for all other users [Rossi et al. 2014]. Moreover, from the mobile app side, all data stored in the isolate storage are deleted every time the user logs off the mobile app by the code behind the Legend page.
The architecture scalability depends on the speed of the mobile app to process XML documents. The mobile app does not have to create a mPHMR: it has just to update the value of the same fields of the clinical document. The most time consuming phase can occur when a different number of mPHMR templates is received: for example in case of pain evaluation scale the questionnaire is divided into three sessions that correspond to different mPHMRs to be stored in the isolate storage.

The flexibility of the architecture to manage different case studies is based on the possibility to configure both the templates of the EHR system (by the O.U. administrator) and of the mobile app (by the developer) sharing the same data model. The reliability of the system is guaranteed by the generation of a unique identifier for a new patient (equivalent to MPI) by the EHR system, which implies that it is not possible to associate the patient to two different MPIs. In addition, the system generates the app user accounts derived from the MPI. In this way, the user’s credentials on the mobile app guarantee the insertion of the correct patient’s identification in the Header during the generation of the mPHMR. Interoperability is guaranteed by the standard-based architecture [Marceglia et al. 2015a, Marceglia et al. 2015b].

In summary, the Three-Tier architecture of the system implements a service-oriented architecture (SOA) approach, where the middle tier includes specific services aimed to create, read, and exchange the anonymized XML-based CDA-2 structured documents (mPHMRs). This makes the architecture independent of the systems on which it is implemented. In addition, the middle tier of the architecture supports the development of a new software solution both on the EHR side and the mobile app side.
as the mPHMR creation and interpretation are managed by the web service. The introduction of new data protection rules or of new health information exchange standards can require modifications to the functions of the web service even if the management of anonymous documents could easily fulfil new data protection requirements. For this reason, the adoption of mPHMR-derived standards could be a promising solution for the generation of clinical documents by the mHealth app.

The information exchanged between the EHR system and the mobile app in the case study are modelled in chapter 2 using UML use case and activity diagram related to the entire integrated care process named “tDCS integrating home monitoring”. The following UML diagrams show in more detail the system architecture from both the two sides: EHR system and mobile app side.

### 3.3.1 UML use case diagram

Figures 3-5-A and 3-5-B depict UML use case diagrams of the integrated home monitoring system dedicated to patient undergoing transcranial Direct Current Stimulation (tDCS) treatment. In figure 3-5-A, the UML diagram from the EHR side can be seen. When doctors log into the EHR system and select an Electronic Health Record, they can access the patient’s data. The use case “read data in EHR” includes the use case “view parameters of the last tDCS stimulation” because a form inside the EHR manages a list of all the tDCS treatment prescriptions. Here the doctor can find the archive of stimulation parameters and electrode montages dedicated to the patient in order to define the optimal stimulation setting. Inside the EHR the doctor can also read the results of daily evaluation scale performed by patient or caregiver at home.

The rating scales results are considered monitoring parameters in order to measure the daily health status of patient and the disease progression. From the analysis of both results of home evaluations and the latest stimulation setting, the doctor can evaluate the efficiency of the tDCS treatment over a period of time. If the treatment turns out to be inadequate to the patient’s health status, the doctor can summon the patient for a medical examination and can modify the electrical stimulator settings or improve the caregiver’s training in case of an improper use of the device. On this occasion, the doctor either registers the new stimulation setting (use case “new tDCS parameters”) in the EHR in the list of tDCS treatments prescribed, or adjusts the mobile app content to better support the caregiver at home (use case “new content in App”). In this first UML diagram, the actor “mobile App user” refers to both the patient and the caregiver independently from their role while in the second UML diagram “mobile App side” the two users are distinguished (figure 3-5-B). In this model, the association lines depict which items of the app menu can be accessible to different
users, according to the role and the app configuration prescribed by the clinicians. In general, both the two roles can access to education on tDCS and operative instructions for a safe home treatment. Instead, the evaluation scale implemented in the mobile app always depends on the patient’s pathology and the author of the evaluation can be different according to the instructions related to the rating scale. For example, the Hamilton scale [Hamilton 1960] can be used for the evaluation of depression: in this rating scale the patient is observed and evaluated by the caregiver. On the contrary, the McGill questionnaire [Melzack 1975 and Hawker 2011] can be used to evaluate a person experiencing significant pain: in this case the author is the patient himself. In the UML model an <<extend>> relationship connects the use case “App content configuration” with all the use cases representing an item of the app menu. This means that all items are optional and can be inserted into the behavior of app configuration according to the prescription of the clinician.

**Figure 3-5-A: UML use case diagrams for tDCS integrated care system.** This model refers to the EHR side where the doctor can access the EHR of the patient in order to read result from home monitoring measurements or to read previous tDCS prescriptions. From the analysis of rating scale’s results and tDCS setting the doctor can decide to insert new data into the EHR. He can register new stimulator setting or change the configuration of mobile app menu.
3.3.2 UML activity diagram

The sequence of activities in the integrated care process “tDCS integrating home monitoring” is displayed in the UML activity diagram (Figure 3-6). It describes the workflow from the starting point, where the specifications of a new tDCS monitoring system are defined, to the finish point where the monitoring data reveals that the home treatment is adequate for the patient and the care services are confirmed by the clinician. The tDCS is a neuromodulation technique for the treatment of different neurological diseases.

The activity "tDCS home monitoring system specifications" refers to the pathologies to be considered in the care services and the relative treatments or monitoring parameters needed for the implementation of a dedicated care pathway. A multidisciplinary team of health professionals (doctor, nurse, technician, physiotherapist, social worker, etc.) performs this activity.

The administrator of the Operative Unit in the EHR system configures the template of EHR according to the specifications received (activity “O.U. Admin configures EHR”) and communicates the contents of the application (such as: images, operative instructions, rating scales dedicated to the pathologies) and the monitoring parameters to the developer of the mobile app (activity
“Communication of mobile app content”). The administrator of the Operative Unit and the mobile app developer have to share the same data model. Using this information, the app administrator creates the mobile app and the web service for the connection to the EHR system (activity “App admin creates new mobile app and connect it to the O.U.”).

At the same time (fork F1), the administrator of the Operative Unit can create accounts for health professionals with different roles (activity “O.U. Admin creates accounts for health professionals”).

During the patient admission and the first visit, patient is expected to communicate to the doctor the person to enrol into the integrated care process with the role of caregiver (“App user identification” activity). During the visit, the doctor can also (fork F2) define the personalized care pathway (activity “definition of the personalized care pathway”) and create the EHR dedicated to the patient (activity “doctor creates EHR of the patient”).

Inside the EHR doctor can insert both clinical data (for example: anamnesis, diagnosis, images, result of initial evaluation scale) and the personalized configuration of the mobile App. Using a dedicated module, the doctor can choose the operative instructions and the tDCS information to include in the mobile app (according to the caregiver’s and patient’s level of education) or he/she can select the rating scales. These activities in the UML diagram are represented by the block “inside EHR doctor configures mobile App content”. Result of this activity can be joined with output of previous activities (join J1): using all these information the EHR system generates the account for the mobile app user (with different roles) that the clinician has to communicate to the caregiver and the patient. Both the app content configuration and the accounts are available to the web service for the data exchange with the mobile App.

Now the integrated system is fully implemented, patient can be discarged and data collection starts. If the patient is in hospital the data are inserted into the EHR by the health professional; when the patient is at home they are collected by the mobile app. The patient and the caregiver can access to the mobile app and execute the planned activity according to the care pathway. When the rating scale for the daily evaluation of the patient is saved the mobile app automatically sends the data to the web service.

In this way, a unique database is used to merge all data (join J2) and the clinician can view both the clinical data and the monitoring parameters inside the HER. By comparing (join J3) the result of the activity “monitoring progress of neurodegenerative course” with the planned personalized care pathway, the doctor can evaluate whether the treatment is adequate (branching B2). In case of a
positive result, she/he can confirm the care pathway and the patient can continue to use the same configuration of mobile app at home (END point of the process). On the contrary, if treatment turns out to be ineffective, the doctor can (fork F3) change the electrical stimulator setting (activity “Change stimulation parameters”) or adjust the care service and improve the caregiver’s training in case of improper use of tDCS device or electrode montage (activity “Adjust care services and training of caregivers”). At the end of these two activities (join J4) doctor can update of the personalized care pathway. The result influence both (fork F4) the activity “Definition of the personalized care pathway” and “Inside EHR doctor updates configuration mobile app content”. This loop can be repeated until the tDCS treatment became adequate to the patient.
Definition of the personalized care pathway

Doctor creates EHR for the patient

App User identification

Inside EHR doctor configures mobile app content

O.U. Admin configures EHR

tDCS home monitoring system specifications

Communication of mobile app content

App admin creates new mobile app and connects it to the O.U.

EHR system generates accounts for app users

Communication of mobile app content

Inside EHR doctor updates configuration mobile app content

Is the patient in hospital?

Data collection inside EHR from health professionals in hospital

Data collection from mobile app used at home

Data storage

Monitoring progress of neurodegenerative course

Check if the treatment is adequate

B1

yes

no

B2

yes

no

Confirm care services and continue the treatment

Update of the personalized care pathway

Adjust care services and training of caregivers

Change stimulation parameters (tDCS device)

Patient discharge

Patient admission and first visit

O.U. Admin creates accounts for health professionals

Data collection inside EHR from health professionals in hospital

Inside EHR doctor configures mobile app content

O.U. Admin configures EHR

Student configures EHR

Communication of mobile app content

O.U. Admin creates accounts for health professionals

Data collection from mobile app used at home

Data collection from EHR from health professionals in hospital

Data storage

Monitoring progress of neurodegenerative course

Check if the treatment is adequate

B2

yes

no

Confirm care services and continue the treatment

Update of the personalized care pathway

Adjust care services and training of caregivers

Change stimulation parameters (tDCS device)
Figure 3-6: UML activity diagram of the integrated care process “tDCS integrating home monitoring system”. The starting point is the specifications’ definition regarding the tDCS home monitoring system dedicated to some kinds of neurological diseases. The administrators of the EHR system and the mobile app have to share data model of the monitoring parameters and all the possible content of the mobile app. During the first visit, the doctor creates the EHR dedicated to the patient and inside it she/he can personalize the configuration of the mobile app content. EHR system generates app user accounts for patient and caregiver respectively. Clinical data are inserted into EHR by health professional and monitoring parameters by the mobile app at home. Using a unique database allows clinician to view inside the EHR both the data types. Comparing results of monitoring activity with the care pathway defined for the patient, the doctor can decide if the treatment is adequate. In case of an effective treatment, he can confirm the care services and allow the patient to continue to use the mobile app and tDCS stimulator at home (end point of the diagram). At contrary, if the treatment reveals to be ineffective, the doctor can change the stimulator setting or care services, improve the training of caregiver otherwise change the mobile app content and define a new personalized care pathway.

3.3.3 UML sequence diagram

The UML sequence diagrams (Figure 3-7 and Figure 3-8) show the communications between the objects and the messages that trigger those communications in the tDCS home monitoring system. A sequence diagram is an interaction diagram that drafts objects as lifelines running down the page, with their interactions over time represented as messages drawn as arrows from the source lifeline to the target lifeline. Figure 3-7 shows the UML sequence diagram from the EHR side, meanwhile figure 3-8 drafts the UML sequence diagram from the mobile app side.

From the EHR side, the process starts with the first medical examination. Doctor accesses to the EHR system and creates a new EHR for the patient. Personal data are stored in a local registry on the workstation under the responsibility of the health professional. The local registry is a list of MPI, name, surname, date of birth, sex and fiscal code. Only the doctor can manage this list in order to associate the Electronic Health Record to the MPI: on the platform, data are de-identified for the physician and unidentified for users with the role of researcher on the platform [Rossi et al. 2014]. Into the EHR doctor inserts clinical data and the personalized configuration of the mobile app content using a particular module that automatically creates two accounts for users of the mobile app with different roles: the patient and the caregiver. All data are stored in the database, “DB” in the UML diagram. When the user at home logs in the mobile app using their smartphone, the patient or the caregiver are required to insert the username and the password communicated by the clinician during the medical examination. The object “account verification” is part of the web service dedicated to the communication between the mobile app and the EHR system. It receives the credentials and searches for them in the database “DB”. If the credentials are valid, it communicates to the mobile app that the user is allowed to access. During the user’s navigation of the mobile application pages, the software asks the web service for the app content configuration dedicated to the patient and the relevant XML templates. The web service retrieves this information from the database and structures each template
updating some of the fields in the Header, such as the identification number of the EHR for a correct data storage. The web service sends the personalized content and the pre-configured XML templates to the mobile app which can at this point set the main menu dedicated to the user according to the last configuration prescribed by the clinician. At the end of each planned activity, performed at home according to the care pathway, the mobile app sends the corresponding mPHMR to the web service. It reads the report and save data in the database. During follow-up controls in hospital, the doctor logs in the EHR system and, using the local registry, can search for the patient and open the corresponding EHR. Inside the EHR, the doctor views the data collected at home and the last stimulation setting registered during the previous examination. By using the monitoring results, the doctor can evaluate the efficacy of the care pathway. If the monitoring process reveals that the treatment is not adequate for the patient’s present health status the health professional can call the patient for a new medical examination in order to change the stimulator setting.
Figure 3-7: UML sequence diagram of the integrated care process “tDCS integrating home monitoring system” from the EHR side. There are two starting points: one is the first visit when a new patient is enrolled into the integrated care system and the second is a control of the clinician during the follow-up period. A local registry is used for the de-identification of data on the web-based platform. The doctor can insert into EHR both clinical data and mobile app content configurations. A unique database is accessible from the EHR system and from the web service dedicated to the data exchange with the mobile app. Each time the user at home accesses to the mobile app the web service control the validity of the credentials and eventually retrieve the last app configuration with the relative XML templates. The mobile app receives XML templates that are pre-configured for data collection into the correct EHR. During follow-up controls the doctor can view inside the EHR all data collected at home. Evaluating the monitoring results, he can decide to confirm the care pathway or to call the patient to a visit in order to change the stimulation parameters.

Figure 3-8 shows the UML sequence diagram from the mobile app side. When the web service transmits the grant, the mobile application identifies the role and the user can navigate the second page of the app. This page shows a colour legend used to differentiate activities planned according to the care pathway. When the user touches the icon for the navigation towards the main menu, the software calls the web service in order to retrieve the content configuration prescribed by the clinician inside the EHR. After receiving this configuration, the mobile app saves the relative XML templates in the isolate storage of the application. The user now can access the main menu which includes only the items dedicated to their role according to the care pathway dedicated to the patient. From the app menu, the user can select the item corresponding to the planned activity he wants to perform. For example, if the selected item is a rating scale, at the end of the questionnaire filling up the software automatically retrieves the corresponding XML template and completes the clinical document with the ratings and the identification number of the user (author). The mobile app sends the resulting mPHMR report to the web service in order to store the data in the patient’s EHR.
When the credentials verification grants access to the mobile App, the Login page of the mobile app identifies the role of the user. In the second page, the user finds a colour legend of different kinds of activities that can be included into the care pathway of the patient. When the Legend page receives the app content prescribed into the EHR and the relative XML templates, the software saves the templates into the isolate storage of the application and then configures the content of the following page: the app menu. When the user wants to perform an evaluation scale, he selects the corresponding page (in the model generalized into “Item menu” page). At the end of the activity, this page retrieves the corresponding XML template and inserts results and the identification number of the user. It finally sends the resulting mPHMR to the EHR system.
4. SYSTEM DESCRIPTION

This chapter describes the system architecture and the developed integrating home monitoring system. The main result of the thesis is an innovative template of anonymized mPHMR reports dedicated for the data exchange between the EHR system and the mobile application. The chapter includes the following paragraphs:

- Document exchange between the healthcare professional side and the patient’s side: it defines elements of Header and Body of the innovative anonymized mPHMR (mHealth Personal Health Monitoring Report) template.
- Healthcare professional side: a web-based platform used as an EHR system and characterized by de-identified data management. This is the "Care Pathway" module of the integrated home monitoring system.
- Patient’s side: the mHealth app dedicated to the patient and the caregiver at home. This is the "Caregiver Support" module.
- Integration: it deals with the integration between the “caregiver support” and “care pathway” modules in order to realize the integrated home monitoring system.
- Validation: it refers to the validation test of the prototype developed for the use-case dedicated to patient undergoing tDCS treatment.

tDCS home monitoring system is the first implementation of the communication protocol, but it is not the only possible realization of the system architecture defined in the first paragraph.
4.1 mPHMR

The present study defines a new template for home monitoring report, named “mHealth Personal Healthcare Monitoring Report“, dedicated to the exchange of anonymized clinical documents between mobile apps and EHR systems. It is similar to the PHMR defined by HL7 as a draft standard for trial use [HL7, 2010] in the context of remotely monitoring patients as both documents carry personal healthcare monitoring information according to HL7 CDA2 base standard. The PHMR is typically the final stage of the reporting sequence from patient data recorded in a remote (often home) environment by sensor devices to the healthcare provider. On the contrary, the mPHMR does not report the measurements captured by monitoring devices, it allows mobile app to manage anonymous clinical document. This paragraph describes constraints on mPHMR Header and Body elements for data exchange between mobile app and EHR systems.

In general, there are two actors that exchange a CDA2 document: the consumer and the source. The document consumer is the application role that receives the CDA2 and the source is the application role that creates the CDA2 document. In the present scenario “tDCS Integrating home monitoring system“ there are two actors that exchange mPHMR: the mobile application and EHR system. Both are consumer and source because during the app personalization the EHR system generates preconfigured mPHMR and sends them to the mobile app, meanwhile during the evaluation of the patient at home the mobile app fills in mPHMR and send it to the EHR system. In this use-case, data can be viewed only by authorized clinician inside the EHR of the patient so it is not necessity to share also a style sheet file for the rendering of mPHMR. According to the new communication protocol, mobile apps and EHR systems share only anonymized files according to the mPHMR format.

In order to guarantee comprehensive high-quality clinical content in health records, mPHMR includes terminologies’ mapping with SNOMED CT: a clinically validated, semantically rich, controlled vocabulary [IHTSDO, 2014]. The following table lists the terminology mapping for observation elements inside mPHMR considering the tDCS use-case.
<table>
<thead>
<tr>
<th>Concept ID</th>
<th>Preferred Term Description ID</th>
<th>Description Text</th>
<th>Fully Specified Name ID</th>
<th>Fully Specified Name description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>273503001</td>
<td>408954017</td>
<td>Hamilton rating scale for depression</td>
<td>666154014</td>
<td>Hamilton rating scale for depression (assessment scale)</td>
<td>UMLS information CUI: [C0451203] Hamilton rating scale for depression Semantic Types: Intellectual Product [T170]</td>
</tr>
<tr>
<td>418363000</td>
<td>2576577012</td>
<td>Itching of skin</td>
<td>2573305010</td>
<td>Itching of skin (finding)</td>
<td>UMLS information CUI: [C0033774] Pruritus Semantic Types: Sign or Symptom [T184]</td>
</tr>
<tr>
<td>255234002</td>
<td>380400010</td>
<td>After</td>
<td>646243015</td>
<td>After (attribute)</td>
<td>UMLS information CUI: [C0231290] Status post Semantic Types: Temporal Concept [T079]</td>
</tr>
<tr>
<td>288556008</td>
<td>428223015</td>
<td>before</td>
<td>682904012</td>
<td>Before (attribute)</td>
<td>UMLS information CUI: [C0332152] Before Semantic Types: Temporal Concept [T079]</td>
</tr>
<tr>
<td>469022007</td>
<td>2942788013</td>
<td>Entry phone</td>
<td>2935168013</td>
<td>Entry phone (physical object)</td>
<td>UMLS information CUI: [C3881588] Entry phone Semantic Types: Manufactured Object [T073]</td>
</tr>
<tr>
<td>133932002</td>
<td>213673014</td>
<td>caregiver</td>
<td>738684019</td>
<td>Caregiver person</td>
<td>UMLS information CUI: [C0085537] Caregiver Semantic Types: Professional or Occupational Group [T097]</td>
</tr>
<tr>
<td>116154003</td>
<td>186889013</td>
<td>Patient</td>
<td>675470013</td>
<td>Patient person</td>
<td>UMLS information CUI: [C0030705] Patients Semantic Types: Patient or Disabled Group [T101]</td>
</tr>
<tr>
<td>223493006</td>
<td>336340011</td>
<td>Documenting observations</td>
<td>610520013</td>
<td>Documenting observations (procedure)</td>
<td>UMLS information CUI: [C0557070] Documenting observations Semantic Types: Health Care Activity [T058]</td>
</tr>
<tr>
<td>308292007</td>
<td>451618016</td>
<td>Transfer of care</td>
<td>704826010</td>
<td>Transfer of care (procedure)</td>
<td>UMLS information CUI: [C1531390] Transfer of care Semantic Types: Health Care Activity [T058]</td>
</tr>
</tbody>
</table>

Table 4-1: Terminology mapping with SNOMED CT for Observation Types in mPHMR dedicated to tDCS use-case. The code value in observation elements of mPHMR is set equal to the corresponding SNOMED concept ID.
The description of mPHMR is divided into the following two paragraphs: Header and Body of the clinical document. This template refers to WebBioBank as EHR system but it can be generalized for other EHR systems.

4.1.1 Header of mPHMR

With respect to the PHMR, the Header of mPHMR is de-identified according to the new communication protocol for the data exchange between mobile app and EHR system. The innovative aspect of the present study is that now the author of the clinical document is not a clinician or a sensor device but it is the user of mobile app: patient or caregiver. Users are authorized to access to the mobile app using credentials defined by the EHR system during the configuration of app content by the clinician. The caregiver’s and the patient’s credentials are different, so the users can be identified during the access to the mobile application. During the mPHMR generation at home, the mobile application can automatically insert the user’s identifier (‘uID’) into the Header. This variable is the same as the patientID (‘pID’) if the author of the XML document is the patient or the same as ‘cID’ if the user is the caregiver. No personal data or address are included in the mPHMR. Table 4-2 lists the principal differences between the original PHMR and the mPHMR.

<table>
<thead>
<tr>
<th>ORIGINAL PHMR</th>
<th>mHealth-PHMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHMR FIELD</td>
<td>CONTENT</td>
</tr>
<tr>
<td>ClinicalDocument/id</td>
<td>Document OID</td>
</tr>
<tr>
<td></td>
<td>@root @extension</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>ClinicalDocument/record</td>
<td>Id, Addr, Telecom, patient/name</td>
</tr>
<tr>
<td>Target/patientRole</td>
<td>patient/administrativeGenderCode</td>
</tr>
<tr>
<td></td>
<td>patient/birthTime</td>
</tr>
<tr>
<td>ClinicalDocument/author</td>
<td>timeValue, assignedAuthor/id</td>
</tr>
<tr>
<td></td>
<td>assignedAuthor/addr</td>
</tr>
<tr>
<td></td>
<td>assignedAuthor/telecom</td>
</tr>
<tr>
<td></td>
<td>assignedAuthor/assignedPerson</td>
</tr>
<tr>
<td></td>
<td>assignedAuthor/assignedOrganization</td>
</tr>
<tr>
<td>ClinicalDocument/custodian</td>
<td>assignedCustodian/representedCustodian/organization</td>
</tr>
<tr>
<td></td>
<td>assignedCustodian/representedCustodian/organization/name</td>
</tr>
</tbody>
</table>

Table 4-2: Comparison between PHMR and mPHMR Header. In mPHMR the elements “patientRole” and “author” are de-identified according to the app configuration from the EHR system. Author identification depends on the user actually login into the mobile app. During the app configuration, the element “ClinicalDocument/id” is configured equal to the identifier number of the Electronic Health Record where data collected at home has to be archived. “ClinicalDocument/custodian” is configured equal to the Operative Unit (OU) where the EHR of the patient is stored in WebBioBank.
The Header of mPHMR is composed by the following xml-elements:

- **ClinicalDocument**: all documents begin with the root element ClinicalDocument which contains attributes for namespace declaration. The namespace for CDA R2 is “urn:hl7-org:v3” and in mPHMR all elements are shown unprefixed, assuming that the default namespace is declared to be “urn:hl7-org:v3”.

  ```xml
  <ClinicalDocument xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance" xsi:schemaLocation="urn:hl7-org:v3 ..\..\..\0.Standards\HL7\CCD\CDASchemas\cda\Schemas\CDA.xsd">
  ```

- **RealmCode**: this element is mandatory according to Italian CDA2 requirements (HL7 Italia, 2009) because it identifies the belonging domain of the document. In tDCS use-case, the clinical document has to comply with regional constraints defined by Italian realm.

  ```xml
  <realmCode code="IT"/>
  ```

- **TypeId**: is a reference to the CDA release 2 specification. This element has two attributes: root="2.16.840.1.113883.1.3" and extension="POCD_HD000040". The first attribute refers to the OID of HL7 Registered model and the second attribute is the unique identifier for CDA2.

  ```xml
  <typeId root="2.16.840.1.113883.1.3" extension="POCD_HD000040"/>
  ```

- **TemplateId**: this element identifies the template that defines constraints on the content. For PHMR the root attribute is equal to “2.16.840.1.113883.10.20.9” which is an OID. The present study defines a templateid equal to “2.16.840.1.113883.10.XX.YY” for mPHMR.

  ```xml
  <templateId root="2.16.840.1.113883.10.XX.YY"/>
  ```

- **Id**: is the unique identifier of a clinical document. The id element uniquely and universally distinguishes a document from all other documents. This element has two attributes: root and extension. The root value is equal to “wbb.IDEHR” where ‘wbb’ means WebBiobank as an EHR system and ‘IDEHR’ is the identifier number of the patient’s EHR in WebBioBank. This value is automatically assigned to the mPHMR files during the app configuration inside the EHR by the clinician. Meanwhile the extension attribute corresponds to the data and time of creation of the document and it is filled in by the mobile application when the user saves data.

  ```xml
  <id root="wbb.IDEHR" extension="yyyymmddhhmmss+-ZZzz"/>
  ```
- **SetId:** this element is mandatory according to HL7 Italia (CDA2-prescrizione, 2009). This identifier is common to the future different versions of the document. In tDCS use case the attributes of this element have the same value as the element “ClinicalDocument/Id” because it is the first version.

  ```xml
  <setId root="wbb.IDEHR" extension="yyyyMMddhhmmss+|ZZzz" />
  ```

- **versionNumber:** the version number of the document. mPHMR is a new template so the attribute value is set to 1.

  ```xml
  <versionNumber value="1"/>
  ```

- **Code:** the code element at the root level of the document specifies the particular kind of document that is being created. This element has two attributes: the code that contains the string indicating the type of document and the codesystem that is the OID of the organization that defined the string (LOINC). Because of mPHMR is a new template, in this study this element is equal to the LOINC codification of PHMR: root=”53576-5” and codeSystem=”2.16.840.1.113883.6.1”.

  ```xml
  <code code="53576-5 " codeSystem="2.16.840.1.113883.6.1"/>
  ```

- **Title:** The title element must be present and specifies the local name used for the document in mPHMR. In tDCS use-case, all documents generated by mobile applications has to include the following title: “Mobile Document: tDCS home monitoring”.

  ```xml
  <title>Mobile Document: tDCS home monitoring</title>
  ```

- **EffectiveTime:** is the document creation time. Date and times are coded according to HL7 adoption of ISO8601 and include the time zone. In mPHMR this elements has one attribute value equal to “YYYYMMddhhmmss+|ZZzz” where +|zzzz is the time zone.

  ```xml
  <effectiveTime value="20141031213058+0200"/>
  ```

- **ConfidentialityCode:** is a required contextual component of CDA and represents the level of confidentiality of the information in the document. The codeSystem refers to an HL7 OID that contains the code (http://wiki.hl7.de/index.php/2.16.840.1.113883.5.25). As in the mPHMR data are de-identified the level of confidentiality is equal to low (L). Moreover in tDCS use-case WebBioBank limits the re-identification process only to authorized person who owns files with a correspondence between identification number and registry of patients: into the database all data are always de-identified. A web service receives the mPHMR from the mobile app and stores the de-identified data into database of the EHR system.
**LanguageCode:** is the language used when writing a document. The language codification is “nn-CC” where “nn” is legal ISO-639-1 language code in lower case and ‘CC” ISO-3166 country code in upper case. In general, PHMRs could be readable by medical practitioners, caregivers, and patients. In the present case-study xml files characterized by mPHMR template are automatically managed by the mobile app and the EHR system. Moreover the EHR system and a dedicated webservice installed on the same virtual machine automatically parse the XML file and stored data into the corresponding table of the EHR. Only the doctor can view the data sent by the mobile app inside the patient’s EHR. In tDCS use-case the language is set to English due to scientific publication of the study.

```xml
<languageCode code="en-US"/>
```

**Recordtarget:** represents the person whose chart (EHR) this document belongs to. Typically this is the patient who is the subject of the report. These elements must have only one element recordTarget/patientRole that includes the following child-elements:

- **patientRole/Id:** supplied by the EHR system that is defining patient. The identification number for patient in WebBiobank is IDBAC (equivalent to master patient index, MPI) so the attributes are:

  ```xml
  <id root="wbb_pID" extension="pID" assigningAuthorityName="WebBioBank"/>
  ```

  where the extension value correspond to IDBAC and it is assigned when the mobile app generates the mPHMR. In particular during the user’s authentication on the mobile application the system retrieves the IDBAC of the corresponding patient and saves it on the isolate storage: at the end of each session the app automatically deletes all local data.

- **patientRole/Addr:** the patient’s address. In the PHMR it includes streetAddressLine, city, state, postalCode and country to support communication between the receiver of the document and the patient or any other person or organization mentioned within it. Instead in the mPHMR data are de-identified so the attribute NullFlavor is set to MSK (masked). According to HL7 NullFlavor vocabulary this means that there is information on the item available but it has not been provided by the sender due to security, privacy or other reasons. There may be an alternate mechanism for gaining access to this information. In the tDCS use-case, the EHR system WebBioBank exchanges with mobile app only de-identified...
data with the biographical information of the patients using a local personal registry file.

```
<addr nullFlavor="MSK"></addr>
```

- **patientRole/telecom:** also this information of patient is masked in mPHMR.

```
<telecom nullFlavor="MSK"/>
```

- **patientRole/patient:** also this information of patient is masked in mPHMR.

```
<patient nullFlavor="MSK"></patient>
```

- **Author:** the element represents the humans and/or the machine that created the document. It includes two child elements: time and assignedAuthor. The former represents the date and hour (including time zone) when the document is created: it is updated by the mobile application when mPHMR is created and sent to EHR system. The assignedAuthor is the user of mobile app who fills in the form (for example: patient evaluating scale) and created the clinical document by clicking the Save button. The ID element of assignedAuthor has three attributes:

```
<author>
  <time value="20141031213058+0200"/>
  <assignedAuthor>
    <id root="wbb_uID" extension="uID" assigningAuthorityName="WebBioBank"/>
    <telecom use="WP" value="tel:+39xxxx-xxxxxx"/>
  </assignedAuthor>
</author>
```

where the extension value corresponds to the userID and it is assigned when the mobile app generates the mPHMR. In particular during the user’s authentication on the mobile application the system retrieves the IDBAC of the corresponding patient and creates a userID equal to ‘IDBAC_p’ when the user login is the patient or equal to ‘IDBAC_c’ when caregiver is login into the mobile app. All these data are saved on isolate storage of the application: at the end of each session the app automatically deletes all local data. The element “telecom” is the phone number of the device where the mobile app is installed for the use at home. During the app content configuration the clinician needs to insert the phone number of the smartphone used at home, so that the EHR system can send the mPHMR template with this element prefilled to the mobile app.

- **Custodian:** The custodian element represents the organization in charge of maintaining the document, the steward entrusted with the care of the document. In the mPHMR these elements
includes the identification data of the Operative Unit on the EHR system. In WebBiobank an Operative Unit can be a hospital (in case of multi-centre clinical study) or a hospital department (in case of single-centre configuration of the EHR system). However of each Operative Unit in the database of WebBioBank is stored the contact of the corresponding chief doctor. Based on this requirement of the EHR system, the element Custodian of mPHMR is defined as:

```xml
  <custodian>
    <assignedCustodian>
      <representedCustodianOrganization>
        <id root="wbb_OUID" extension="OUID" assigningAuthorityName="WebBioBank"/>
        <name root="wbb_OUname" extension="OUname" assigningAuthorityName="WebBioBank"/>
        <addr nullFlavor="MSK"/>
        <telecom nullFlavor="MSK"/>
      </representedCustodianOrganization>
    </assignedCustodian>
  </custodian>
```

Where child element “id” corresponds to the identification number of the Operative Unit in WebBiobank. Its attribute extension is defined during the app configuration by the EHR system, but the value is updated during the creation of the mPHMR based on the data received by mobile app from EHR system. Also the child element “name” is assigned by the mobile app at the moment of the document generation whereas the address and the telephone of the Operative Unit are stored inside the EHR system so in the mPHMR they are masked.

- **InformationRecipient**: this element records the intended recipient of the information at the time when the document is created. The intended recipient is the health chart (EHR) of the patient, in which case the receivedOrganization is the scoping organization of that chart. In “tDCS Integrating home monitoring” the Operative Unit of WebBioBank corresponds both to the infomrationRecipient and the Custodian of the mPHMR. So this element is composed of:

```xml
  <informationRecipient>
    <intendedRecipient>
      <id root="wbb_OUID" extension="OUID" assigningAuthorityName="WebBioBank"/>
      <addr nullFlavor="MSK"/>
      <telecom nullFlavor="MSK"/>
    </intendedRecipient>
    <informationRecipient>
      <name root="wbb_OUname" extension="OUname" assigningAuthorityName="WebBioBank"/>
    </informationRecipient>
  </informationRecipient>
```

where the extensions “OUID” and “OUname” are filled by the mobile app when the document is generated and the address and the telephone number are masked.
- **DocumentationOf/ServiceEvent**: The main activity being described by a mPHMR is the monitoring of a patient over a period of time. This is shown by setting the value of ClinicalDocument/documentationOf/serviceEvent/@classCode to MOBILE (mobile Monitoring Program) and indicating the period of time over which the person's health was monitored in ClinicalDocument/documentationOf/serviceEvent/effectiveTime. In tDCS use-case, the child element “Low” represents the data of the last app content configuration by the clinician according to the care plan dedicated to the patient. In this use-case there is no expiration date (corresponding to “high” child element of EffectiveTime in PHMR) of the app personalization because the care plan updating depends on the effect of the tDCS treatment on the patient. The id elements include a reference to the primary key column of the table in which the app configurations prescribed by the clinician are stored with WebBioBank.

```xml
<documentationOf>
  <serviceEvent classCode="MOBILE">
    <id root="wbb_IDappContent" extension="IDtDCS_app_APPcontent"
         assigningAuthorityName="WebBioBank"/>
    <effectiveTime>
      <low value="8/1/2015 12:00:00 AM"/>
    </effectiveTime>
  </serviceEvent>
</documentationOf>
```

### 4.1.2 Body of mPHMR

A mHealth Personal Healthcare Monitoring Report has a structuredBody element whose content makes up the human-readable text of the document and it provides the structured representation of the information contained in the document itself. This information is organized into sections and subsections. Whenever possible, the elements in the structured body of a mPHMR conform to the constraints of HL7’s Continuity of Care Document (CCD) specification (published April 1, 2007).

The Body of the mPHMR has an XML structured content. The XML structured content is always inserted into the structuredBody element and is organized in sections which are either Required (R) or Optional in the mPHMR (table 4-3). Each section needs to have a LOINC code.

<table>
<thead>
<tr>
<th>Section</th>
<th>LOINC code</th>
<th>Required(R)/Optional(O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Equipment</td>
<td>46264-8</td>
<td>R</td>
</tr>
<tr>
<td>Vital Signs</td>
<td>8716-3</td>
<td>O</td>
</tr>
<tr>
<td>Purpose</td>
<td>48764-5</td>
<td>O</td>
</tr>
<tr>
<td>Medications</td>
<td>10160-0</td>
<td>O</td>
</tr>
<tr>
<td>Results</td>
<td>30954-2</td>
<td>R</td>
</tr>
</tbody>
</table>

*Table 4-3: StructuredBody sections in mPHMR. Medical Equipment and Results are required in mPHMR because they include information regarding the smartphone used at home (medical equipment where the mobile app is installed) and*
data regarding patient evaluation scale (in result section) to be stored in the corresponding EHR. Other section are optional for mPHMR. At contrary in CCD all section are optional and in PHMR two sections (Vital Signs and Results) are mandatory.

The section “Result” in mPHMR is composed of the following XML-elements:

- **structuredBody/component/section/templateID**: indicating conformance of the section content to the constraints specified in CCD (root=“2.16.840.1.113883.10.20.1.14”) and PHMR (root=“2.16.840.1.113883.10.20.9.14”).

  ```xml
  <section>
    <templateId root="2.16.840.1.113883.10.20.1.14"/>
    <templateId root="2.16.840.1.113883.10.20.9.14"/>
  </section>
  ```

- **structuredBody/component/section/code**: refers to the coding system of the section in LOINC standard (codeSystem: 2.16.840.1.113883.6.1). For example the code value for section Result according to table 4-3 is:

  ```xml
  <code code="30954-2" codeSystem="2.16.840.1.113883.6.1"/>
  ```

- **structuredBody/component/section/title**: describes the title of the section.

  ```xml
  <title>Results</title>
  ```

- **structuredBody/component/section/text**: information to be rendered for the user who views the document. It is mandatory according to CDA2, while in this use case the mPHMR is not viewed by users. The EHR system and the WCF service parse the xml file and store data in the corresponding table into the database of WebBioBank automatically. In this way, only authorized clinicians can access the patient’s EHR and read data collected at home. Inside the EHR of WebBioBank data are displayed in a form where the fields correspond to the columns of the table in the database. However, in tDCS use case, the text subsection of Result includes the user’s answers in order to comply with CDA2 constricts.

  ```xml
  <text>
    <paragraph>Chronic Pain Scale Results: McGill Pain Questionnaire section 2</paragraph>
    - <table name="table2" border="1" width="100%">
      - <tbody>
        - <tr>
          <th>Date/Time</th>
          <th>1. Which word or words would you use to describe the pattern of your pain?</th>
          <th>2. Does liquor increase or decrease pain?</th>
          <th>3. Do stimulants, such as coffee, increase or decrease pain?</th>
          <th>4. Does eating increase or decrease pain?</th>
          <th>5. Does heat increase or decrease pain?</th>
          <th>6. Does cold increase or decrease pain?</th>
          <th>7. Does damp increase or decrease pain?</th>
      </tbody>
  ```
8. Does weather changes increase or decrease pain?
9. Does massage or use of a vibrator increase or decrease pain?
10. Does pressure increase or decrease pain?
11. Does no movement increase or decrease pain?
12. Does movement increase or decrease pain?
13. Does sleep or rest increase or decrease pain?
14. Does lying down increase or decrease pain?
15. Does distraction (TV reading etc.) increase or decrease pain?
16. Does urination or defecation increase or decrease pain?
17. Does tension increase or decrease pain?
18. Does bright lights increase or decrease pain?
19. Does loud noises increase or decrease pain?
20. Does going to work increase or decrease pain?
21. Does intercourse increase or decrease pain?
22. Does mild exercise increase or decrease pain?
23. Does fatigue increase or decrease pain?

<table>
<thead>
<tr>
<th>Measurement Condition</th>
<th>Tester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before stimulation</td>
<td>Patient</td>
</tr>
</tbody>
</table>

- **structuredBody/component/section/entry**: represents the structured content provided for further computer processing (e.g., XML parsing and database updating). COMP value as typeCode means that the section has components.

- **structuredBody/component/section/entry/Observation**: it is a clinical statements. Observation appears directly under the entry element when it is a primary clinical act
statement in a section. The mPHMR for evaluating scale in tDCS use-case, primary clinical act statement of the section Result is the first question of the evaluating scale.

```xml
<observation classCode="OBS" moodCode="EVN">
  <templateId root="2.16.840.1.113883.10.20.1.31"/>
  <templateId root="2.16.840.1.113883.10.20.9.8"/>
  <id root="273593005-s2-q-01" name="question1"/>
  <code code="273593005" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" displayName="McGill pain questionnaire"></code>
  <effectiveTime value="20080501123333-0500"/>
  <value xsi:type="PQ" value="3" unit="points"/>
</observation>
```

Where:

- @classCode = “OBS” means a numeric Observation
- Template ID refers the fact that the observation complies with CCD (CCD numeric observation root: 2.16.840.1.113883.10.20.1.31) and PHMR (PHMR numeric observation root: 2.16.840.1.113883.10.20.9.8).
- Id is the unique identifier of the observation. The name refers to the number of the question in the questionnaire and the root is composed of: the SNOMED code of the evaluating scale and a string ‘-sY-q-XX’ where Y is the number of the section of the questionnaire and XX is the number of the question (XX = 01).
- Code refers to terminology mapping with SNOMED CT vocabulary for the evaluating scale (for example the code for Hamilton evaluating scale in SNOMED CT is: 273503001).
- effectiveTime corresponds to the time of filling in the questionnaire by the user app. The mobile app updates its value during the mPHMR generation at the end of the patient’s evaluation.
- Value is the patient’s or caregiver’s answer to the question of the evaluation scale. In the evaluation scale each answer corresponds to a score (type:quantity, unit: points).

**structuredBody/component/section/entry/Observation/EntryRelationship/Observation:**

observation appears directly under the entryRelationship when it is being related to another clinical act. In the mPHMR for evaluating scale in tDCS use-case, all the question of the questionnaire are related to the first question of the evaluating scale (primary clinical act statement of the section Result).

```xml
<entryRelationship typeCode="COMP">
  <observation classCode="OBS" moodCode="EVN">
    <id root="273593005-s2-q-02" name="question2"/>
    <code code="273593005" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" displayName="McGill pain questionnaire"></code>
    <value xsi:type="PQ" value="-1" unit="points"/>
  </observation>
</entryRelationship>
```
Where:

- @classCode = “OBS” means a numeric Observation
- Id is the unique identifier of the observation. The name refers to the number of the question in the questionnaire and the root is composed of the SNOMED code of the evaluating scale and a string ‘-q-XX’ where XX is the number of the question (XX >=2).
- Code refers to terminology mapping with SNOMED CT vocabulary
- Value is the patient’s or the caregiver’s answer to the question of the evaluation scale. In the evaluation scale each answer corresponds to a score (type:quantity, unit: points).

In the mPHMR of each patient’s evaluation in tDCS use case, not only the questions in the questionnaire are related to the first question of the evaluating scale (primary clinical act statement of the section Result) but also the measurement condition and tester. The measurement condition refers to the time when the questionnaire is filled: it can be filled in before or after tDCS home treatment. Tester refers to the user who filled in the form: the patient or the caregiver. So in the mPHMR at the end of the observations related to the questions the code is the following:

```xml
<entryRelationship typeCode="COMP">
  <observation classCode="OBS" moodCode="EVN">
    <id root="273503001-q-Mcondition" name="measurement condition"/>
    <code code="255234002" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" display="After"/>
    <value xsi:type="string" value="After stimulation"/>
  </observation>
</entryRelationship>
```

where:

- Id is the unique identifier of the observation. The name refers to the measurement condition of the questionnaire and the root is composed of the SNOMED code of the measurement condition and a string ‘-q-Mcondition’.
- Code refers to terminology mapping with SNOMED CT vocabulary for the measurement condition: the code 255234002 corresponds to the ‘after tDCS’ condition and 288556008 to the ‘before tDCS’ condition.
- Value is a string that is the measurement condition.

The value and the code of this observation are updated by the mobile application during the generation of the mPHMR. At the end of the Observation of evaluating scale in mPHMR there is the following code:

```xml
<entryRelationship typeCode="COMP">
  <observation classCode="OBS" moodCode="EVN">
    <id root="273503001-q-tester" name="tester"/>
    <code code="133932002" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" displayCode="Caregiver"/>
    <value type="string" value="Caregiver"/>
  </observation>
</entryRelationship>
</observation>
```

where:

- Id is the unique identifier of the observation. The name refers to the tester: the person who fills in the questionnaire (user login into mobile app) and the root is composed of: the SNOMED code of the measurement condition and a string ‘-q-tester’.
- Code refers to terminology mapping with SNOMED CT vocabulary for the tester: the code 133932002 corresponds to the ‘caregiver’ and 116154003 to the ‘patient’.
- Value is a string that corresponds to the person who fills in the form.

The tester of the questionnaire depends on the evaluation scale: Hamilton needs to be filled in by a caregiver who evaluates the patient at home, meanwhile McGill pain questionnaire needs to be filled in by the patient himself. So the observation Tester in tDCS use case is fixed in the mPHMR template that EHR system sends to the mobile app at the user login.

The section “Medical Equipment” in mPHMR is composed of the following xml-elements:

- `structuredBody/component/section/templateID`: indicating conformance of the section content to the constraints specified in CCD (root="2.16.840.1.113883.10.20.1.7") and PHMR (root="2.16.840.1.113883.10.20.9.1").
**structuredBody/component/section/code**: refers to the coding system of the section in LOINC standard (codeSystem: 2.16.840.1.113883.6.1). For example the code value for section Medical Equipment according to table 4-3 is:

```xml
<code code="46264-8" codeSystem="2.16.840.1.113883.6.1"/>
```

**structuredBody/component/section/title**: describes the title of the section.

```xml
<title>Medical Equipment</title>
```

**structuredBody/component/section/text**: information to be rendered for the user who views the document. It is mandatory according to CDA2 but in this use case users do not view the mPHMR. The EHR system and the WCF service parse automatically the XML file and store data in the corresponding table in the database of WebBioBank. In this way only authorized clinicians can access the patient’s EHR and read the data collected at home. Inside the EHR of WebBioBank data are never viewed as documents, like pdf or XML: all data are displayed in a form in which the fields correspond to the columns of the table in the database. In tDCS use case, the text subsection of Medical Equipment includes details regarding the smartphone used at home by the patient and the caregiver. The smartphone is a medical device because the mobile app installed on it manages and shares data with the EHR system. The details of the medical equipment are provided by the clinicians in the EHR system: during the app content personalization the doctor asks the patient and the caregiver which smartphone will be used at home during the integrated tDCS home monitoring process.

```xml
<text>
<table border="1" width="100%">
  <tbody>
    <tr>
      <th>Device Type</th>
      <th>Device Model</th>
      <th>Device Manufacturer</th>
      <th>Device ID</th>
      <th>mobile App name</th>
      <th>mobile App Revision</th>
    </tr>
    <tr>
      <td name="device_type">smartphone</td>
      <td name="device_model">Nokia Lumia</td>
      <td name="device_manuf">Nokia</td>
      <td name="device_id">1F-3E-46-78-9A-BC-DE-F1</td>
      <td name="device_App_name">tDCS_home_WP</td>
      <td name="device_App_version">1.0.0.0</td>
    </tr>
  </tbody>
</table>
</text>
```
structuredBody/component/section/entry: Each medical device is coded through a device definition organizer (type code = “comp”, classcode = “cluster”, moodcode = “evn”, templateid @root is 2.16.840.1.113883.10.20.9.4)

<entry typeCode="COMP">
<organizer classCode="CLUSTER" moodCode="EVN">
<templateId root="2.16.840.1.113883.10.20.9.4"/>

structuredBody/component/section/entry/organizer/participant: the device definition Organizer must contain a “participant” with typecode “SBJ” that contains the PHMR instance (templateid 2.16.840.1.113883.10.20.9.9)

<participant typeCode="SBJ">
<participantRole classCode="MANU">
<templateId root="2.16.840.1.113883.10.20.1.52"/>
<templateId root="2.16.840.1.113883.10.20.9.9"/>
{id root="1.2.840.10004.1.1.0.0.1.0.0.1.2680" assigningAuthorityName="EUI-64" extension="1F-3E-46-78-9A-BC-DE-F1"/> <!--PHMR:EUI-64 device ID in extension-->
<code nullFlavor="OTH">
<originalText>Unregulated Device</originalText>
</code>
<code code="469022007" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" displayName="Entry phone"/>
<manufacturerModelName>
Manufacturer:Nokia
Model: Nokia Lumia
phone ID: 1F-3E-46-78-9A-BC-DE-F1
mobile App name: tDCS_home_WP
mobile App revision: 1.0.0.0
</manufacturerModelName>
</playingDevice>
<scopingEntity>
<desc>Nokia</desc>
</scopingEntity>
</participantRole>
</participant>

Participant is the “Product Instance Reference”. It contains a participantRole with classCode = “MANU” that is the Product Instance and has:

- two templateID; CCD Product Instance template (CCD templateId 2.16.840.1.113883.10.20.1.52) and the other one where @root is 2.16.840.1.113883.10.20.9.9 that refers to PHMR.
- id element where @root is OID of the device numbering space and @extension is a valid device ID within that space. (e.g. @root is 1.2.840.10004.1.1.0.0.1.0.0.1.2680 and @extension is a valid EUI-64 device ID). The Device ID can be found in the advanced setting of the smartphone and can be IMEI (International Mobile Equipment Identity), MEID (Mobile Equipment Identifier) or MAC address assigned by the
manufacturer of a network interface controller (NIC) and are stored in its hardware. So this information depends on the smartphone used at home and is inserted into the mPHMR automatically by the mobile application.

- code element where @nullFlavor is OTH (other) containing an originalText element describing the regulatory status of the device in plain text (e.g., " Regulated Device ") or " Unregulated Device" );

- playingDevice/code element indicates the type of device, where @code= 469022007 is the equivalent SNOMED CT code for an “entry phone”.

- A playingDevice/manufacturerModelName that contains data items from the Continua data model (no constraints on the formatting, is plain text): Model, Unspecified, SerialNumber, PartNumber, HardwareRevision, SoftwareRevision. The manufacturerModelName may also contain device certification information.

- scopingEntity/desc contains the manufacturer's name.

The section “Purpose” represents the specific reason for which the clinical document is generated, such as in response to a request or to perform a planned activity. In tDCS use case, according to the care plan dedicated to the patient and the app content configuration the activities are the evaluation of the patient at home before or after the tDCS treatment and a report of the stimulation results. In the mPHMR this section is composed of the following xml-elements:

- **structuredBody/component/section/templateID**: indicating conformance of the section content to the constraints specified in CCD (root="2.16.840.1.113883.10.20.1.13").

  ```xml
  <section>
  <templateId root="2.16.840.1.113883.10.20.1.13"/>
  </section>
  ```

- **structuredBody/component/section/code**: refers to the coding system of the section in LOINC standard (codeSystem: 2.16.840.1.113883.6.1). For example the code value for section Purpose according to table 4-3 is:

  ```xml
  <code code="48764-5" codeSystem="2.16.840.1.113883.6.1"/>
  ```

- **structuredBody/component/section/title**: describes the title of the section.

  ```xml
  <title>Purpose</title>
  ```

- **structuredBody/component/section/text**: information to be rendered for the user who views the document.
Transfer of Care

- **structuredBody/component/section/entry/act**: the Purpose section contains a clinical statement including one or more purpose activities (templateId 2.16.840.1.113883.10.20.1.30). The mPHMR represents the <Purpose> object as a relationship between two classes – the source represents the act of creating a summary document, the target is the reason for creating the document, and the relationship type is “RSON” (has reason). The purpose activity contains exactly one Act / code, with a value of “223493006” corresponding to SNOMED codification for “Documentation observations”. The target of Act/entryRelationship/@typeCode in a purpose activity can be an Act. In tDCS use-case the act is the transfer of care from hospital to home environment.

```xml
<entry contextConductionInd="true" typeCode="DRIV">
  <act classCode="ACT" moodCode="EVN">
    <templateId root="2.16.840.1.113883.10.20.1.30"/>
    <code code="223493006" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" displayName="Documentation observations"/>
    <statusCode code="completed"/>
    <entryRelationship contextConductionInd="true" typeCode="RSON">
      <act>
        <code code="308292007" codeSystem="2.16.840.1.113883.6.96" displayName="Transfer of care"/>
        <statusCode code="completed"/>
      </act>
    </entryRelationship>
  </act>
</entry>
```

Annex A of the thesis lists the mPHMR Data Model to CDA Mapping considering the tDCS use-case.

### 4.2 The healthcare professional side: the Electronic Health Record (EHR) dedicated to tDCS patient

The "Care Pathway” module representing the EHR side was implemented using the proprietary system named WebBioBank [Rossi et al. 2014, see Methods section]. The "Care Pathway” module consists of the following activities: definition, monitoring, and updating of the home treatment plan customized for each patient. These activities are carried out by members of a multidisciplinary clinical team (doctors, nurses, physiotherapists, speech therapists and psychologists) who can access the web-based platform through authentication. In particular, the module “Care Pathway” allows the clinician to manage the local registry of patients and users, to prescribe tDCS treatments in terms of stimulation parameters and electrode montage, to configure the scales and exercises on the mHealth app according to the care plan assigned to each patient and to analyse the data sent by the mHealth app. The members of the multidisciplinary clinical team can use a specific module included inside each
EHR to configure the ”Caregiver Support”. In so doing, they are able to create the connection between the personalized mHealth app and the corresponding EHR. Moreover, during the first visit, they define the care pathway for the patient selecting the type and number of the evaluation scales or the rehabilitation exercises to include into the mHealth app.

The mHealth app dedicated to each single patient can be configured in terms of menu items, that are the evaluation scales, the operative instructions and the home exercises but also in terms of file contents, namely the patient and user identifiers for the header of the clinical document generated by the single app. Figure 4-1 shows an example of an EHR dedicated to a tDSCS patient on the WebBioBank.

![Figure 4-1: “Care Pathway” module. The upper part of the image shows the patient list of an operative unit on the web-based platform WebBiobank. The operative unit is configured for tDSCS patient so all EHRs are characterized by the same template. Each EHR is divided into three sections: pre tDSCS evaluation scales, tDSCS treatment and post tDSCS evaluation scales. Sections include modules for data collecting and mobile app personalization.](image)

When the doctor accesses the Operative Unit, he can see the list of patients and from there he can select the EHR of the patient he is interested in and open it. On the web-based platform there are no personal data, therefore, in order to recognize the right EHR, the clinician has to use a personal local registry, an .xml file matching the IDEHR and the patient’s details (name, surname, date of birth, tax code). Without this local file, the users of WebBioBank can only see the date of creation of the EHR, the name of the operative unit where the EHR is stored and the serial number of the stimulator assigned to the patient (upper part of the figure 4-1). Inside the EHR (bottom of figure 4-1) the doctor can view the following sections:

- ”Pre tDSCS Evaluation Scales”: it includes modules where the doctor can insert a patient’s evaluation during visit and he/she can verify the results of an evaluation performed at home using the mobile app. The evaluation scales used, vary according to the pathology of the
patient: the Hamilton Anxiety Rating Scale is employed for depression while the McGill Pain Questionnaire for the chronic pain rating. The choice of these two rating scales is due to the availability of SNOMED codifications for the mPHMR. Data collected in this section are useful for the clinician during the tDCS prescription.

- “tDCS treatment”: this EHR section includes modules for the tDCS treatment prescription, both in terms of stimulation parameters and electrode montage, and for the mobile app personalization. Inside the module “tDCS result from mobile app” the doctor can view the reports filled by his/her patient at home and related to any adverse effect perceived after the stimulation. The innovative aspect of the app is the module “mobile app personalization” which allows the configuration of the app content according to the pathology, the disease progression and the caregiver’s level of education. Only the doctor can insert the mobile app configuration dedicated to the patient while the system automatically generates the accounts for its users with two different roles: the one of the patient and the one of the caregiver. In this way, when a user at home accesses the mobile app, he can see, according to his role, different items and he can also check the last prescription of the clinician.

- “Post tDCS Evaluation Scales”: the third section of the EHR includes the evaluations of patient performed at home after each tDCS treatment. This section is similar to the first one, but in this section data are collected at home and analysed by the clinician to evaluate the effect of the treatment. While comparing the last tDCS prescription with the results of home evaluation, the clinician can optimized the stimulation protocol.

The data collected at home can be seen in real time by the doctor inside the EHR thanks to the newly created system architecture characterized by a unique database in which data exchange between the mobile app and the EHR system is managed by a dedicated web service. This service can both access the database and the interpreter mPHMRs. In particular, the service sends the personalized content and pre-configured XML templates to the mobile app in order to guarantee the correct data storage of mPHMRs. When the service receives a report from the mobile app it can interpret the PMHR and store the results into the corresponding EHR. The advantages of the "Care Pathway” module are:

- Configuration of EHR template according to the pathology or the clinical trial
- Access to the web-based platform with different user’s roles allowing multidisciplinary team coordination and workflow
- Management of de-identified data for doctors and anonymized data for other roles (such as researchers)
- Real time data collection from home environment to EHR
- Immediate comparison between tDCS protocol and patient evaluations in order to optimized the treatment, adjusting the stimulation parameters according to the disease progression.

4.3 The patient’s side: mobile application for Windows phone

The “Caregiver support” is a mobile application dedicated to those patients treated with tDCS (transcranial Direct Current Stimulation) and to their caregivers. It aims at supporting non-specialized people during home tDCS treatment, at collecting data related to patients’ evaluation at home and at sending this data to each patient’s EHR using a preconfigured mPHMR template. The mobile app has been developed for Windows Phone and it consists into 14 pages. Figure 4-2 shows the different types of pages: log in page (1), legend page (2), menu page (3), patient evaluation scale (4a), education for patient and caregiver (4b), operative instructions (4c, 4d) and report of each stimulation (4e).

![Figure 4-2: “Caregiver support” module. The mobile app includes the following pages: 1) log in page, 2) legend page, 3) menu page, 4a) depression rating scale, 4b) education about tDCS, 4c) operative instruction for electrode hydration before each stimulation, 4d) operative instruction for electrode placement, and 4e) stimulation report.](image-url)
The first page is dedicated to the user authentication: the user can insert the credentials provided by doctor during the configuration of the app on the day of the first visit. As already mentioned, the credentials of the patient differ from the ones of the caregiver as both the app content and the mPHMR compilation depend on the role of the user during tDCS home monitoring. When a user inserts valid credentials, he can access the application and view some menu items according to the last app configuration decided by the doctor through WebBiobank. The second page (Figure 4-3) describes the legend of colours used for the items in the app menu:

- green colour: it represents operative the instructions or information for tDCS usage. It is addressed to all users;

- orange colour: it displays the modules to be filled only by the caregiver (for example the Hamilton Rating Scale);

- purple colour: it highlights the modules to be filled by the patient himself (for example the McGill Pain Questionnaire)

![Screenshot of app]

*Figure 4-3: the second page of the mobile app. It is a colour legend of app menu items.*
In this page there is a confirmation button that invokes the web method “GetEvaluationScaleXml” (see paragraph 4.4) for the configuration of the app content and, once received the message, it navigates to the third page. In the third page (Figure 4-2 image 3) the user can view the app menu including the information, operative instructions and evaluating scale according to the personal care plan for home tDCS treatment. In general, the menu includes the following items:

- Hamilton scale before tDCS (depression scale evaluation, filled in by the caregiver)
- McGill questionnaire before tDCS (chronic pain evaluation, filled in by the patient)
- Electrode position and hydration (operative instructions about tDCS)
- Education for tDCS (information about transcranial Direct Current Stimulation)
- tDCS results (adverse event report)
- Hamilton scale after tDCS (depression scale evaluation, filled in by the caregiver)
- McGill questionnaire after tDCS (chronic pain evaluation, filled in by the patient)

The items corresponding to the Hamilton scale or to the McGill questionnaire are displayed according to the pathology of the patient and the role of the user (patient or caregiver).

From the app menu the user can access to the following pages:

- “Evaluating scale before tDCS” page: this page includes the Hamilton scale or the McGill questionnaire of the patient before tDCS treatment. The type of evaluation scale used depends on the pathology (depression or chronic pain) and the results are stored in the EHR of the patient. When the user selects the “Save” button, the app updates the XML template with the current evaluation of the patient, sends the anonymized mPHMR to the EHR and immediately deletes it from the isolated storage of the mobile application.
- “Electrode position and hydration” page: a fixed page describing the operative instructions for the correct electrode preparation before each stimulation. The safety and efficacy of the tDCS treatment depends on this important phase so this page is always visible to all users. The page also includes a picture of the head with the electrode montage that corresponds to the pathology of the patient. During the configuration of the app the doctor can select the
appropriate image for the correct electrode positioning and for cables connection to the DC stimulator.

- “Education for tDCS” page: this is a default page with general information regarding tDCS. Here, the app user can find a description of the tDCS treatment, the difference between active and return electrode, and between anodal or cathodal stimulation.

- “tDCS result” page: a page which is always visible to users. It includes the report of each stimulation including the electrode impedance in KiloOhm and the number of failures of the device during the stimulation. The patient or caregiver can write notes on this page regarding adverse events after the stimulation. This report is not part of the mPHMR template.

- “Evaluating scale after tDCS” page: this is similar to the first item of the menu, but here the resulting XML is characterized by the SNOMED code “255234002” corresponding to the measurement condition: after the stimulation.

### 4.4 Integration between mobile app and EHR system

The “tDCS Integrating home monitoring” system is based on a WCF service. Windows Communication Foundation (WCF) is a framework for building service-oriented applications. While using WCF, it is possible to send data as asynchronous messages from one service endpoint to another. In this case one service endpoint is part of a continuously available service hosted by IIS on the virtual machine where is installed WebBioBank, and the other endpoint is a client of a service (mobile application) that requests data from the dedicated service named “WCF_mobile”. The two endpoints share anonymous messages: clinical documents in XML format that comply with mPHMR.

The service contract ‘IEvaluationScaleService.cs’, created by defining a C# interface, specifies what operations the service “WCF_mobile” supports. Each method in the interface corresponds to a specific service operation. In this case, the service contract includes two methods named: “GetUserApp” and “GetXmlTemplate”. Both of them require as input data the password of the user logged into the mobile app; this parameter corresponds to the ID BAC of the patient in WebBiobank. The first method selects from the database of WebBioBank (table [wH_DirectTable].[tDCS_app_APPcontent]) the lastest app configuration prescribed by the doctor for the corresponding patient. Safety inside the GetUserApp is guaranteed by account verification. At the same time, the use of the date (yyyy/mm/dd) enables the doctor to easily identify the latest app configuration stored inside the EHR. The “GetXmlTemplate” extracts the IDEHR and the pathology from the latest app configuration stored in the database. After doing that, according to the pathology,
this method extracts the corresponding types of XML templates from the table [mobileapp] [EvaluationScaleXml], it updates their Header elements using the IDEHR of the chart and the identification number of the Operative Unit where the EHR is stored on WebBioBank. The so pre-configured templates of mPHMR are sent from the web service to the mobile application (client of the service). To sum up with, the “WCF_mobile” service supports two operations: the management of user authentication and app content setting dedicated to the patient according to the latest app configuration recommended by the clinician inside the EHR.

The integration, between “Care Pathway” and “Caregiver support” modules, is performed during the following two phases:

- **User authentication in “Caregiver support”:** while configuring the app on WebBioBank, the system releases two user accounts dedicated to the patient and the caregiver respectively. When the user at home inserts his/her credentials into the first page of the mobile app, the web service “WCF_mobile” verifies whether the account is valid and whether there is an app configuration assigned to this user using the method “GetUserApp”. In case of valid credentials, the user can access the application and view the data and time of the latest app content personalization. On the contrary, the access to the mobile application is denied to the user in order to avoid unauthorized messages from the mobile app to the patient’s EHR.

- **Loading app content in “Caregiver support”:** during the app configuration on WebBiobank the doctor can select the content of the mobile application according to the pathology of the patient. When the user at home logs in the mobile application and clicks on the confirmation button on the second page, the system refers to the web method “GetXmlTemplate”. The client of the service receives, as asynchronous message, templates of XML files which are pre-configured for the corresponding patient and it saves them into the isolated storage of the mobile application. The items of the menu on the third page of the app change according to the type and the number of XML templates received. In this way, the content of the “caregiver support” module depends on the pathology of the patient. For example, in case of depression, only one mPHMR template (“Hamilton.xml”) is received and the menu of the app includes the button “Hamilton scale before tDCS” and “Hamilton scale after tDCS”. As for chronic pain the client of the WCF service receives three mPHMR templates corresponding to the three sections of McGill Pain Questionnaire: “McGill_s1.xml”, “McGill_s2.xml” and “McGill_s3.xml”. In this case the menu of the app includes two items: “McGill scale before tDCS” and “McGill scale after tDCS” with the corresponding sections. All the templates of mPHMR, stored in the isolated storage of the mobile application, include the identification
number of chart (IDEHR) and the Operative Unit where the EHR is managed on WebBioBank (Header elements: Custodian, informationRecipient and DocumentOf). At the end of each patient evaluation, when the app user clicks on the save button, the mobile application generates the real mPHMR report and sends it to the web service in order to archive data into the database of WebBioBank. In conclusion, the difference between a pre-configured XML template and a real mPHMR is the app’s insertion of the identification number of the patient and of the user into the Header, of the details of the medical device (smartphone) and of the answers to the questionnaire. The real mPHMR corresponds to a daily clinical document that includes all the information for the archiving into the correct EHR.

The following figure summaries the integration process between the mobile application and the EHR system.

The WCF service used in the first prototype is not the unique technological solution that can implement the interface between the mobile app and the EHR system creating the “tDCS Integrating home monitoring” system described above. Other web services or technologies can implement the middle tier of the new system architecture. In any case, the web service has to communicate with a unique database, according to the protocol described above. Moreover, it has to code and decode mPHMR reports.
“tDCS Integrating home monitoring” system: an example of integration between mobile app and EHR system. “Caregiver support” module consists in a mobile application used at home by patient and his/her caregiver. “Care pathway” module is composed by a web-based platform for the EHR management (named WebBioBank) and a WCF service developed for anonymous data exchange with mobile application (named WCF mobile). Both the EHR system and WCF service are installed on the same virtual machine on cloud (Azure virtual machine). WCF mobile manages user authentication on mobile app, the configuration of the app according to the last prescription of the care plane dedicated to the patient. It pre-configures templates of mPHMR according to the identification numbers of the chart of the patient and of the Operative Unit where the EHR is stored in WebBioBank. When the mobile app receives these files, it archives them into the isolated storage of the application. Save buttons of mobile app do not save local data but update on one of these templates, generate a real mPHMR and immediately send it to WCF service.

4.5 Validation results

The first experiment demonstrates a correct app personalization and data exchange between the mobile app and the EHR system. The mobile app content complies with the configuration prescribed by the doctor inside the EHR of the patient and generates mPHMR for the correct data storage into the EHR. Results of a brief visual test shows that running the mobile app with different emulators does not alter the quality of visualization on the screen. The second experiment displays that using either a memory-constrained Windows Phone emulator either a real smartphone does not affect the performance. The analysis reveals a good quality level of the app according to reports generated by the Windows Performance Analysis Tool [App monitoring for Windows Phone site]. Certification requirements regarding app launch time, responsiveness and maximum memory usage by the app are fulfilled.

Table 4-4 and 4-5 show validation test results of the first and second experiments.

<table>
<thead>
<tr>
<th>EXPERIMENT 1</th>
<th>Action</th>
<th>Expected result</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>The doctor creates a new EHR in WebBioBank and fills in the module for the configuration of app content according to the pathology of the patient. Then he creates a second EHR for another patient and configures the app for a different pathology.</td>
<td>Inside each EHR, the module for the configuration of the app content is filled. The item includes the configuration of app menu and two user accounts: one for patient and one for caregiver.</td>
<td>In the database, the corresponding table has two rows: in each row data for the app configuration, the identification number IDEHR and user accounts are stored correctly. The app accounts have to be different in the two rows of the table because the doctor has inserted two prescriptions into two EHRs.</td>
<td></td>
</tr>
<tr>
<td>Log in the mobile app with the patient’s and the caregiver’s accounts.</td>
<td>The user can access to the application and the menu is in compliance with the pathology of the patient and the role of user.</td>
<td>Evaluation scales change according to the pathology of the patient: McGill questionnaire for chronic pain and Hamilton for depression.</td>
<td></td>
</tr>
</tbody>
</table>
Hamilton scale appears into the menu only if the user logged in is the caregiver.

<table>
<thead>
<tr>
<th>In the mobile app patient fills in the McGill questionnaire and clicks on the save button.</th>
<th>The mobile app sends to the web service the mPHMR.</th>
<th>In the database, data are stored into the correct table. If the doctor logs in the web-based platform, he can see the result of the McGill scale inside the EHR of the corresponding patient. The doctor can see the author and the date of the new item inside the EHR.</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the mobile app the caregiver fills in the Hamilton scale and click save button.</td>
<td>The mobile app sends to the web service the mPHMR.</td>
<td>In the database, data are stored into the correct table. If the doctor logs in the web-based platform, he can see the results of the Hamilton scale inside the EHR of the corresponding patient. The doctor can see the author and the date of the new item inside the EHR.</td>
</tr>
</tbody>
</table>

Table 4-4: results of experiment 1 for system validation. The first column describes actions that the tester has to do, the second column shows the expected result for each action and the third column is the result of the test.

The first experiment demonstrates the correct implementation of the integrated system: all the expected results are achieved. Results in table 4-4 are achieved using the same smartphone emulator during the debug. Meanwhile debugging the mobile app using emulators with different display configurations, reveals that each phone automatically scales the images to the correct size of screens and navigation is always guarantee therefore it is not necessary to improve the quality of the visualization.

Table 4-5 shows results of the final experiment regarding the maximum memory used by the mobile app. This test consists in repeating the same operation with emulator or the registered smartphone for the performance analysis. During the debug of the mobile app the Windows Performance Analysis Tool is used to view memory use and performance parameters: startup time, total data uploaded, total data downloaded, max memory used and average memory used.
Table 4-5: results of experiment 2 for system validation. The first column describes which devices to use during the debug, the second column shows which actions to perform and the third column is the result of the test.

<table>
<thead>
<tr>
<th>Device</th>
<th>Action</th>
<th>Result</th>
</tr>
</thead>
</table>
| Run the app using the emulator: WVGA 512 MB | Log in the mobile app and navigate to the menu page. Select and fill in the Hamilton scale. | Startup time: 0.59 sec  
Total data uploaded: 2.48 KB  
Total data downloaded: 0.04 MB  
Max memory used: 44.60 MB  
Average memory used: 27.33 MB |
| Run the app using the emulator: WVGA 512 MB | Log in the mobile app and navigate to the menu page. Select the McGill questionnaire and fill in the first session. | Startup time: 0.52 sec  
Total data uploaded: 3.23 KB  
Total data downloaded: 0.11 MB  
Max memory used: 36.30 MB  
Average memory used: 21.50 MB |
| Run the app using a physical mobile device connected to the computer | Log in the mobile app and navigate to the menu page. Select and fill in the Hamilton scale. | Startup time: 0.76 sec  
Max memory used: 82.22 MB  
Average memory used: 41.53 MB |
| Run the app using a physical mobile device connected to the computer | Log in the mobile app and navigate to the menu page. Select the McGill questionnaire and fill the first session. | Startup time: 0.70 sec  
Max memory used: 59.78 MB  
Average memory used: 39.80 MB |
| Run the app using a physical mobile device connected to the computer | The mobile app generates a report where the Section Medical Equipment includes technical details corresponding to the device connected to the PC | Manufacturer: Microsoft  
Model: RM-1072_1013  
Phone ID: ‘gBlrXiIxK8blXorMWvrPallwmes=’  
Mobile app name: tDCS_home_WP  
Mobile app revision: 1.0.0.0  
(see figure 4-5) |

Figure 4-5: mPHMR generated by the physical mobile device connected to the computer: the section Medical Equipment includes details of the smartphone and the application.
5 DISCUSSION AND CONCLUSIONS

Electronic health information exchange is a priority in national policies in order to achieve a more cost-effective health care system. Due to the diffusion of mHealth apps, the integration between mobile tools and EHR systems is a predicted consequence.

The American Medical Association has recently published eight priorities fostering better usability of EHR systems and suggesting the introduction of mobile apps in health care processes [AMA, 2014]. In addition to this, the FDA guidance in the USA and public consultation on mHealth in the form of a Green Paper in Europe are the first attempts to regulate mHealth apps as real medical devices. In this context, where specific standards dedicated to mHealth apps are lacking and low usability of EHR systems obstructs electronically health information exchange, it is imperative to focus the attention on how mobile tools can favour the integration between healthcare enterprises. MHealth apps are so widely spread in daily activities that they can really accelerate the realization of the “health IT ecosystem” vision suggested by HIE. A standard and literature review [Marceglia et al. 2015b] shows that the information exchange between health documental systems is always mediated by structured standard clinical documents. In the present scenario, a two-way exchange from professional health information systems to patient-managed digital health systems, based on structured standard clinical document, can represent a turning point.

The present study deals with the definition of a new system architecture for an integrated home monitoring system where clinical documents comply with a new standard based format dedicated to mHealth apps. The aim of the thesis is to include into an electronic health record (EHR) data acquired in a domestic environment, and to allow the exchange of such data among clinicians, caregivers, patients according to a newly developed protocol for mobile applications. In order to achieve this objective it was necessary to:

I. study current literature and available standards regarding both the electronically health information exchange and the mobile apps.

II. analyse a use case in order to design a specific protocol for the data exchange between patient’s mobile applications and professional EHR systems: from requirement identification to the system architecture, definition and modelling

III. provide a proof-of-concept of such integration.
During the study, it was significant to examine how to extend the use of recognized protocols to a direct data exchange between mHealth apps and EHR systems for a harmonized cooperation among different users actively involved in this healthcare scenario (professionals, caregivers and empowered patients).

5.1 Comparison with other studies

In literature there are many studies related to the interoperability issues arising from electronically data exchange between different EHR systems and health applications. In most cases, the application creates a direct connection between the patient and the health professional with the aim to allow the citizen to view his/her own personal medical report. In only one study the patient at home can also insert data into a mobile application connected to a dedicated web-based platform (OncoSys) integrated with the local health system. The goal of this thesis is not to develop a new integrated care system but to demonstrate that a dedicated standard for data exchange is necessary whenever a smartphone is used for an integrated home care service. Moreover, any communication protocol or standardized format presently available has to be remodelled so that it can share clinical documents between the EHR system and the mHealth app.

The system developed in the present study is different from others, both in terms of architecture and in terms of the type of messages shared between the EHR system and the mobile app. The middle tier of the Three-Tier system architecture is innovative because it implements specific services with the aim to create, read, and exchange the new structured document based on HL7 standards. This tier represents the interface between the mobile app and the EHR system so that the same database is used. The connector is a newly developed dedicated web service, in which the XML used to code and to decode data complies with mPHMR, a new anonymous format dedicated to clinical documents’ exchange between mobile apps and EHR systems. This architecture allows a good system scalability, flexibility and reliability.

The introduction of a new data protection rule or of a new health information exchange standard can require modifications to the functions of the web service, even if the manager of an anonymous document could easily fulfill new data protection requirements. For this reason, the adoption of mPHMR-derived standards could be a promising solution for the generation of clinical documents with mHealth apps. The implementation of a prototype reveals that an integrated home monitoring system based on mPHMR can easily meet the requirements of traceability when the author of a message is not a health professional. In the present system, the author’s identification number is stored
with the data collected at home into the database. In this way, when the clinician opens the EHR, he/she can see the monitoring parameters and the author of the relative message, that is, the user of the mobile app.

From a social and clinical point of view, the integrated health care system proposed in this study represents a technological solution satisfying the need of a patient’s empowerment and involving a trained caregiver in the daily management of his patient at home. Mobile personal health applications (mHealth apps) can enhance direct communication between patients and health professionals as they favour the sharing of medical and scientific knowledge and the acquisition of practical skills and operational instructions for safe daily management of diseases. According to health professionals, this integrated care system is different from the others because it does not require data entry from different databases. So far, mHealth apps have been developed as stand-alone systems that may communicate with healthcare professionals through dedicated channels such as ad-hoc developed web platforms or through e-mails. In the present system, data are available in real time into the EHR of the patient. Obviously, sharing data between a mobile app and an EHR system generates regulatory and interoperability issues but mPHMR-compliant messages can solve them. Another advantage of this technological solution is the management of de-identified data from the professional side (the EHR system in the hospital) and of anonymized messages from the non-professional side (the mobile medical app used at home). The integrated home care system described in the present thesis appears may represent a reliable solution to bridge the three gaps “communication, safety and interoperability” that at the moment still divide home and professional environments.

5.2 Possible risks

The new integrated system has to presume user authentication both in the home and professional environment to avoid access to health information by unauthorized people. In fact, the main risk is the insertion of clinical data as for instance a patient’s evaluating scale, from the mobile app into the EHR system by users who are neither the patient nor the caregiver enrolled into the monitoring system. However, the telephone number in the Header of mPHMR can identify the author of the clinical document. In this first prototype, this number is the one given by the patient and the caregiver to the clinician during the first visit. A future improvement could be the access of the mobile app to the SIM data in order to automatically retrieve the mobile phone number to be inserted into the Header
of mPHMR. In this way, the doctor could see inside the EHR those monitoring data coming from a different phone number and he could immediately verify who the author of patient’s evaluations is.

If a user of a previous integrated system logs in the mobile app with a wrong password, the system associates the home monitoring reports to a different patient. On the contrary, in the present release of the system, the mobile app can discern the patient through the password inserted by the user during the login. In this way, the user does not need to insert his personal data into the mobile tool for the identification as the role of the user and of the evaluated patient are identified with two parameters: the account credentials. How possible the insertion of a password and the access to the mobile app by a non-enrolled user are, entirely depends on how the patient and caregiver safeguard their credentials. Even if the security of the system architecture is based on anonymous messages, the prototype developed in the present study can be improved using encrypted messages and controls on the phone number of the clinical documents’ author.

5.3 Limits and future developments

The prototype developed in this study includes the web-based platform named WebBioBank as an EHR system because data inside the EHR are de-identified for the health professional user and anonymized for other roles [Rossi et al. 2014]. This allows the desired anonymization of mPHMR. At the same time, this EHR system allows the implementation of the XDS compliant model because it stores data of mPHMR into two tables: metadata of the Header into a registry and clinical data of the Body into a repository. Moreover, it is a web-based platform based on the framework wHospital: normally used for clinical practise where clinical documents are externally exchanged according to HL7 standard but internally data are not stored as documents for a real time clinical data management. Doctors can insert prompt prescriptions or view clinical data, images and results of laboratory exams in real time. In the same way, using WebBioBank researchers can extract all data of the clinical trial into an excel format for further elaboration and processing. In this study, the web service interprets mPHMR for the extraction of results to store into the corresponding EHR and it archives the metadata of each report into a dedicated table of the database. A future improvement could be the realization of an archive of entire mPHMR messages.

Since the aim of the present study is not to develop a real integrated care system but just a proof-of-concept of the new architecture allowing the integration between EHR systems and mobile apps, the prototype has been developed using only one type of mobile app: Windows Phone. A further extension toward a cross-platform mobile application might also introduce the possibility to
validate the system with different mobile devices (Android, iOS). Thanks to the middle tier of the Three-tier architecture this extension of the system could be easily added. Even if the first prototype was implemented using Microsoft technologies both in the mobile and server side, the three-tier architecture enables connections to other technologies, too. Comparing the performance between operating systems or technologies is out of the scope of the current thesis. The main result of the thesis is the definition of a communication protocol and a template of reports (mPHMR). Other systems or technologies, both on the mobile and on the server side (EHR systems), can be added to the prototype because the middle tier manages the message coding and decoding. Adding new service contracts into the web service allows one to define methods dedicated to the data exchange with other technologies or systems. Besides including the opportunity to use a variety of operating systems or technologies, it could be important to develop this integrated care system creating a mobile app entirely dedicated to clinicians. This might be essential in an emergency or in acute disease scenarios where the prompt intervention of the doctor is crucial. In the vision of a future national interoperability between mobile apps and EHR systems of different enterprises the implementation of regional registries for mPHMR messages should also be evaluated. In this case, it would be necessary to define of a common minimum set of metadata to include into the Header of mPHMR.

Finally, the results obtained in this study may guide the decision to confirm or to adjust the current HL7 protocol and to include cases where patients and caregivers are actively involved into the integrated health care process through a mobile application, taking into consideration not only the technical point of view but also issues regarding access to health personal records.

5.4 Conclusions

In conclusion, we developed an integrated home monitoring system composed by a mHealth app and an EHR system in order to include into an electronic health record data acquired in a domestic environment and to support caregiver at home. This new system allows the exchange of such data between clinicians, caregivers, patients according to a newly developed protocol for mobile applications: mPHMR. We demonstrated that actual HL7 standards (such as: PHMR, CDA2 or CCD) cannot be used when a clinical document is generated at home using smartphones. In this new scenario, where authors are not health professionals and sensitive information are exchanged outside hospitals, it is necessary to identify author and to use an anonymized report. For these reasons we
proposed a new anonymized standard, named mPHMR, that can solve regulatory and interoperability issues coming from data sharing between a mobile app and an EHR system.
REFERENCES


American Medical Association (AMA) site. http://www.ama-assn.org/ama


Fregni F, Boggio PS, Nitsche M, Marcolin MA, Rigonatti SP, Pascual-Leone A. Treatment of major depression with transcranial direct current stimulation. Bipolar Disord 2006, 8:203-4. (c)


Health Information Exchange (HIE) site. http://www.healthit.gov/providers-professionals/health-information-exchange/what-hie

Health Level 7 web site (www.hl7italia.it)


IHE. Integrating the Healthcare Enterprise. IHE Patient Care Coordination (PCC) Technical 491 Framework. 04-Oct-2013


Marceglia S, Fontelo P, Rossi E, Ackerman MJ. A Standards-Based Architecture Proposal for Integrating Patient mHealth Apps to Electronic Health Record Systems. Applied Clinical Informatics. Accepted on 7 May 2015 (b)


Medicare’s Blue Button site (http://www.medicare.gov/manage-your-health/blue-button/medicare-blue-button.html)


TreC. Cartella Clinica del Cittadino. www.trec.trentinosalute.net


W3C site. Web Services Architecture. On line at: http://www.w3.org/TR/ws-arch/

wHospital web site. http://www.whospital.it/en/


ANNEX A

mPHMR Data Model to CDA Mapping: tDCS use-case

The following table shows how items in the mPHMR data model are mapped to constructs in this mPHMR CDA specification. This table is meant to serve as a quick reference, not a complete set of constraints. Please refer to the relevant sections in paragraph 4.1 of the thesis. The columns “mobile app” and “EHR system” indicate if the value in mPHMR is updated during the generation of the Report from the mobile app or during the app personalization according to the care plane inside the EHR of the patient.

Note: All XPath statements reference elements in the CDA namespace; for readability no namespace prefixes are shown.
<table>
<thead>
<tr>
<th>Class</th>
<th>Attribute</th>
<th>CDA XPath</th>
<th>Value</th>
<th>Comments for mobile app used at home</th>
<th>Mobile app</th>
<th>EHR system</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPHMReport</td>
<td>Creation Data/Time</td>
<td>/ClinicalDocument/effectiveTime</td>
<td>[@value = &quot;YYYYMMddhhmmss+[-Z]zz&quot;]</td>
<td>Date and times are coded according to HL7 adoption of ISO8601 and include the time zone (+</td>
<td>-ZZzz).</td>
<td></td>
</tr>
<tr>
<td>Document Identifier</td>
<td>id</td>
<td>/ClinicalDocument/id</td>
<td>[@root=&quot;wbb.IDEHR&quot;][@extension=&quot;yyyyymddhhmmss+[-Z]zz&quot;]</td>
<td>The IDEHR is insert into mPHMR template during the app configuration by the EHR system. The extension corresponds to the date and time of creation of mPHMR by the mobile app.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Document Code</td>
<td>code</td>
<td>/ClinicalDocument/code</td>
<td>[@code=&quot;53576-5&quot;][@codeSystem=&quot;2.16.840.1.113883.6.1&quot;]</td>
<td>Because of mPHMR is a new template, in this study this element is equal to the LOINC codification of Personal health monitoring report Document.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Language</td>
<td>languageCode</td>
<td>/ClinicalDocument/languageCode</td>
<td>[@code=&quot;en-US&quot;] or [@code=&quot;ita-ITA&quot;]</td>
<td>In tDCS use-case the language is set to English due to scientific publication of the study.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Version</td>
<td>versionNumber</td>
<td>/ClinicalDocument/versionNumber</td>
<td>[@values=&quot;1&quot;]</td>
<td>mPHMR is a new template so the version number is 1.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Version</td>
<td>setld</td>
<td>/ClinicalDocument/setld</td>
<td>[@root=&quot;wbb.IDEHR&quot;][@extension=&quot;yyyyymddhhmmss+[-Z]zz&quot;]</td>
<td>If versionNumber is specified then setld should also be specified. In tDCS use-case the attribute of this elements has the same value to the element &quot;ClinicalDocument/Id&quot; because it is the first version.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Reference</td>
<td>typeId</td>
<td>/ClinicalDocument/typeId</td>
<td>[@root=&quot;2.16.840.1.113883.1.3&quot;][@extension=&quot;POCD_HD000040&quot;]</td>
<td>It is a reference to the CDA release 2 specification.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Realm</td>
<td>realmCode</td>
<td>/ClinicalDocument/realmCode</td>
<td>[@code=&quot;IT&quot;]</td>
<td>In tDCS use-case, the clinical document has to comply with regional constraints defined by Italian realm.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Template</td>
<td>templateId</td>
<td>/ClinicalDocument/templateId</td>
<td>[@root=&quot;2.16.840.1.113883.10.XX&quot;]</td>
<td>PHMR[@root=&quot;2.16.840.1.113883.10.20.9&quot;] but mPHMR is different so it’s necessary a new OID such as &quot;2.16.840.1.113883.10.XX.YY&quot;</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Confidentiality</td>
<td>ConfidentialityCode</td>
<td>/ClinicalDocument/ConfidentialityCode</td>
<td>[@code=&quot;L&quot;][@codeSystem=&quot;2.16.840.1.113883.5.25&quot;]</td>
<td>codeSystem = HL7 OID code=L = because of de-identified data</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Actors and Identification</td>
<td>Document Author</td>
<td>/ClinicalDocument/author/Time</td>
<td>[@value = &quot;yyyyymddhhmmss+[-Z]zz&quot;]</td>
<td>It complies with ISO8601 and includes the time zone (+</td>
<td>-ZZzz).</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>/ClinicalDocument/author/assignedAuthor/Id</td>
<td>/ClinicalDocument/author/assignedAuthor/Id</td>
<td>[@root=&quot;wbb_uID&quot;][@extension=&quot;uID&quot;][@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Author of mPHMR is the user login into mobile app who is identified by uID. Th extension is updated by mobile app during the generation of mPHMR.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Class</td>
<td>Attribute</td>
<td>CDA XPath</td>
<td>Value</td>
<td>Comments for mobile app used at home</td>
<td>Mobile app</td>
<td>EHR system</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>-----------</td>
<td>-------</td>
<td>--------------------------------------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>Mobile app</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Custodian</td>
<td>/ClinicalDocument/ author/assignedAuthor/telecom</td>
<td>[@use=&quot;WP&quot;] [@value=&quot;tel:+39XXX-XXXXXXX&quot;]</td>
<td>The phone number depends on the smartphone used at home. The value is updated by clinician during the app configuration in EHR.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>/ClinicalDocument/ custodian</td>
<td></td>
<td>mPHMR Contains required child element assignedCustodian</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>/ClinicalDocument/ custodian/assignedCustodian</td>
<td></td>
<td>assignedCustodian requires a representedCustodianOrganization that in tDCS use-case corresponds to the Operative Unit in WebBioBank</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>/ClinicalDocument/ custodian/representedCustodianOrganization/id</td>
<td>[@root=&quot;wbb_OUID&quot;] [@extension=&quot;OUID&quot;] [@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Identification number of the Operative Unit in WebBioBank that includes the EHR of the patient. The extension is defined during the app configuration by the EHR system. But the value is updated during the creation of mPHMR based on the data received by mobile app from EHR system.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>../representedCustodianOrganization/name</td>
<td>[@root=&quot;wbb_OUname&quot;] [@extension=&quot;OUname&quot;] [@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Also the child element “name” is defined by EHR system but its attribute extension is updated by the mobile app at the moment of the document generation.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>../representedCustodianOrganization/addr</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Address of the Operative unit is stored in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>../representedCustodianOrganization/telecom</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Telephone number of the Operative Unit is stored in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject</td>
<td>Patient id</td>
<td>/ClinicalDocument/ recordTarget/ patientRole/id</td>
<td>[@root=&quot;wbb_pID&quot;] [@extension=&quot;pID&quot;] [@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Patient object of mPHMR is de-identified both in EHR system and into mobile App. HE/SHE is identified by pID. The extension is updated by mobile app during the generation of mPHMR.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient address</td>
<td>/ClinicalDocument/ recordTarget/ patientRole/addr</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Patient’s registry of the Operative Unit is managed in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient telephone number</td>
<td>/ClinicalDocument/ recordTarget/ patientRole/telecom</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Patient’s registry of the Operative Unit is managed in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

*Annex A: mPHMR data model*
<table>
<thead>
<tr>
<th>Class</th>
<th>Attribute</th>
<th>CDA XPath</th>
<th>Value</th>
<th>Comments for mobile app used at home</th>
<th>Mobile app</th>
<th>EHR system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>/ClinicalDocument/recordTarget/patientRole/Patient</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Patient’s registry of the Operative Unit is managed in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>InformationRecipient</td>
<td>IntendedRecipient: Identification</td>
<td>ClinicalDocument/informationRecipient/intendedRecipient/id</td>
<td>[@root=&quot;wbb_OUID&quot;] [@extension=&quot;OUID&quot;] [@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Identification number of the Operative Unit in WebBioBank that includes the EHR of the patient. The extension is defined during the app configuration by the EHR system. But the value is updated during the creation of mPHMR based on the data received by mobile app from EHR system.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>InformationRecipient</td>
<td>IntendedRecipient: address</td>
<td>ClinicalDocument/informationRecipient/intendedRecipient/address</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Address of the Operative Unit is stored in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>InformationRecipient</td>
<td>IntendedRecipient: telecom</td>
<td>ClinicalDocument/informationRecipient/intendedRecipient/telecom</td>
<td>[@nullFlavor=&quot;MSK&quot;]</td>
<td>Telephone number of the Operative Unit is stored in EHR system so in mPHMR is masked.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>InformationRecipient</td>
<td>name fo OU</td>
<td>ClinicalDocument/informationRecipient/intendedRecipient/informationRecipient/name</td>
<td>[@root=&quot;wbb_OUname&quot;] [@extension=&quot;OUname&quot;] [@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Also the child element “name” is defined by EHR system but its attribute extension is updated by the mobile app at the moment of the document generation.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Class</td>
<td>Attribute</td>
<td>CDA XPath</td>
<td>Value</td>
<td>Comments for mobile app used at home</td>
<td>Mobile app</td>
<td>EHR system</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>----------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ClinicalDocument/Documentatinof/ServiceEvent/id</td>
<td>[@root=&quot;wbb_IDappContent&quot;] [@extension=&quot;IDtDCS_app_APPcontent&quot;] [@assigningAuthorityName=&quot;WebBioBank&quot;]</td>
<td>Also the child element “id” is defined by EHR system but its attribute extension is updated by the mobile app at the moment of the document generation. IDtDCS_app_APPcontent is the identity number of the last app content configuration for the patient.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ClinicalDocument/Documentatinof/ServiceEvent/Effective Time</td>
<td>[@value=&quot;yyyymmdd&quot;]</td>
<td>In tDCS use-case, the child element “Low” represents the data of the last app content configuration by the clinician according to the care plane dedicated to the patient.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>PHM Section</td>
<td></td>
<td>/component/section/Results/Template/Section/templateId</td>
<td>[@root=&quot;2.16.840.1.113883.10.20.1.14&quot;] [@root=&quot;2.16.840.1.113883.10.20.9.14&quot;]</td>
<td>Also section Result of mPHMR complies with CCD and PHMR standards</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Section Code</td>
<td>/Section/code</td>
<td>[@code=&quot;30954-2&quot;] [@codeSystems=&quot;2.16.840.1.113883.6.1&quot;]</td>
<td>LOINC codification for section Result</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Section Title</td>
<td>/Section/title</td>
<td>&lt;title&gt;Results&lt;/title&gt;</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Text</td>
<td>/Section/text</td>
<td>&lt;text&gt;....&lt;/text&gt;</td>
<td>In tDCS use-case, the text subsection of Result include the question of the evaluation scale and the answer of app user.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Entry</td>
<td>section/entry</td>
<td>[@typeCode=&quot;COMP&quot;] for Result section [@typeCode=&quot;DRIV&quot;] for Purpose section</td>
<td>The section Result has components. The section Purpose the narrative was rendered from the CDA Entries, and contains no clinical content not derived from the entries.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Observation</td>
<td>section/entry/Observation</td>
<td>[@classCode=&quot;OBS&quot;] [@moodCode=&quot;EVN&quot;]</td>
<td>Observation appears directly under the entry element when it is a primary clinical act statement in a section. The mPHMR for evaluating scale in tDCS use-case, primary clinical act statement of the section Result is the first question of the evaluating scale. Numeric observation.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Class</td>
<td>Attribute</td>
<td>CDA XPath</td>
<td>Value</td>
<td>Comments for mobile app used at home</td>
<td>Mobile app</td>
<td>EHR system</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Observation</td>
<td>/templateID</td>
<td>[@root=&quot;2.16.840.1.113883.10.20.1.31&quot;]</td>
<td>Also section Result of mPHMR complies with CCD and PHMR standards</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Observation</td>
<td>/ID</td>
<td>[@root=&quot;273593005-s2-q-01&quot;]</td>
<td>Id is the unique identifier of the observation. The name refers to the number of question of the questionnaire and the root is composed by: the SNOMED code of the evaluating scale and a string 'sY-q-XX' where Y is the number of the section of questionnaire and XX is the number of the question (XX = 01).</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Observation</td>
<td>/code</td>
<td>[@code=&quot;273593005&quot;]</td>
<td>Code refers to terminologies’ mapping with SNOMED CT vocabulary for the evaluating scale (for example the code for Hamilton evaluating scale in SNOMED CT is: 273503001).</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Observation</td>
<td>/effectiveTime</td>
<td>[@value=&quot;yyyy-mm-dd hh:mm:ss+</td>
<td>-zz&quot;]</td>
<td>EffectiveTime corresponds to the time of filling in the questionnaire by the user App. The mobile app updates its value during the mPHMR generation at the end of the patient evaluation.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Observation</td>
<td>/value</td>
<td>[@xsi:type=&quot;PQ&quot;]</td>
<td>Value is the answer of the patient or caregiver to the question of the evaluation scale. All the evaluation scale at each answer corresponds a score (type:quantity, unit: points).</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>EntryRelationship</td>
<td></td>
<td>[@typeCode=&quot;COMP&quot;]</td>
<td>The section Result has components</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>EntryRelationship/Observe</td>
<td></td>
<td>[@classCode=&quot;OBS&quot;]</td>
<td>Observation appears directly under the entryRelationship when it is being related to another clinical act. The mPHMR for evaluating scale in tDCS use-case, all the question of the questionnaire are related to the first question of the evaluating scale (primary clinical act statement of the section Result).</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>EntryRelationship/Observe/Id</td>
<td></td>
<td>[@root=&quot;273593005-s2-q-02&quot;]</td>
<td>Id is the unique identifier of the observation. The name refers to the number of question of the questionnaire and the root is composed by: the SNOMED code of the evaluating scale and a string 'q-XX' where XX is the number of the question (XX &gt;= 02).</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Class</td>
<td>Attribute</td>
<td>CDA XPath</td>
<td>Value</td>
<td>Comments for mobile app used at home</td>
<td>Mobile app</td>
<td>EHR system</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>--------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
</tbody>
</table>
| EntryRelationship/Observation/code |                                            | EntryRelationship/Observation/code                                        | [@code="273593005"]  
[@codeSystem="2.16.840.1.113883.6.96"]  
[@codeSystemName="SNOMED CT"]  
[@displayName="McGill pain questionnaire"] | Code refers to terminologies’ mapping with SNOMED CT vocabulary for the evaluating scale (for example the code for Hamilton evaluating scale in SNOMED CT is: 273503001). | X          | X           |
| EntryRelationship/Observation/value |                                            | EntryRelationship/Observation/value                                        | [@xsi:type="PQ"]  
[@value="x"]  
[@unit="points"] | Value is the answer of the patient or caregiver to the question of the evaluation scale. In evaluation scale at each answer corresponds a score (type:quantity, unit: points). | X          | X           |
| Device (medical equipment)       | Device Id                                  | //participant[templateId/@root="2.16.840.1.113883.10.20.9.9"]/id          | @root is OID of device numbering space and @extension is a valid device ID within that space         | e.g. @root is 1.2.840.10004.1.1.0.0.1.0.0.0.1.2680 and @extension is a valid EUI-64 device ID.  
Its attribute extension is updated by the mobile app at the moment of the document generation.      | X          | X           |
| Device Type                      |                                            | //participant[templateId/@root="2.16.840.1.113883.10.20.9.9"]/participantRole[templateId/@root="2.16.840.1.113883.10.20.9.9"]/playingDevice/code | [@code="469022007"]  
[@codeSystem="2.16.840.1.113883.6.96"]  
[@codeSystemName="SNOMED CT"]  
[@displayName="Entry phone"] | SNOMED mapping for the smartphone (default value) | X          | X           |
| Manufacturer                     |                                            | //participantRole[templateId/@root="2.16.840.1.113883.10.20.9.9"]/scopingEntity/desc | <scopingEntity>  
<desc>Nokia</desc>  
</scopingEntity> | e.g. Nokia.  
Its value is updated by the mobile app at the moment of the document generation. | X          | X           |
<p>| Manufacturer                     |                                            | //participantRole[templateId/@root=&quot;2.16.840.1.113883.10.20.9.9&quot;]/playingDevice/manufacturerModelName | Free text | Its value is updated by the mobile app at the moment of the document generation. | X          | X           |</p>
<table>
<thead>
<tr>
<th>Class</th>
<th>Attribute</th>
<th>CDA XPath</th>
<th>Value</th>
<th>Comments for mobile app used at home</th>
<th>Mobile app</th>
<th>EHR system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production Spec</td>
<td>Model</td>
<td>//participantRole[templateId/@root=&quot;2.16.840.1.113883.1.20.9.9&quot;]/playingDevice/manufacturer ModelName</td>
<td>Free text</td>
<td>Its value is updated by the mobile app at the moment of the document generation.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Phone ID</td>
<td>//participantRole[templateId/@root=&quot;2.16.840.1.113883.1.20.9.9&quot;]/playingDevice/manufacturer ModelName</td>
<td>Free text</td>
<td>Its value is updated by the mobile app at the moment of the document generation.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mobile app name</td>
<td>//participantRole[templateId/@root=&quot;2.16.840.1.113883.1.20.9.9&quot;]/playingDevice/manufacturer ModelName</td>
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<td>Its value is updated by the mobile app at the moment of the document generation.</td>
<td>X</td>
<td></td>
</tr>
<tr>
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<td>Mobile app version</td>
<td>//participantRole[templateId/@root=&quot;2.16.840.1.113883.1.20.9.9&quot;]/playingDevice/manufacturer ModelName</td>
<td>Free text</td>
<td>Its value is updated by the mobile app at the moment of the document generation.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Regulatory Information</td>
<td>Regulatory Status</td>
<td>//participantRole[templateId/@root=&quot;2.16.840.1.113883.1.20.9.9&quot;]/code[@nullFlavor=&quot;OTH&quot;]/originalText</td>
<td>&lt;originalText&gt;Unregulated Device&lt;/originalText&gt;</td>
<td>Smartphone = unregulated device (default value)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Purpose</td>
<td>Template</td>
<td>/Section/templateld[@root=&quot;2.16.840.1.113883.10.20.1.13&quot;]</td>
<td></td>
<td>Also section Purpose of mPHMR complies with CCD standards</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Section Code</td>
<td>/Section/code[@code=&quot;48764-5&quot;] [@codeSystems=&quot;2.16.840.1.113883.6.1&quot;]</td>
<td></td>
<td>LOINC codification for section Purpose</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Section Title</td>
<td>/Section/title</td>
<td>&lt;title&gt;Purpose&lt;/title&gt;</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Class</td>
<td>Attribute</td>
<td>CDA XPath</td>
<td>Value</td>
<td>Comments for mobile app used at home</td>
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<td>------------</td>
<td>------------</td>
</tr>
</tbody>
</table>
| Text  | /Section/text | `<text> 
<table>....</table> </text>` | | In tDCS use-case, the text subsection of Purpose is transfert of care between hospital and home. | | X |
| Entry/Act | /Section/Entry/Act/ [@classCode="ACT"] [@moodCode="EVN"] | Clinical Statement templates for Purpose activity according to CCD | X |
| | /Section/Entry/Act/templateID [@root="2.16.840.1.113883.10.201.30"] | | |
| | /Section/Entry/Act/code [@code="223493006"] [@codeSystem="2.16.840.1.113883.6.96"] | SNOmed CT codification for the activity “Documentation observations” | X |
| | /Section/Entry/Act/statusCode [@code="completed"] | The intended acts is fully complete | X |
| | /Section/Entry/Act/entryRelationship [@typeCode="RSON"] | the relationship type is “RSON” that means “has reason” | X |
| | /Section/Entry/Act/entryRelationship/Act/code [@code="308292007"] [@codeSystemName="SNOMED CT"] [@codeSystem="2.16.840.1.113883.6.96"] [@displayName="Transfer of care"] | In tDCS use-case the act is the transfer of care from hospital to home environment. | X |
| | /Section/Entry/Act/entryRelationship/Act/StatusCode [@code="completed"] | The intended acts is fully complete | X |

Table 1: mPHMR Data Model to CDA Mapping: tDCS use-case

Annex A: mPHMR data model