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PITES-ISA: NEW SERVICES BASED ON TELEMEDICINE AND E-HEALTH AIMED AT INTEROPERABILITY, PATIENT SAFETY AND DECISION SUPPORT

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Prólogo

La Plataforma de Innovación en Telemedicina y e-Salud (PITES) constituye un marco de actuación en red para la investigación y la innovación en soluciones, servicios y herramientas basadas en Tecnología de la Información y la Comunicación (TIC) dirigidos al soporte de los nuevos modelos de asistencia. Formalmente, PITES es una agrupación de nodos de innovación tecnológica con base en unidades clínicas para la implementación de entornos de aplicaciones, herramientas, e infraestructuras TIC, seguras, accesibles, e interoperables conforme a estándares abiertos tal que permiten implementar soluciones de telemedicina móvil personal y de e-salud para el soporte de nuevos modelos asistenciales dirigidos a la condición crónica, fragilidad y dependencia, acelerando la transferencia del conocimiento a la práctica clínica.

La definición anterior trata de englobar todos los componentes y ámbitos de actuación que abarca PITES. La primera parte pone de manifiesto los elementos y ámbitos intrínsecos a PITES que son consecuencia de las decisiones de conformación de la propia plataforma:

- basar la plataforma en unidades clínicas;
- dirigir la actividad fundamentalmente hacia la innovación de producto, principalmente, innovación tecnológica, pero también innovación en procesos y nuevos modelos de atención;
- implementar soluciones TIC accesibles, seguras, interoperables y conforme a estándares abiertos, como soporte a procesos de atención que generen o hagan viables nuevos modelos de asistencia.

La segunda parte de la definición hace referencia a los elementos y condiciones de contorno que han actuado como referencia en la conformación y evolución de PITES:

- un contexto sociosanitario condicionado por los patrones dominantes epidemiológicos y demográficos relacionados con la condición crónica, el envejecimiento, la fragilidad y la dependencia;
- una práctica médica irreversible e indisolublemente vinculada a las TIC, y en este ámbito el desarrollo de la telemedicina y la e-salud;
- unos modelos asistenciales con una alta complejidad organizativa, que integran los cuidados sanitarios y sociales, que requieren una mayor participación e interacción de actores, y en los que los pacientes y su entorno comienzan a formar parte activa y central en los procesos de asistencia;
- una absoluta necesidad de habilitar vías efectivas para transferir el conocimiento y la innovación a un contexto de gran complejidad como es la práctica clínica.

Los antecedentes de PITES son diversos y conformaron el origen de los ámbitos de trabajo, los intereses de colaboración y los grupos que actualmente conforman o han formado parte de la plataforma. Cabe destacar fundamentalmente dos acciones:

- la Red Temática de Investigación en Servicios de Salud Basados en Telemedicina que, durante el periodo 2003 a 2006, formó parte de las Redes de Temáticas de Investigación Colaborativa financiadas por el Fondo de Investigación Sanitaria (G03/117). La red, constituida por 13 grupos de investigación en 10 Comunidades Autónomas (8 hospitales y servicios de salud, 5 universidades y un organismo público de investigación), dirigió su actividad hacia la consolidación y extensión de la investigación en modelos formales de sistemas y servicios para la atención domiciliaria; el desarrollo de protocolos, guías y normas para el Sistema Nacional de Salud; y la propuesta de procedimientos estructurados para la evaluación de las nuevas tecnologías sanitarias;
- los acuerdos de colaboración AIRMED entre el Instituto de Salud Carlos III y la Fundación Vodafone España que, durante el periodo 1998 a 2008, dieron cobertura a la investigación, desarrollo, despliegue y evaluación formal de nuevos modelos de atención extrahospitalaria soportados por tecnologías móviles e Internet. Los trabajos se centraron fundamentalmente en la propuesta, despliegue experimental y evaluación de nuevos modelos de cuidados basados en la autogestión de la condición crónica y las situaciones de dependencia a través de tecnologías de telemonitorización e interacción

sobre servicios basados en redes GSM y la web. En colaboración con organizaciones sanitarias, se abordaron múltiples escenarios, niveles de atención y condiciones de salud (hipertensión arterial, insuficiencia cardiaca, asma, prevención secundaria de factores de riesgo cardiovascular, tratamiento de anticoagulación oral, entre otros), y se introdujo y desarrolló en concepto de plataforma tecnológica para la investigación colaborativa.

La red PITES se constituye formalmente en 2009 como una red de nodos con base en unidades clínicas con el objetivo de innovar en telemedicina y e-salud. La decisión de basar los nodos de la red en unidades clínicas posibilita una mayor ventaja en los siguientes aspectos:

- el abordaje de cuestiones interdisciplinares y dominios transversales;
- la efectividad en la inserción de productos tecnológicos en procesos y organizaciones;
- la identificación de factores innovadores y el refuerzo de la capacidad de innovación;
- el establecimiento de puentes en el entorno sociosanitario;
- la preparación para adopción de innovaciones (preparación de mercado).

En PITES se combina la innovación en productos (bienes y servicios tecnológicos), la innovación en nuevos procesos y organización y la innovación por la compartición de recursos entre sus nodos (conocimiento e infraestructuras). La innovación en PITES se ve impulsada desde los usuarios (profesionales sanitarios y no sanitarios, pacientes y su entorno) a través de las interacciones generadas durante la construcción de prototipos y el uso cotidiano de productos y procesos durante los periodos de evaluación formal. Alineados con el Reto de Salud, Cambio Demográfico y Bienestar de la Estrategia Española de Ciencia, Tecnología e Innovación, las actuaciones de PITES se pueden agrupar en 3 ámbitos:

- Modelos de asistencia: propuesta y diseño de nuevos modelos y procesos de asistencia para cuidados integrados, continuidad asistencial, atención personalizada y soporte a la autogestión; modelos orientados a los interfaces entre los niveles de atención especializada y primaria, el domicilio del paciente/ciudadano y la asistencia social; modelos "tech-enabled", es decir, no es tanto dar soporte TIC a modelos de asistencia existentes, sino hacer viables nuevos modelos a partir de nuevas propuestas TIC.
- Tecnologías para la asistencia: implementación de servicios y aplicaciones en tres amplias áreas:
  - Telemonitorización: biomédica, actividad, ambiental, etc., dirigidas al paciente/ ciudadano como soporte a modelos de atención extrahospitalarios.
  - Encuentro e interacción virtual: entornos colaborativos (profesional-profesional, profesional-paciente); asistencia virtual al paciente/ cuidador (formal, informal); capacitación; interacción en tiempo real, diferido, social.
  - Gestión de información y conocimiento: intercambio de información clínica/ historia clínica electrónica; herramientas de ayuda a la decisión; extracción de conocimiento; normalización en el campo asistencial (uso de normas, modelos de datos, open-data, big data); repositorios de información semánticamente interoperables para uso primario y secundario.

  En el área tecnológica, PITES dispone de una infraestructura TIC (plataforma tecnológica PITES) como recurso compartido complementario para el soporte de las actividades investigación y experimentación colaborativa entre sus nodos.
- Evaluación formal: propuestas metodológicas y búsqueda de evidencia científica sobre la eficacia, efectividad y eficiencia de los nuevos modelos y tecnologías mediante la realización de estudios experimentales.

Formal y administrativamente, la red PITES se articula a través de un proyecto de investigación. Por este motivo, en ocasiones, la red es referida como proyecto PITES. Se trata de un proyecto coordinado financiado a través de fondos públicos en el marco de la Acción Estratégica de Salud (AES) dentro del Plan Estatal de Investigación Científica y Técnica y de Innovación. El proyecto establece un marco de trabajo de tres años renovable a través de convocatoria pública competitiva. El proyecto inicial (PITES) se desarrolló durante los años 2010 a 2012 en el marco de la AES 2009. La primera renovación (PITES-ISA), objeto de esta publicación, se ha desarrollado entre los años 2013 y 2016 en el marco de la AES 2012. Actualmente, está en curso la segunda renovación (PITES-TIISS) que se desarrolla durante el periodo 2016-2018 en el marco de la AES 2015.

En el marco del proyecto coordinado PITES, cada nodo de la red desarrolla un subproyecto propio. En primer lugar, la red consensua un objetivo general para el proyecto coordinado, orientado a los ámbitos generales de actuación de PITES; posteriormente, cada nodo establece los objetivos específicos para su subproyecto, de acuerdo con sus necesidades e intereses locales o regionales, y alineados con el objetivo general. El requisito de coordinación del proyecto ha sido asumido por Unidad de Investigación en Telemedicina y e-Salud del Instituto de Salud Carlos III.

En el marco de desarrollo del proyecto PITES-ISA, la red PITES ha estado conformada por seis nodos: Hospital Universitario Puerta de Hierro Majadahonda (Madrid); Hospital de Barbastro (Aragón); Hospital Universitario Virgen del Rocío (Andalucía); Hospital Clínic Barcelona (Cataluña); Complejo Hospitalario Universitario A Coruña (Galicia); y, como nodo coordinador, la Unidad de Investigación en Telemedicina y e-Salud del Instituto de Salud Carlos III. El objetivo general consensuado para el proyecto PITES-ISA dirige las actuaciones hacia los entornos de aplicaciones y herramientas TIC para la interoperabilidad, la seguridad (técnica y del paciente) y la ayuda a la decisión (clínica y procedimental), orientadas a desarrollar soluciones extendidas de telemedicina móvil personal y de e-salud.

Esta publicación presenta seis artículos cuyo objetivo es presentar algunos de los resultados más relevantes alcanzados en los respectivos subproyectos que se han llevado a cabo en el marco de PITES-ISA.

El primero de los seis artículos incluidos en este libro se refiere al subproyecto correspondiente al nodo coordinador. Sus autores son componentes del grupo de la Unidad de Investigación en Telemedicina y e-Salud del Instituto de Salud Carlos III de Madrid. Lleva por título **"Reformulating the database persistence of the PITES interoperability platform".** En el trabajo se describe la utilidad de los sistemas de EHR estandarizados, como la plataforma de interoperabilidad PITES, para resolver el problema demográfico y de la proliferación de información médica, a través del uso secundario de la EHR. Es un sistema interoperable que utiliza un modelo dual basado en el estándar ISO/EN 13606 y esto afecta profundamente al sistema de persistencia en base de datos. En el trabajo se evalúan los DBMS relacionales y no relacionales (NoSQL) para implementar la persistencia del sistema de EHR estandarizado utilizado en la plataforma interoperable PITES.

El segundo artículo, titulado **"Implementation of an early detection service for COPD exacerbations: experimental evaluation for an early discharge, hospital-at-home programme",** tiene como autores a investigadores del Hospital Universitario Puerta de Hierro en Madrid; también incluye autores pertenecientes a la Unidad de Investigación en Telemedicina y e-Salud del Instituto de Salud Carlos III de Madrid. En el mismo se describe la implementación y evaluación mediante metodología de ensayo clínico, un protocolo de telemonitorización y ayuda a la decisión para dar soporte a programas de hospitalización domiciliaria por alta precoz de pacientes con EPOC. La evaluación se ha dirigido a demostrar la mejora de la eficiencia y la similitud en la eficacia, satisfacción, adhesión al tratamiento e impacto en bienestar y vida diaria, en relación a los programas convencionales de hospitalización domiciliaria basados en la atención presencial domiciliaria diaria por profesionales sanitarios.

El tercer artículo, titulado **"Servicio Aragonés de Salud: Results of the PITES ISA T-CUIDAENCASA: Platform of Innovation in home ehealth services project"** tiene como autores a investigadores del Sector Sanitario de Barbastro. En el mismo se presenta una plataforma dirigida a promover la colaboración entre profesionales en la prestación de cuidados integrados en cuidados paliativos en pacientes que puedan adaptarse a la hospitalización domiciliaria, con una atención de alta calidad y manteniendo su seguridad clínica, y al mismo tiempo brindar a todos los profesionales las herramientas necesarias para compartir datos clínicos para proporcionar este tipo de asistencia.

El cuarto trabajo, bajo el título **"PITeS ISA in Andalusia: Clinical Decision Support System for the prescription of genetic testing in the gynecological cancer risk and screening the risk of thromboembolism during hospitalization",** correspondiente a los trabajos desarrollados en el subproyecto del Hospital Universitario Virgen del Rocío, se describe un conjunto de herramientas genéricas y servicios dirigidos a proporcionar soporte a la decisión, haciendo uso de arquitecturas orientadas a servicio y estándares tecnológicos, y su pilotaje en dos escenarios: la estandarización de los criterios de prescripción de los tests genéticos BRCA1 y BRCA2; y el cálculo del factor de riesgo para la monitorización la evolución del tromboembolismo venoso.

El quinto trabajo, lleva por título **"PITES-ISA in Catalonia: Innovation in Integrated Care Services for Chronic Patients",** tiene como autores a investigadores del Hospital Clinic Barcelona, y presenta actividades con un enfoque hacia la integración de cuidados y fundamentos de medicina personalizada, orientadas a tres ámbitos: el despliegue regional de servicios asistenciales; banco de pruebas en Cataluña para el liderazgo como sitio de referencia en EIP-AHA; y la transferencia y explotación de nuevos productos y servicios.

El sexto trabajo, que completa los contenidos del libro, lleva por título **"Development of a Telemedicine System for Rheumatology Patients",** tiene como autores a investigadores del Complejo Hospitalario Universitario de A Coruña. En el mismo se describe la implementación de un sistema de telemedicina orientado a dar soporte a las deficiencias detectadas actualmente en la atención al colectivo de pacientes reumatológicos: falta de continuidad asistencial, gasto excesivo en actividades terapéuticas, dificultades en el cumplimiento de las guías clínicas y la aparición de un alto número de eventos adversos durante el tratamiento.

Esperamos que el contenido de este libro pueda servir de referencia para futuras investigaciones en este dominio.

Para concluir, queremos agradecer a todos los autores el esfuerzo en la realización y la calidad de sus contribuciones.

Mario Pascual y Adolfo Muñoz
Madrid, 2017

Foreword

The PITES Telemedicine and e-Health innovation platform constitutes a network intervention framework for research and innovation in solutions, services and tools based on Information and Communications Technologies (ICTs) aimed at supporting the new assistance models. Formally, PITES is a grouping of nodes of technological innovation based on clinical units aimed at the implementation of environments of applications, tools and ICT infrastructures, secure, accessible, and interoperable, compliant with open standards permitting to implement personal mobile telemedicine and e-Health solutions to support new healthcare models for chronic condition, frailty and dependence, accelerating the transfer of knowledge to clinical practice.

The previous definition tries to include all components and intervention scopes of PITES. The first part presents the elements and scopes inherent to PITES that are consequence of the decisions conforming the platform itself:

- to base the platform on clinical units;
- to direct the activity fundamentally to product innovation, mainly technological innovation, but also innovation in processes and new assistance models;
- to implement accessible ICT solutions, secure, interoperable and conforming to open standards, as support to processes of attention generating or make viable new assistance models.

The second part of the definition addresses the elements and contour conditions that have acted as references in the conforming and evolution of PITES:

- a socio-sanitary context contrived by the dominant epidemiological and demographic patterns related to the chronic condition, ageing, frailty and dependence;
- a medical practice irreversible and indissolubly linked to ICTs, and in this scope the development of telemedicine and e-Health;
- healthcare models with a high organizational complexity, integrating social and health care, requiring a higher participation and interaction of actors, in which patients and their environment are starting to take an active and central part in the assistance processes;
- an absolute necessity to habilitate effective ways to transfer the knowledge and the innovation to a context of great complexity such as clinical practice.

The precedents of PITES are diverse and have conformed the origins of the work environments, the interests of collaboration and the groups that currently conform or have formed part of the platform. There are two actions to mention:

- the Thematic Research Network on Health Services Based on Telemedicine. Between 2003 and 2006 it took part of the Thematic Collaborative Research Networks financed by the Sanitary Research Fund (G03/117). This network, constituted by 13 research groups from 10 Autonomous Regions (8 hospitals and health services, 5 universities and one public research centre), conducted its activity to the consolidation and extension of the research in formal models of systems and services for home attention; the development of protocols, guidelines and norms for the National Health System; and the proposal of structured procedures for the evaluation of new sanitary technologies;
- the AIRMED collaboration agreements between the Institute of Health Carlos III and the Foundation Vodafone España that, from 1998 to 2008, have given coverage to the research, development, deployment and formal evaluation of new models of extra-hospital attention, supported by mobile technologies and Internet. Works were focused in the proposal, experimental deployment and evaluation of new healthcare models based on the self-management of the chronic condition and the dependence situations through tele monitoring technologies and interaction with GSM networks based services and the Web. In collaboration with healthcare organizations multiple scenarios, levels of attention and health conditions (arterial hypertension, heart failure, asthma, secondary prevention of cardiovascular

risk factors, oral anticoagulation treatment, and others) were addressed, and the concept of technological platform for collaborative research was introduced and developed.

The PITES network is constituted formally in 2009 as a network of nodes based on clinical units aimed at innovating in telemedicine and e-health. The decision to base the nodes of the network on clinical units makes possible advantages in the following aspects:

- to address multidisciplinary issues and transversal dominions;
- the effectivity in the insertion of technological products in processes and organizations;
- to identify innovation factors and to improve the capacity to innovate;
- to establish bridges in the socio-sanitary environment;
- to prepare for the adoption of innovations (market preparation).

In PITES, product innovation (technological goods and services), innovation in new processes and organization and innovation through resources sharing between nodes (knowledge and infrastructures) are combined. Innovation in PITES is driven by users (health and non-health professionals, patients and their environments) through the interactions generated during the prototypes construction and everyday use of products and processes during periods of formal evaluation. Aligned with the Health, Demographic Change and Well-being Challenge of the Spanish Science, Technology and Innovation Strategy, PITES interventions may be grouped in 3 scopes:

- Assistance models: proposal and design of new assistance models and processes for integrated care, care continuity, personalized attention and support to self-management; models oriented to the interfaces between specialized and primary attention levels, the home of the patient/citizen and social care; "tech-enabled" models, that is, not giving ICT support to existing care models, but to make viable new models from new ICT proposals.
- Technologies for care: services implementation and applications in three broad areas:
  - Tele-monitoring: biomedical, activity, ambience, etc., directed to the patient/citizen as support to extra-hospital care models.
  - Virtual meeting and interaction: collaborative environments (professional-professional, professional-patient); virtual assistance to patient/care-giver (formal, informal); capacitation; real time, pre-recorded, social interaction.
  - Information and knowledge management: clinical information interchange/electronic health record; decision aid tools; knowledge extraction; healthcare standardization (use of norms, data models, open data, big data); semantically interoperable information repositories for primary and secondary use.

  In the technological area, PITES has an ITC infrastructure (PITES technological platform) as a complementary shared resource to support the research and collaborative experimentation activities between its nodes.
- Formal evaluation: methodological proposals and scientific evidence search about the efficacy, effectiveness and efficiency of the new models and technologies through the performance of experimental studies.

Formal and administratively, the PITES network is constructed through a research project. Sometimes it is known as the PITES project. It is a coordinated project financed through public funds coming from the Strategic Health Action (AES) in the Scientific and Technical Research and Innovation State Plan. The project establishes a three years framework renewable in competitive public call. The initial project (PITES) was developed through the years 2010-2012 in the AES 2009. The first renewal (PITES-ISA), the subject of this publication, has been developed between 2013 and 2016 in the framework of the AES 2012. Currently its second renewal is into effect (PITES-TISS) for the period 2016-2018 in the AES 2015.

In the framework of the PITES coordinated project, each node of the network performs a different subproject. In the first place, the network agrees a general objective for the coordinated project, orientated to the general scopes of intervention of PITES; subsequently each node establishes the specific objectives for its subproject, according to its necessities and local or regional interests, and aligned with the general objective. The coordination requisite of the project has been assumed by the Telemedicine and e-Health Research Unit of the Institute of Health Carlos III.

The PITES network, in the PITES-ISA Project, has been makeup of six nodes: University Hospital Puerta de Hierro Majadahonda (Madrid); Barbastro Hospital (Aragón); University Hospital Virgen del Rocío (Andalucía); Hospital Clínic Barcelona (Cataluña); University Hospital Complex A Coruña (Galicia); and as hub node, the Telemedicine and e-Health Research Unit of the Institute of Health Carlos III. The general agreed objective of the PITES-ISA project directs the interventions to applications environments and ICT tools for interoperability, security (technical and patient) and the aid to decision (clinical and procedural), orientated to developing extended solutions of personal mobile telemedicine and e-Health.

This publication includes six articles whose objective is to present some of the most relevant results achieved in the respective subprojects carried out in the framework of PITES-ISA.

The first of the six articles included in this book corresponds to the hub node. Authors are members of the Telemedicine and e-Health Research Unit of the Institute of Health Carlos III. This work is entitled **"Reformulating the database persistence of the PITES interoperability platform".** It describes the usefulness of standardized EHR systems, such as the PITES interoperability platform, to resolve the demographic and the medical information proliferation problems, through the secondary use of the EHR. It is an interoperable system using a dual model based on the ISO/EN 13606 standard, and this affects strongly the structure of the underlying database persistence system. Relational and non-relational (NoSQL) DBMSs are evaluated from the standpoint of time response (algorithmic complexity) to implement the database persistence of the standardized EHR system used in the PITES interoperable platform.

The second article, entitled **"Implementation of an early detection service for COPD exacerbations: experimental evaluation for an early discharge, hospital-at-home programme",** authored by researchers of the University Hospital Puerta de Hierro, Madrid; includes authors from the Telemedicine and e-Health Research Unit of the Institute of Health Carlos III, Madrid. It describes the implementation and evaluation through a clinical trial methodology, a tele-monitoring protocol and decision aid to support home hospitalization programme due to early discharge of patients suffering EPOC. Evaluation is directed to demonstrate the efficiency improvement, and the similarity in efficacy, satisfaction, treatment adherence and impact on well-being and everyday life, related to the conventional hospital-at-home programmes based on everyday domiciliary face-to-face attention by healthcare professionals.

The third article, entitled **"Servicio Aragonés de Salud: Results of the PITES ISA T-CUIDAENCASA: Platform of Innovation in home ehealth services project"** is authored by researchers of the Barbastro Health Sector. It presents a platform aimed at promoting collaboration between professionals in the provision of integrated care in palliative care to patients that may adapt to home hospitalization, giving a high-quality attention and maintaining their clinical security, and at the same time giving professionals the necessary tools to share clinical data to provide this kind of healthcare.

The fourth work, under the title **"PITeS ISA in Andalusia: Clinical Decision Support System for the prescription of genetic testing in the gynaecological cancer risk and screening the risk of thromboembolism during hospitalization",** correspond to work developed by the University Hospital Virgen del Rocío subproject. It describes a set of generic tool s and services aimed at providing decision support, making use of service oriented architectures and technological standards, and its deployment in two scenarios: the standardization of the prescription criteria of genetic tests BRCA1 and BRCA2; and the computation of the risk factor to monitoring the evolution of poisonous thromboembolism.

The fifth work, entitled **"PITES-ISA in Catalonia: Innovation in Integrated Care Services for Chronic Patients",** is authored by researchers of the Hospital Clínic Barcelona and presents interventions with an approach to the integration of healthcare and personalized medicine fundaments, orientated to three different scopes: the regional deployment of healthcare services; test bench in Catalonia for leadership as reference site in EIP-AHA; and the transference and exploitation of new products and services.

The sixth and last work, entitled **"Development of a Telemedicine System for Rheumatology Patients",** is authored by researchers from the University Hospital Complex A Coruña. It describes the implementation of a telemedicine service orientated to give support to currently detected deficiencies in the attention to rheumatologic patients: lack of healthcare continuity, excessive expense in therapeutic interventions, difficulties in the achievement of clinical guidelines and the emergence of a high number of adverse events during treatment.

We hope that the content of this book may serve as a reference for future research in this domain.

To conclude, we would like to express our gratitude to all authors for their effort in the elaboration and for the quality of their contributions.

Mario Pascual y Adolfo Muñoz
Madrid, 2017

CHAPTER 1

REFORMULATING THE DATABASE PERSISTENCE OF THE PITES INTEROPERABILITY PLATFORM

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Index terms: *Data Mining, Electronic Health Record system, Learning Health System, NoSQL DBMS, Precision Medicine, Relational DBMS, semantic interoperability.*

ABSTRACT

KMSs (or EHR systems, for short) constitute one form to address the demographic and the exponential proliferation of information problems affecting world widely to the health care systems. KMSs use a dual model to store and maintain EHR extracts, in order to provide semantic interoperability between them and to be sustainable and evolutionary as medical knowledge changes and evolves. EHR systems are an excellent tool to implement Precision Medicine, which has substituted Personalized Medicine to include the important ambient aspects of the patient, not only the biogenetic information, in an individualized fashion. EHR systems are also an excellent tool to implement Evidence-based Medicine through the virtuous circle of the Learning Health System. It accelerates the process of generation of new medical knowledge and translation of new evidence. The PITES platform at the ISCIII includes an EHR system that stores, validates, anonymizes, queries and manages ISO/EN 13606 standardized EHRs and archetypes. The PITES EHR system may be utilized to conduct secondary use (research) of the standardized medical information held in the EHR extracts. Its persistence system has been evaluated comparing the relational and non-relational (NoSQL) approaches. Several experiments using 6 complexity varying queries on three size growing databases have been performed on it in order to calculate the algorithmic complexity (response times) of the two database persistence approaches. Results show linear behavior in the two methodologies, but document-based NoSQL DBMSs seem more appropriate when the size of the database is extremely high ('epidemiological' queries in research use) or in the edition and visualization of EHR extracts, considered as document-based tasks. However, each different problem and scenario requires a different database persistence solution.

1.1 STANDARDIZED INTEROPERABLE KNOWLEDGE MANAGEMENT SYSTEMS

Paradoxically, strong advances in medical knowledge have led to a considerable problem. Uninterrupted progress in medicine has made people live much longer, and require much more from the public healthcare system. In addition, these increasing

quantities of elder people are often suffering a number of different illnesses simultaneously [1].

This is a big demographic problem demanding greater resources for longer periods of time from the healthcare system, which is suffering permanent financial restrictions.

At the same time, the growing number of clinical computational devices and power has caused the generation of a huge amount of medical information which needs to be analyzed, processed and understood. However, the vast majority of this information is still wasted or misunderstood while health organizations and systems show poor agreement on how to organize, give sense, interchange or understand it. On the other hand, this phenomenon opens also the possibility to learn and extract an enormous volume of new medical knowledge. The success with these huge challenges depends more than ever on the appropriate development and intelligent use of ICT and e-Health applications.

Maintaining, communicating and understanding this huge amount of information arises severe semantic and organizational interoperability problems. World-wide efforts are being undertaken in order to resolve these problems, and they will continue in the long term [2] [3].

One way to address these issues is the design and development of standardized interoperable Knowledge Management Systems (KMS). KMSs permit to communicate and understand medical information and knowledge in the form of standardized Electronic Health Record (EHR) extracts.

Communication and understanding of medical information between such KMSs is possible since the documents they store, i.e. EHR XML extracts, are normalized following a standard such as the ISO/EN 13606 norm. Standardization permits EHR extracts to be semantically interoperable, so that any other standardized KMS can interpret and understand correctly their content.

An EHR extract is defined as a unit of communication of all or part of an EHR document and is also an instance of the ISO/EN 13606 Reference Model (RM, see below).

KMSs (or EHR systems, for short) manage, store, edit and communicate standardized medical information and constitute one method to address the demographic and information proliferation challenges discussed above. Medical information may be standardized, communicated, interpreted and understood, so that the huge amount of it generated every day, corresponding to an ever increasing number of people, may be given sense and more medical knowledge may be extracted from it. The huge amount of information problem may be reduced to treatable and understandable proportions.

1.2 ELECTRONIC HEALTH RECORDS

EHRs have been in use since the sixties, when IBM and the Children's Hospital in Akron (Ohio) collaborated in the development of a system whose main objective was to centralize and share medical information, and to improve administrative efficiency [4].

EHR KMSs or EHR systems (for short) have enormously evolved since then, and today we can see medical practitioners to introduce or query medical information from EHRs using tablets or cellular phones. However, this tremendous technological evolution has not resolved the main problem of the traditional medical record i.e. the great heterogeneity in its structure and content [5]. This great complexity is in direct relation with the extraordinary variety of biomedical knowledge, and its rapid evolution. As a consequence of this heterogeneity, different EHR systems may not interpret and understand each other.

In addition, early EHR systems used a single-level architecture, in which medical knowledge stored in the EHR was hard-wired in the software design. This means that, if medical knowledge undertakes any change due to its rapid evolution, the single-level EHR system is unable to evolve accordingly, since the software needs to be rewritten, and the whole system becomes unmaintainable in practice.

This two-fold problem has been overcome using a double-level architecture that separates medical knowledge from medical information. This architecture is usually known as the dual model and it provides semantic interoperability to EHR systems i.e. they are able to understand each other, and practical maintainability as medical knowledge evolves.

1.3 SEMANTIC INTEROPERABILITY THROUGH THE DUAL MODEL

Semantic interoperability between EHR systems and documents has been achieved normalizing then through several standards such as ISO/EN 13606, openEHR and HL7 [6] [7] [8] [9].

The ISO/EN 13606 and openEHR standards define a dual model that separates information and knowledge into two levels of abstraction. This means that EHR extracts are constructed using the building blocks provided by the ISO/EN 13606 Reference Model (RM) [10] and their semantics is defined by the constraints imposed by the ISO/EN 13606 archetypes [11] [12] [13] [14] [15] to it.

Archetypes are special data structures constraining the RM and holding medical knowledge. Now, if medical knowledge changes, only the archetypes need to be changed. Any two EHR systems sharing archetypes may interpret and understand each other. Archetypes are stored as special files written in Archetype Definition Language (ADL) [16].

1.4 PERSONALIZED MEDICINE AND PRECISION MEDICINE

The emergence some twenty years ago of new biogenetical technologies has changed the way medicine investigates illnesses and diseases, and the way patients are attended, producing huge amounts of new data of particular interest for clinical research [17].

This progress in genomic technology has brought Personalized Medicine twenty years ago. Personalized Medicine argues that a greater capacity to generate data about the patient should be translated into patient-adapted medical care.

However, genetic factors are only responsible of a reduced percentage of complex diseases (the most prevalent). As a result, progress is needed in the research of gen-ambience interactions.

Generalized in 2011, Precision Medicine overcomes the vision of Personalized Medicine, recognizing the fundamental role played by ambient factors, measured at the individual level, in the development of illnesses.

Here is where EHR extracts enter the picture, since they provide the necessary ambience information at the individual patient level. Connecting clinical assistance and scientific research, the patient-centered information of EHRs may be used to promote evidence-based medicine and to learn new useful medical knowledge, permitting the development of Precision Medicine.

1.5 LEARNING HEALTH SYSTEM

This section and its references is mainly extracted from the excellent resume provided in [5].

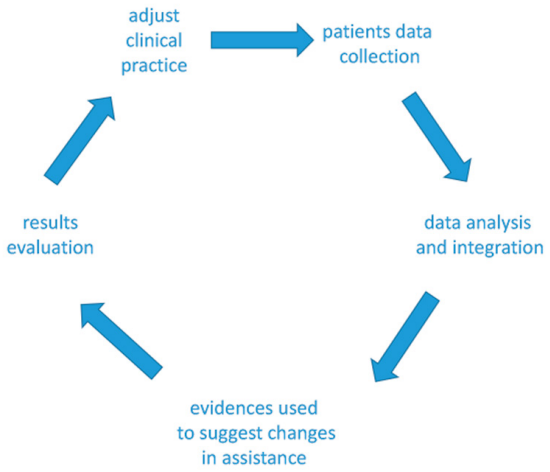
Evidence-based medicine states that medical decisions should be an objective process based on the evidences at disposal of the clinical professionals [18].

However, the process of generation of new evidences has been expensive and slow, as is the process of translational implementation of these new evidences, requiring up to 17 years [19].

The notion of Learning Health System (LHS) emerges as a way to accelerate the process of generation of new medical knowledge and translation of new evidence. It aims at a change in the healthcare system so that it is oriented to the generation of cycles of permanent improvement based on the communication between clinical practice and clinical research as shown in Figure 1 [20].

Relevant clinical knowledge should be available in the moment of patient assistance so that a meaningful use of information is performed [21].

Figure 1. The virtuous circle of the Learning Health System



LHS also promotes a cultural change in the way research is performed, since not only researchers will be the generators of working hypothesis, but also data analysis

methods will be. Learning from data will also increment reproducibility and consistency of obtained results [22]. This increments the necessity of multidisciplinary teams and the importance of Data Scientists, but also the evolution of the EHR systems in order to permit the LHS.

EHR extracts should not only store data coming from clinical practice, but also research data coming from other systems. All these data will consequently be available to be jointly exploited.

There are also initiatives to develop models to include genomic data in EHRs, such as the HL7 Clinical Genomics Working Group [23].

In addition, EHR extracts store information relating not only raw observations, but also metadata describing their structure and meaning i.e. their context and how they were obtained. This will increment considerably their capacity to be exploited and to generate new knowledge in the LHS.

1.6 THE PITES PLATFORM AT THE ISCIII

The PITES platform [24] contains as one of its subparts a standardized interoperable EHR system conforming the ISO/EN 13606 international norm. The PITES EHR system includes a standard EHR extracts and archetypes web server implemented using services-oriented architecture (SOA). The main objective of the PITES interoperable EHR system is the standardization, validation, communication, sharing and understanding clinical information in order to make a secondary i.e. research use of it.

Information coming from legacy heterogeneous non-normalized geographically disperse data warehouses may be collected and normalized at once using the powerful characteristics of the dual model i.e. the medical knowledge representation provided by archetypes.

This can be achieved using archetype-based data transformation technologies, such as the LinkEHR studio tool [25] [26]. This tool uses a mapping from the structure of the non-normalized heterogeneous information into the standard structure of archetypes to generate homogenized standardized information [27].

In order to manage all this homogenized and shared medical information for research purposes, the PITES EHR system users may:

- upload and store EHR extracts;
- validate EHR extracts;
- visualize EHR extracts;
- query EHR extracts, using standard query languages;
- download and retrieve EHR extracts;
- upload and store archetypes;
- validate archetypes;
- visualize archetypes;
- download and retrieve archetypes.

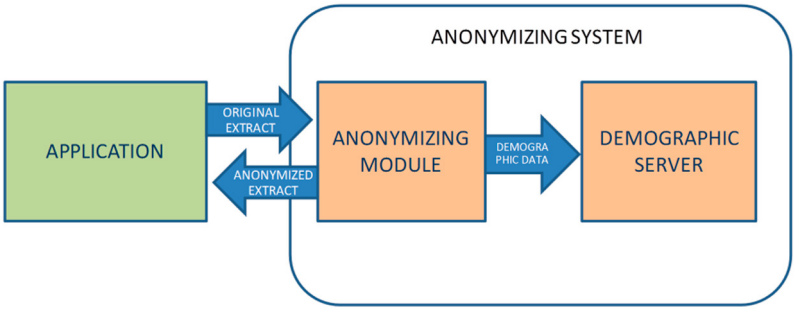
Access policies to regulate information obtainment are established and implemented. It defines the following hierarchical structure of roles:

- public user, with only basic visualization permission;
- registered user, authorized to register and visualize specific projects, and to validate EHR extracts and archetypes;
- collaborator user or system, allowed to store, validate, visualize, query and retrieve a large set of extracts and archetypes; a system can also integrate all the functionalities of those services to its own system.

Medical data as included in EHR extracts constitutes sensitive information that needs to be properly anonymized so that it may be used by third parties without the possibility of being re-identified.

A sophisticated anonymization service developed by our Unit in the PITES project [28] is featured in the EHR system. It consists of two main modules (see Figure 2, extracted from [29]): a demographic server [30] and an anonymizing module. Due to security reasons, the two modules are installed in the Information System of the organization collaborating with the EHR system. This permits that only the system of the organization where information has been generated might have access to the demographic server's data, which otherwise could dishonestly be used to re-identify the patient corresponding to a given EHR extract.

Figure 2. The structure of the anonymizing system



1.7 EXAMPLE OF SECONDARY USE OF THE EHR SYSTEM: A DATA MINING PROJECT

Our research Unit is carrying out a Data Mining project, using the EHR system, with EHR extracts data from several hospitals, including the Barcelona Clinical Hospital (HCB) and the Fuenlabrada University hospital (HUF). At the time of writing, the following hospitals were initiating this process: 12 de Octubre University Hospital, Madrid, Virgen del Rocío University Hospital (HUVR), Seville, A Coruña University Hospital Complex (CHUAC) and Barbastro Sanitary Sector (SSB).

When medical information as collected and stored in the platform is used for research, one way to gain medical knowledge from it is the extraction of so-called Association Rules. Association rules (AR) are a form of knowledge representation that can be learned from a knowledge database, using several Machine Learning algorithms [31]. They identify different regularities that underlie the dataset, and they predict different consequences and aspects, based on given antecedent facts.

Medical information from non-normalized databases is usually non-structured. It is very difficult to isolate, for instance, individual problems of patients, and also

several attributes of each problem, such as their duration, initial and final date or gravity.

Standardized clinical information might be a solution to these problems, because the medical knowledge is systematized and structured through the use of archetypes. For instance, we may isolate the problems of a patient, and understand their duration, dates or gravity, with this information being included as antecedents of association rules.

Several attributes of the problems of a patient such as initial and final dates, or severity, are encoded in the EHR extracts, and they ate queried using SQL and put together in different rows of a file.

This file is processed in order to produce a csv (comma separated values) file to be processed by an AR ML algorithm from the Weka workbench [32]. This algorithm produces an ordered list of ARs representing the medical knowledge underlying the database. When contrasted with experts' opinion and medical practice they can produce useful new medical knowledge. However medical practitioners are not going to accept it immediately [33], and more research needs to be carried out in order to optimize this process.

1.8 DATABASE PERSISTENCE OF THE PITES EHR SYSTEM

Standardized EHR extracts as those maintained in the PITES EHR system are information files that need to be stored physically in that system. The special nature of standardized medical knowledge that requires the separation into two levels of the dual model can have profound consequences on the way information in EHR documents is structured and how it gets stored logically and physically in a database management system (DBMS). The dual model used by standardized EHR documents requires the organization of the information following a specific structure, following the structure constrained by archetypes, and this structure may affect very distinctly to very different DBMSs.

1.8.1 Relational approach: Object Relational Mapping (ORM)

For decades DBMSs have been dominated by the relational paradigm [34]. This model has a well-established theoretical background based on relational calculus and algebra that has long guaranteed consistency and efficiency within database systems. However, the complex structure of the information adopted by the normalized EHR documents may cause the direct application of the relational model following this structure (Object Relational Mapping, ORM) [35] to be complicated and inefficient.

ORM maps every element of the EHR XML extract into relational tables. In order to do so, the W3C XML Schema of the ISO/EN 13606 RM is translated to a Java classes' representation using JAXB (Java XML Binding) technology, and these classes are in turn translated to a MySQL relational database using JPA (Java Persistence API). The big number of resulting relational tables induces many expensive join operations, and the query performance in terms of time response is poor.

1.8.2 Relational improvements

Relational improvements on the ORM include the openEHR Node + Path system and the archetype relational mapping (ARM) persistence solution.

Node + Path persistence [36] is based on the serialization of information objects (entire extract trees) into single blobs, requiring only one column in a relational database table. Additional indexing columns are added for attribute values in order to provide some query ability.

ARM builds a new relational database schema, different from the direct relational schema used in ORM. Information elements of an EHR extract as constrained in the archetypes are mapped into tables, key, foreign key and columns. The structure of the information in the archetypes is used to define a new relational schema.

1.8.3 NoSQL approach: document-based MongoDB

A NoSQL (Not Only SQL) database provides a mechanism for storage and retrieval of data modelled on means other than the tabular relations used in relational databases [37] [38]. A document-based NoSQL database system stores documents in any format like XML [39] or JSON (JavaScript Object Notation) [40] as data [41]. NoSQL databases may be appropriate in specific solutions, while in many others they do not substitute relational DBMSs. They store documents as entire blobs. They have no schema and do not support either joins or ACID (atomicity, consistency, isolation, durability) properties [42]. So they may be very inefficient if a subpart of a document references parts of other such documents through an indirection link, because the whole referenced document(s) must be processed sequentially [43]. However if the main task carried out by the DBMS is a document-based task, a non-relational database may be appropriate. This is because NoSQL data stores allow stored data to remain in a form that more closely approximates its true representation [42], and also because of the special persistence policies of EHR documents.

1.9 EVALUATION OF STANDARDIZED EHR DATABASE SYSTEMS

In order to evaluate the relational ORM and two NoSQL MongoDB and eXist DBMSs we have performed several experiments. We have executed six different complexity growing queries in three increasing databases of 5000, 10,000 and 20,000 extracts in order to compute the response times (algorithmic complexity) of each database. Queries were performed against problems information of each patient, which include a number of attributes such as name, initial date, resolution date or severity. Node + Path and ARM relational improvements have been evaluated from appropriate results available in the literature.

The results of these experiments may be consulted in [44]. Here we present a brief resume of the main conclusions available in that research work:

a. Relational model-based databases and NoSQL document-based databases behave linearly as database size grows. However, relational databases present a much steeper linear slope than NoSQL databases. As a direct consequence, if database size is not very big, improved relational systems behave reasonably well, but if database size is extremely high i.e. 'epidemiological' queries in secondary use (research), NoSQL databases will often be more appropriate.

b. Standardized medical information visualization and edition is a document-based task, performed on a very small subset of the whole database, and NoSQL systems fit better for several reasons, including information structure similarity, which permits manageability, and intuitive processing. Moreover, due to medical storage policies, database consistency is not compromised.

However, as a corollary, [44] concludes that there is not a 'better' persistence solution, it depends strongly on the specific situation and problem to be solved, and an appropriate solution should be adopted for each specific case.

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CHAPTER 2

IMPLEMENTATION OF AN EARLY DETECTION SERVICE FOR COPD EXACERBATIONS: EXPERIMENTAL EVALUATION FOR AN EARLY DISCHARGE, HOSPITAL-AT-HOME PROGRAMME

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Index terms: *COPD, home hospitalization, early discharge, telemonitoring.*

ABSTRACT

Objective: A telemonitoring and decision-support protocol was implemented and evaluated to provide support for an early discharge, hospital-at-home programmes for COPD patients. The evaluation aimed to show the improvement in terms of efficiency with respect to the total number of home visits, and the similarity in terms of efficacy (non-inferiority in health outcomes), satisfaction, adherence to treatment, and impact on wellbeing and daily life with respect to conventional programmes based on daily, face-to-face home care by health professionals.

Methods and procedures: We developed and deployed a telemedicine service based on a telemonitoring protocol, which enabled regular online home-based transmission of biomedical parameters and hospital-based clinical follow-up. For evaluation purposes, we conducted a randomised controlled clinical trial using 116 patients split into two groups (with intervention based on telemedicine service, and conventional control based on face-to-face visits). The main variable was time from discharge to first exacerbation, and the secondary variables were satisfaction (Satisfad10), anxiety-depression (STAI), therapeutic adherence (Morisky-Green), and impact on wellbeing and daily life (CAT). Visits took place at commencement and discharge, with follow-up at one and six months.

Results: A high proportion (95.7%) of the originally established sample size was attained (56 control, 55 intervention), with follow-up being completed by 95.7% at one month and 72% at six months. No significant differences were observed at commencement (baseline conditions; days of hospitalisation prior to the study), or in the main variable ($p=0.89$) and number of exacerbations during ($p=0.28$) or post home-hospitalisation. The difference in the total number of visits proved to be statistically significant ($p=0.0001$), i.e., 5.1 ± 2.2 for control versus 3.9 ± 1 for intervention. However, no significant differences were observed in: SATISFAD10 ($p=0.052$); CAT (baseline $p=0.07$, month $p=0.64$); STAI (state $p=0.15$, trait $p=0.55$); or Morisky-Green (baseline $p=0.7$, month $p=0.69$). Patients rated their satisfaction with the intervention as very high, and reported subjective reassurance and ease of use.

Conclusions: Given that the study has not yet been completely finalised, the telemonitoring-based, early discharge, hospital-at-home programme has succeeded in showing comparable efficacy in terms of health outcomes, adherence and satisfaction, and greater efficiency in terms of use of health resources (lower number of home visits).

Clinical impact: Implementation of this type of follow-up protocol could potentially optimise health-resource performance.

Trial registration: ClinicalTrials.gov, NCT01951261, Early Assisted Discharge for COPD Exacerbations with Telemonitoring. https://clinicaltrials.gov/ct2/show/NCT01951261

2.1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a very frequent, increasingly prevalent chronic disease. It is currently the fourth leading cause of death worldwide [1]. Moreover, future trends would appear to be clearly pessimistic [2], with the World Health Organisation (WHO) forecasting that, as from 2020, it will cause 27% of all deaths, thus ranking it in third place, only behind cardiovascular diseases and cancer, and making it the leading preventable cause of death. According to the IBERPOC [3] and EPI-SCAN studies [4], which collected data on the disease in Spain, 8-10% of the country's adult population is estimated to be suffering from COPD.

COPD has considerable repercussions at an economic and social level. Its high morbidity and related disability are often underestimated by patients and carers [5]. The disease causes continuous deterioration in the quality of life of the patient, who experiences growing difficulty in doing any type of physical activity. In European Union (EU) countries, a total of 66,155 working days per 100,000 population are lost every year as a result of respiratory tract diseases; among these, COPD is the principal cause of disease-related work absenteeism, accounting for 62.4% of this total and causing up to 35% of permanent occupational disabilities [6]. At a national level, COPD, and COPD exacerbations in particular, give rise to 10% to 12% of all primary care visits, 35% to 40% of pneumology visits, 1% to 2% of hospital emergencies, and close on 10% of hospital admissions, with a mean hospitalisation time of 10.9 days and a mean cost per episode of €450/day. Overall, COPD is reckoned to account for approximately 93,000 hospitalisations per year and 2% of the health cost. According to the Spanish Society of Pneumology and Thoracic Surgery (Sociedad Española de Neumología y Cirugía Torácica/SEPAR) and the National Council on COPD in Primary Care (Consejo Nacional sobre EPOC en Atención Primaria), the total annual cost of COPD in Spain (social, occupational and health) is estimated to be 3,000 million euros, with each COPD patient costing a total of 2,000 euros per year. It is estimated that 40% to 50% of this cost is due to hospital care, and another 40% to pharmacological treatment and oxygen therapy. In light of all these data, it is undeniable that at present, appropriate care of the COPD patient poses a challenge to the health system –primary and specialised care alike– and in particular, to pneumology departments which have to respond efficiently, thus making it necessary for available resources to be rationally tailored to healthcare demand.

The "National Health System COPD Strategy" approved by the Interterritorial Council of the National Health System (Consejo Interterritorial del Sistema Nacional

de Salud) on 3 June 2009 and published by the Ministry of Health & Social Policy [5], describes the strategic lines, objectives and recommendations to be followed in the care of this disease. The following six strategic lines of action were established: 1) prevention and early detection; 2) chronic patient care; 3) care of patients with exacerbations; 4) palliative care; 5) occupational training; and, 6) research. Within the line of action corresponding to "care of patients with exacerbations", it is recommended that programmes be developed for the care of patients with frequent exacerbations, with the principal objective being seen as the provision of appropriate treatment at home (or at the most suitable healthcare level), based on the best scientific evidence. Under the head of "research", there is a proposal to boost epidemiological, basic, clinical, and translational research into aspects of the prevention and fully integrated care of COPD. Among the principal guidelines laid down, it is recommended that research be conducted into new healthcare models for COPD exacerbations, to enable continuity of care through the use of information and communication technologies (ICT), thereby reducing the number of complications and hospital admissions, increasing the efficiency of healthcare services, and ultimately improving patients' quality of life.

The development of hospital-at-home programmes for COPD exacerbations is proposed as one possibility in the effort to rationalise health costs without detriment to healthcare quality, and achieve more humanised care by seeking to enhance the patient's socio-familial environment. In home care of COPD, the following three possibilities have traditionally been identified [7] [8]:

- Specialised continuing home care, which consists of continuing care administered to a stable patient with advanced COPD (using home oxygen therapy, mechanical ventilation, etc.), aimed at early detection and treatment of decompensations and exacerbations;
- Home hospitalisation in COPD exacerbations are programmes for non-hospital-based care within a hospital-at-home team structure, which cover healthcare necessitated by acute exacerbation, irrespective of other possible existing programmes for general healthcare. They replace the conventional hospital stay required for this process [9]. Patients are selected at hospital emergency services or outpatient care, and are then transferred home (without prior admission), with continuity of specialised medical and nursing care and appropriate healthcare equipment capable of providing 24-hour coverage [9] [10]; and,
- Early discharge, home hospitalisation for COPD exacerbations are programmes based on the structure of the same hospital-at-home team, aimed at reducing the patient's hospital stay. Patients are selected from the hospitalisation areas of pneumology and internal medicine departments [11]. Once patients have been stabilised, they are transferred home under hospitalisation conditions, until they receive their final discharge.

The latter two cases ("hospital-at-home" and "early discharge") are the scenarios targeted by this study. In both cases, current evidence indicates a higher degree of satisfaction on the part of patients and their carers, and of the health professionals involved: direct costs are decreased, compliance with treatment is improved, and hospital emergency visits and admissions in the weeks following discharge are reduced [10]. Traditionally, these scenarios are based on regular home visits by health staff. Accordingly, it would be extremely useful to have tools which made it possible,

on the basis of objective criteria, to envisage and prioritise visits which might require face-to-face actions. This study sought to investigate the combination of traditional home hospitalisation strategies, with the possibility of reliable, secure home telemonitoring of patients' biomedical parameters and vital signs with the support of follow-up and decision-support tools, in order to increase the effectiveness and safety of these programmes and, by extension, the number of patients who would benefit from early discharge, hospital-at-home programmes.

2.2 OBJECTIVES

Focusing on both strategic lines of action (prevention and early detection on the one hand, and research on the other), within the framework of the Innovation Platform for Telemedicine (Plataforma de Innovación para Telemedicina/ PITES-ISA) research project, the general goal was to implement and experimentally evaluate an ICT-based service that would provide support for out-of-hospital follow-up of COPD patients in the context of early discharge, hospital-at-home programmes.

The specific objectives were:

1. To design a general protocol for early detection of COPD exacerbations in out-of-hospital follow-up of COPD patients based on telemonitoring of biomedical parameters and decision-support procedures.

Based on the regular telemonitoring of a set of vital and clinical signs, and analysis of the trends in such parameters, a proposed health condition is automatically generated for the patient, namely, stability, moderate exacerbation, or severe exacerbation. This proposal comprises a decision-making and clinical judgement support element for health professionals.

2. To implement and deploy a telemonitoring and follow-up service for COPD patients under hospital-at-home conditions.

To design, deploy and evaluate a service that would implement the proposed out-of-hospital follow-up protocol. The service enables home-based follow-up and evaluation of the patient's health status. The service provides support for a protocol for home-based telemonitoring of vital and clinical signs, and follow-up by health professionals, using multiparametric monitoring technologies, web-based technologies, GSM networks, and the Internet.

3. To evaluate the early discharge, hospital-at-home programme for patients with exacerbated COPD supported by the telemonitoring service, with respect to traditional programmes based on regular home visits by health staff.

To design and conduct a randomised controlled trial to compare the two modalities of home-hospitalisation-programme delivery, in terms of non-inferiority in health outcomes, efficacy, satisfaction and efficiency, with analysis of variables relating to: health outcomes; use of healthcare resources (number of scheduled and extra home care visits in each arm, hospital emergency visits, unscheduled visits, hospital admissions); satisfaction; impact on wellbeing and daily life; anxiety; adherence to treatment; and compliance with the monitoring protocol evolves.

2.3 METHODS AND PROCEDURES

2.3.1 COPD patient telemonitoring protocol

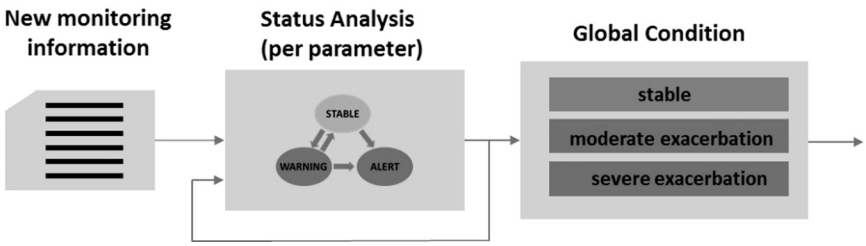
The COPD patient follow-up and control protocol sets regular monitoring of a range of biomedical parameters as a fundamental action. Using this protocol, health professionals (usually nursing staff specialised in pneumology) will make reasoned recommendations about healthcare actions, on the basis of the monitoring data received and the input of a decision-support tool which analyses changes in the patient's health condition (see Figure 1).

The protocol established three possible overall health conditions in the COPD patient:

- Stable (without change or with mild changes);
- Moderate exacerbation;
- Severe exacerbation.

Each of these conditions and the transitions between them are determined by variations in a set of biomedical parameters (vital signs and symptomatology) vis-à-vis the patient's baseline status. While the baseline status determines the patient's reference condition (stable), any improvements or deteriorations will determine stabilisation or exacerbation (and the degree of exacerbation) of COPD.

Figure 1. Monitoring protocol process



The biomedical parameters considered are of two types, namely:

- symptomatic (reported by the patient), i.e., dyspnoea, cough and expectoration; and,
- vital signs (objective values, to be monitored), i.e., temperature, oxygen saturation, breathing rate, heart rate, body mass index, and blood pressure.

The patient's baseline status is defined by the values of each of the above parameters determined under conditions of stability. Temperature is considered baseline if it is under 37 ºC (afebrile). In the case of blood pressure, whatever pressure recorded by the patient is considered baseline, provided that it is within the range of values deemed normal for the population (whether hypertensive or non-hypertensive). Body mass index (BMI) is determined at the patient's first visit, and, once a state of malnutrition or obesity has been ruled out, baseline status will be allocated to this value. At all events, it must be borne in mind that the baseline status of a COPD patient is not a constant and must be regularly re-evaluated (annually/six-monthly) or after episodes of exacerbation.

For each parameter, a status diagram is defined which determines the statuses in which the parameter can remain and the conditions of change. Three possible statuses are set for each parameter. These are:

- Stable, initially corresponding to the baseline status for the parameter in question;
- Warning, corresponding to mild changes in the parameter; and,
- Alert, corresponding to severe changes in the parameter or to the temporary persistence of mild changes (two consecutive telemonitoring sessions).

Transition conditions between statuses are defined by reference to changes in the parameter (see Table 1). In the case of clinical parameters which are of a symptomatic type (dyspnoea, cough, expectoration) and thus subject to self-reporting (subjective determination), scales and questionnaires are used; in the case of vital signs, the telemonitoring values (objective determination) and respective transition thresholds are used.

Table I. Parameter status and conditions of transition between statuses

PARAMETER	STABLE	WARNING*	ALERT
Dyspnoea (less/equal/more/much more) BMRC-ATS scale	Less/equal	More	Much more
Cough (less/equal/more/much more)	Less/equal	More	Much more
Expectoration (less/equal/more/much more) Colour changes (No/Yes)	Less/equal and No	More or Yes	Much more and Yes
Temperature (°C)	< 37°C	37-37.7°C	> 37,7°C
Blood pressure (mm/Hg) (non-diabetic) (diabetic)	≤ 139/89 ≤ 129/79	140-159/89-99 130-149/80-89	≥ 160/99 ≥ 150/90
Breathing rate (bpm)	≤ 20 bpm	21-30 bpm	> 30 bpm or > 30% (basal)
Oxygen saturation (%)	≥ 90%	87-89%	< 87%
Heart rate (bpm)	≤ 100 bpm	100-120 bpm	≥ 120 bpm
Body Mass Index, Body weight changes (kg)	≤ 0 kg	1kg /2 days 1.5kg /4 days 2.5 kg /2 weeks	1 kg /1 day 1.5 kg /2 days 2.5 kg /1 week

** Two consecutive telemonitoring sessions in warning status leads to alert status*

Once the new status for each of the monitored parameters has been determined, a combined analysis of the trend in the respective parameters' statuses is then performed. This analysis will determine a new overall health condition for the patient and, by extension, whether or not there is any need for action (see Table 2). If the stability criteria are not fulfilled, the patient is considered to be suffering from a COPD exacerbation: in such a situation, the degree of exacerbation is determined by applying the criteria to distinguish between "severe" and "moderate".

The complete process goes to form a decision-support tool, which, by way of a result, issues the recommendation to "take action" (moderate or severe exacerbation)

or, alternatively, "take no action" (stability). The final decision on "how to act" depends on the health professional and his/her clinical judgement based on personal experience and information furnished by other data sources (e.g., electronic health records).

Table II. Overall health condition based on current status of and trend in parameters

Parameter	Stable	Moderate exacerbation*	Severe exacerbation**
Dyspnoea	stable or warning	double warning or alert	Not applicable
Cough	stable or warning	double warning or alert	Not applicable
Expectoration	stable or warning	double warning or alert	Not applicable
Temperature	stable or warning	double warning	> 37,7°C and
Blood pressure	Not applicable	Not applicable	Systolic < 90 mm/Hg
Breathing rate	stable or warning	double warning	alert (direct)
Oxygen saturation	stable or warning	double warning	alert (direct)
Heart rate	stable or warning	Not applicable	alert (direct)
Body Mass Index	stable or warning	double warning or alert	Not applicable

** Double warning means two consecutive days in warning status (alert status from warning status)*
*** Alert (direct) means a direct alert status from stable, or a persistent alert status*

2.3.2 COPD patient telemonitoring protocol

2.3.2.1 Adaptation of the protocol to the early discharge, hospital-at-home programme

The proposed telemonitoring protocol is of a general nature, which means that, prior to implementing the technology, the general protocol must be adapted to the specific/local conditions of the early discharge, hospital-at-home programme. These adaptations are geared towards tailoring the protocol to the set of parameters to be telemonitored and the scheduling of the telemonitoring sessions.

The designated goal of the early discharge, hospital-at-home programme is to detect moderate and severe changes in the patient's health condition, and implement the requisite actions in a period not exceeding 24 hours. To this end, the programme establishes an intensive data-recording protocol based exclusively on vital signs, with the following characteristics:

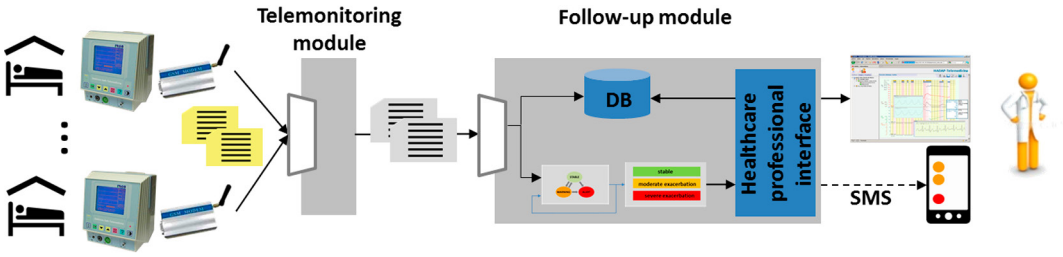
- set of parameters to be telemonitored: a subset of biomedical parameters is selected, namely, temperature, blood pressure, breathing rate, oxygen saturation and heart rate;
- telemonitoring timetable: monitoring is scheduled to take place twice a day (mornings and afternoons) throughout the home hospitalisation period.

2.3.2.2 Technological platform for support of the service

The entire process implemented by the technological platform is asynchronous (see Figure 2). Firstly, home telemonitoring is performed by the patient him/herself (or with the aid of an informal carer); the biomedical data recorded are then transmitted and received; following this, the data are automatically processed and analysed; and finally, the health professional accesses the platform to view the data using the

follow-up tools provided for this purpose. The health professional reviews the data at least once a day. However, when the system detects potential moderate or severe exacerbations in any given patient, mechanisms are triggered to alert the professionals and enable them to take whatever actions are deemed necessary.

Figure 2. Telemonitoring and follow-up platforms

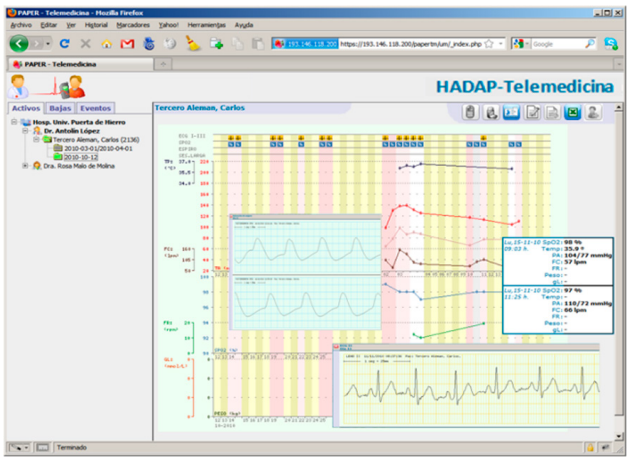


The technological platform that supports the telemonitoring service is fundamentally made up of two modules: a telemonitoring module, which manages the home component of the service, i.e., telemonitoring and shared management of any biomedical monitoring devices that are active in the home; and a follow-up module, which manages the follow-up, decision-support process and presentation of data to the health professionals. A more detailed description of each module is now given below.

- Telemonitoring module: a multiparametric SAFE® device (RGB Medical Devices) was used for biomedical monitoring. The monitor not only has the capability to record the vital signs required by the protocol, but also furnishes 3 ECG deviations (I, II, and III); the device comes equipped with a data-transmission capability over a standard GSM modem (CSD-GSM communication). Data are received in an ASCII-based proprietary file format containing caption headings and data, with information on the following: recording date and time; monitor serial number; monitor "status"; temperature, breathing rate, pulse rate, oxygen saturation and blood pressure values; and lastly, the chain with the sample sequences (8 bit/ 200Hz) of the ECG deviations. During the period of hospitalisation, each monitor is exclusively linked to a specific patient via its serial number. This module manages reception of telemonitoring sessions, analysis of parameter data, and linking of data to the respective patient. Finally, each batch of telemonitoring session data is then sent to the follow-up module for processing.
- Follow-up module: the telemonitoring data packages received are stored in the relevant patient files. The health professionals attached to the home hospitalisation programme have permanent access to a web-based application (see Figure 3), through which the following actions can be taken with regard to patient files: visualization of trends in biomedical parameters and signals; organisation of the information by hospitalisation episodes; specification of baseline status, etc.

With each new transmission of telemonitoring data, an automated data analysis is performed by the decision-support tool, generating new statuses for each parameter and a new proposal of the patient's health condition. If the patient's proposed condition is moderate or severe exacerbation, an SMS alert is texted to the designated health personnel.

Figure 3. Web-based patient follow-up application



The platform is based on "open-source" software components, i.e., apache web servers, mySQL databases and the SUSE Linux Enterprise 11SP3 operating system. Communications are channelled via the Internet (HTTPS protocol), data-reception via standard modems (4 lines enabled), and transfer of SMS via gateway software (PITES) and GSM modems. The services are distributed in 2 virtual XEN machines (telemonitoring and follow-up modules respectively) incorporated in the Carlos III Institute of Health's PITES technological platform. Health-professional access is facilitated by the HTTPS protocol and presentation of X.509v3 digital certificates.

2.3.3 Experimental study for evaluation of a hospital-at-home service

This evaluation of the early discharge, hospital-at-home service sought to corroborate the following three hypotheses (H1, H2, H3). An early discharge hospital-at-home protocol for patients with exacerbated COPD, supported by a telemonitoring and decision-support service, which enables home-based monitoring of vital signs and hospital-based follow-up of trends and progress:

H1 - yields health outcomes that are not inferior to those obtained by a traditional home hospitalisation protocol based on face-to-face regular visits by health staff;

H2 - is more efficient in terms of use of health resources than a traditional home hospitalisation protocol based on regular face-to-face visits by health staff; and,

H3 - in terms of adherence to treatment, satisfaction, and impact on wellbeing and daily life, achieves results in patients and family members similar to those achieved by the traditional home hospitalisation protocol.

To conduct the evaluation, we designed an experimental prospective study in 2 parallel groups, i.e., an intervention group (with the support of the telemonitoring service) and a control group (conventional early discharge/hospital-at-home based on face-to-face visits by health staff). The scope of study was the group of COPD patients attended at the Pneumology Department of the Puerta de Hierro University Teaching Hospital in Majadahonda (Spain). The case-definition used was, "any patient admitted to the Pneumology Department with diagnosis of exacerbated COPD, who, after an initial phase of hospital stabilisation not exceeding 4 days, fulfils the selection criteria and consents to participate in the study".

2.3.3.1 Participation criteria

The inclusion criteria were as follows: diagnosis of COPD (prior to or during admission); patients admitted due to exacerbation of infectious cause, with no age limit; absence of concomitant severe decompensated diseases that might complicate the baseline situation (pneumonia, heart failure, cancer or pulmonary embolism); clinical stability with pH>7.35, pO2>50 mmHg with O2 up to GN3 lpm, or oxygen saturation >90%, pCO2<55, with no evidence of encephalopathy; afebrile for more than 48 h; aerosoltherapy treatment with a maximum frequency of every 6 hours; IV corticoid treatment of less than 40 mg/12 h; control chest radiograph prior to discharge showing no evidence of newly apparent pathology; subjective improvement (patient); and appropriate family environment (availability of informal carer). The exclusion criteria were: neoplasms and other chronic diseases in terminal situation; alcoholism; need for IV medication; inability to understand and participate in the programme; having required admission to the ICU during admission; need for non-invasive mechanical ventilation during the exacerbation; presence of haemodynamic instability criteria; institutionalised patient. The withdrawal criteria were: at patient's request; patient's subsequent inability to use the instrumentation and technology required for the study; patient developing complications that result in readmission to hospital.

2.3.3.2 Determination of the sample

The principal hypothesis (H1) was to ascertain whether, after early discharge, the health outcomes yielded by the experimental treatment (intervention) would not be inferior to those of the reference treatment (control). Since the scientific literature puts the median exacerbation-free time of the reference treatment at 2 months [12], the "non-inferiority" condition requires that the median in the experimental group be similar. It is considered acceptable to set a "non-inferiority" limit of 0.60 units in multiplicative terms with respect to the reference treatment, i.e., to try and show that, at the very least, the experimental treatment affords a median exacerbation-free time of no less than 1.2 months. It is also assumed that the median exacerbation-free time due to other causes unrelated to the study would be 6 months. Under these conditions, it is necessary to include a minimum sample of 58 patients per treatment group (116 in all) to ensure a power of 80% and a significance level of 5%. The inclusion period is 12 months (minimum), with a maximum follow-up of 6 months.

2.3.3.3 Interventions compared

Both groups progressed through the following two phases (see Table 3): a home hospitalisation phase (from leaving hospital to discharge); and a follow-up phase, up to six months from discharge.

During the home hospitalisation phase, control-group patients were subject to the conventional protocol consisting of receiving daily home visits from the nursing staff for follow-up of their health condition. Patients in the intervention group had to perform two telemonitoring sessions daily (mornings and afternoons) autonomously (without the presence of health professionals) or with the aid of an informal carer. During the home hospitalisation phase, a minimum of three visits were made in both groups (initial, intermediate, and discharge). During the home visits (both groups), health education concepts were reinforced. In the case of the intervention group,

additional visits were scheduled only if the medical team decided to do so on the basis of the telemonitoring data received (moderate or severe exacerbations).

During the post-discharge follow-up phase, the actions in both groups were similar, i.e., follow-up visits on termination of the first and sixth months after discharge.

2.3.3.4 Study variables

The main variable was post-discharge exacerbation-free time, i.e., the length of time (in days) from discharge to the patient's first recorded exacerbation. This variable was used as reference to verify the hypothesis of non-inferiority in health outcomes (H1).

The secondary variables were targeted at verifying the hypotheses of greater efficiency (H2), and similarity in term of adherence and satisfaction (H3). Efficiency was fundamentally determined in terms of the use of health resources related with the total number of face-to-face, health staff visits (scheduled and unscheduled) maintaining a similar efficacy (H1). Mean time of home hospitalisation, unscheduled visits to hospital emergencies, primary care and readmissions occurring after discharge were likewise determined. Degree of satisfaction at discharge was ascertained using the Satisfad10 home care satisfaction questionnaire (Encuesta de satisfacción con los servicios de atención domiciliaria); in addition, a specific telemonitoring service satisfaction survey was used for the intervention group, consisting of four questions and answers on a five-point Likert scale, plus a fifth, open-ended question. Aspects of anxiety and depression were studied using the State Trait Anxiety Inventory (STAI) during the home hospitalisation phase, while impact on wellbeing and daily life was gauged using the COPD Assessment Test (CAT). The adherence analysis relating to therapeutic compliance was performed with the aid of the Morisky-Green-Levine questionnaire, at baseline and at six months; in the case of the intervention group, adherence to the telemonitoring protocol was ascertained by comparing the expected number of telemonitoring data transfers to those actually made.

The trial complied with the principles laid down by the Helsinki Declaration and was approved by the Clinical Research Ethics Committee of the Puerta de Hierro University Teaching Hospital. All patients gave their informed consent. Data confidentiality was fully guaranteed under the 1999 Data Protection Act (Ley Orgánica de Protección de Datos 15/1999).

Table III. Visits and information collected (intervention and control groups)

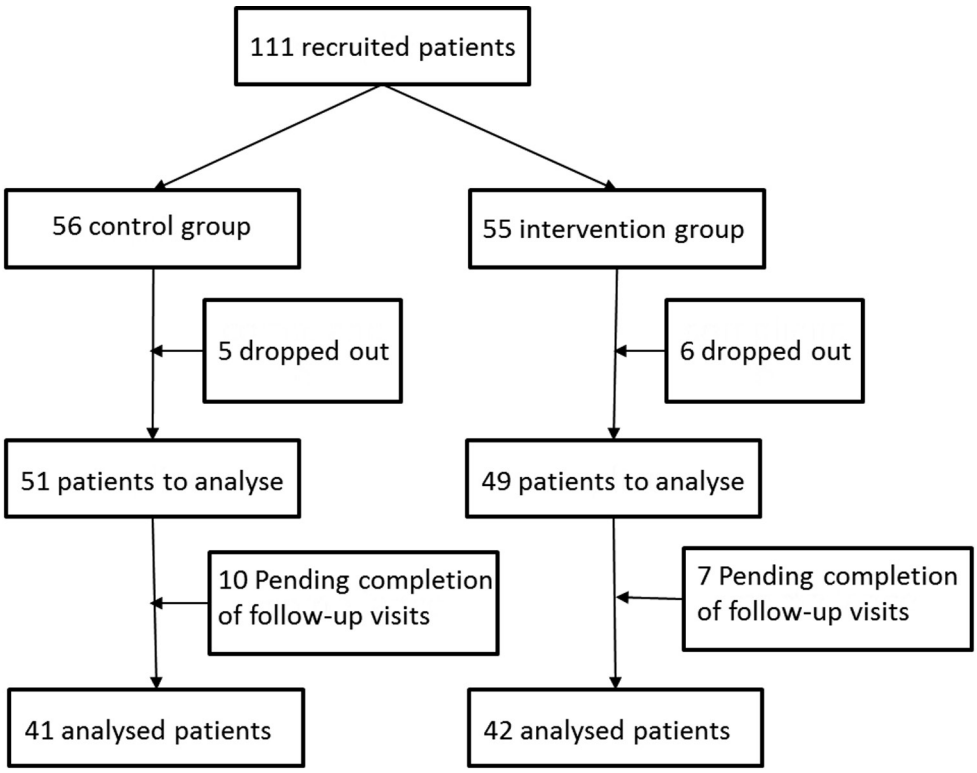
Phase	Visits	Information collected
Hospital	Initial visit	Demographic and clinical information (COPD, and other)
at Home		CAT, Morinsky-Green-Levine, STAI (S/T)
		Number of days at hospital
		Training to use telemonitoring equipment (only intervention group)
	Follow-up at home	Clinical information
	Discharge visit	Number of days at home; number of visits at home (minimum 3)
		SATISFAD, CAT, Morinsky-Green-Levine, STAI (S/T)

Phase	Visits	Information collected
Follow-up (since discharge)	1st month visit	Clinical information (COPD, and other) Number of exacerbations; number of hospital admissions CAT, Morinsky-Green-Levine
	6th month visit (final)	Clinical information (COPD, and other) Number of exacerbations; number of hospital admissions CAT, Morinsky-Green-Levine

2.4 RESULTS

To date, 95.7% of the originally established sample size (116) has been attained (111 patients: 56 control, 55 intervention), with follow-up being completed by 95.7% (111 patients) at one month and by 72% (83 patients) at 6 months. Five patients (2 control, 3 intervention) could not be located for the final visit, and 2 patients (1 control, 1 intervention) were readmitted to the home care programme before completing 6 months of follow-up, thereby also constructively withdrawing from the study. There were 2 patients in the control group and 2 in the intervention group who withdrew from the study due to the need to be readmitted during the home hospitalisation period (see Figure 4).

Figure 4. Recruitment and follow-up



There were no significant differences in demographic and baseline characteristics (see Table 3 bis). Attention should be drawn to the greater number of women with exacerbator phenotype in the control group and the higher number of active male smokers in the intervention group. There were no significant differences in satisfaction, anxiety-depression, or therapeutic compliance (see Table 4). Similarly,

there were no significant differences in the number of days of hospital admission prior to inclusion in the study, with a median of 3 days in the control group and 4 days in the intervention group.

Table III bis. Visits and information collected (intervention and control groups)

Phase	Visits	Information collected
Hospital at Home	Initial visit	Demographic and clinical information (COPD, and other) CAT, Morinsky-Green-Levine, STAI (S/T) Number of days at hospital Training to use telemonitoring equipment (only intervention group)
	Follow-up at home	Clinical information
	Discharge visit	Number of days at home; number of visits at home (minimum 3) SATISFAD, CAT, Morinsky-Green-Levine, STAI (S/T)
Follow-up (since discharge)	1st month visit	Clinical information (COPD, and other) Number of exacerbations; number of hospital admissions CAT, Morinsky-Green-Levine
	6th month visit (final)	Clinical information (COPD, and other) Number of exacerbations; number of hospital admissions CAT, Morinsky-Green-Levine

Table IV. Demographic and baseline characteristics

	Control (n=56)	Intervención(n=55)
Age (years) mean±SD	70 ±9	68 ±9
Gender, % male (n)	62,5 (35)	76 (42)
BMI (mean ±SD)	26,4 ±4,5	27 ±4,5
Smoker %, (n)	32 (18)	42 (23)
SPY (pack-year) mean±SD	54 ±24	59 ±28
Exacerbador %(n)	43 (24)	29 (16)
HOT %, (n)	32 (18)	36 (20)
FEV1 (ml),mean±SD	1224 ±504	1293 ±446
FEV1 (%),mean ±SD	51,5 ±17,5	50 ±16,5
mMRC (median, p25-p75)	2 (1-2)	2 (1-2)
BODEx (median, p25-p75)	3 (2-4)	3 (2-5)
CCI (median, p25-p75)	4,45 (3,6-6,2)	4 (3-5)

BMI: Body Mass Index; SPK: Smoking Pack Years; HOT: Home Oxygen Therapy; I: índice; FEV1: forced expiratory volume in 1 second; mMRC: modified medical research council; CCI: Charlson Comorbidity Index

With reference to the main variable "time to first exacerbation", there were no significant differences between groups, with this being 30 days in the control group and 38 days in the intervention group (p=0.89). During the follow-up phase,

exacerbations were experienced by 16 patients in the control group (42.1%) and 18 in the intervention group (55.8%) (p=0.24). In the control group there were 17 episodes of exacerbation, 4 of which required admission (23.5%); 50% had no exacerbations (p=0.28). In the intervention group there were 25 exacerbations, 11 of which required admission (44%); 50% experienced an exacerbation (p=0.28).

The duration of the home hospitalisation phase had a median of 7 days in both groups. The number of home visits by nursing staff was 5.1 ± 2.2 in the control group versus 3.9±1.0 in the intervention group, with this difference proving statistically significant (p=0.0001).

There were no significant differences in respect of satisfaction with home care services, anxiety and depression, therapeutic adherence, and impact on wellbeing and daily life (see Table 5).

The results of the telemonitoring-service satisfaction survey are shown in Table 6.

Some of the answers to the open-ended question put to the intervention group patients were as follows:

"I found it good. I felt calm. In my opinion, good. It seemed an utter miracle to him, and he liked it a lot. Instead of being in hospital, I prefer to be at home. I was well cared for. Perfect, marvellous."

"I've been happy with the device and it's really been a help to me. God forbid I should need it, but if I do, where can I call to get one?"

"She found the treatment they gave her at home sensational. It worked a treat. There's no problem whatsoever with it. I found it plain sailing."

"He liked it a lot. You feel safer, more secure. I liked it. But they were caught in a spiral of one day at home and the next in hospital. I found it great. Whoever they give to, it's a good idea. It was reassuring."

"What reassured me was that the nurse came. In general, the idea of home care seems very good to me. Very satisfied with the system. I find the device good"

"It was a godsend and it's very simple. I had a problem with the smart phone, which kept using up the battery. I liked it a lot, far better than being in hospital. It was just phenomenal."

"I'd give them 10 out of 10 for the way they treated me and the follow-up and care they gave me. If I could have it again, it'd be fantastic"

"It was good, though there were a couple of glitches in transmission. I'm very happy. It was a novel and extremely good device."

"A very comfortable formula to be at home instead of in hospital. The phone's a disaster. The smart phone has to be changed right away. It drained the battery and had poor coverage. The rest was fine."

"The device could have a better data-transmission unit built into it. When all said and done, I was pretty satisfied, I was being monitored. The device was very good but the smart phone didn't work properly."

"A more than acceptable system. I felt I was being closely monitored all the time."

With respect to the intervention group's adherence to the telemonitoring protocol, the daily average of telemonitoring sessions per patient was 2.23, exceeding the number specified by the protocol (2 sessions per day). This difference amounted to 1.61 extra telemonitoring sessions per patient during the average home hospitalisation period.

On the telemonitoring platform, 6 transmission errors were recorded. There were 17 calls to the technical service involving connection-related matters or monitor-handling problems. A total of 28 SMS alerts were sent to the health professionals, as a result of moderate exacerbations being perceived by the decision-support system.

Table V. Questionnaires

	Control	Intervention	p
SATISFAD10, median (p25-p75)	30 (27-30)	30 (28.5-30)	0.052
CAT initial, median (p25-p75)	15 (9-21)	11 (7-15)	0.07
CAT 1st month, median (p25-p75)	8 (4-11)	8 (5-15)	0.64
STAI state, median (p25-p75)	39 (15-56)	53 (23-58)	0.15
STAI trait, median (p25-p75)	40 (18,5-52)	46 (28-51)	0.55
M-G initial % compliance	78	78,5	0.7
M-G 6th month % compliance	88	84,38	0.69

CAT: COPD Assessment Test; STAI: State Trait Anxiety Inventory; M-G: Morisky- Green

Table VI. Telemonitoring service satisfaction questionnaire

Question	Answer (Likert 1-5)
1. Did you find the device difficult to use?	4,62
2. Did you need help from other people to operate the device?	1,43
3. Faced with a similar problem, would you prefer to use the device again?	4,70
4. ¿Le dio seguridad tener la máquina?	4,57

2.5 DISCUSSION

Our results suggest that protocolised telemonitoring-based home follow-up and control of patients admitted due to COPD exacerbation is as effective as conventional protocols based on face-to-face visits. No significant differences were observed in time from discharge to first exacerbation (p=0.89). Time to first exacerbation was similar and in line with data reported in the literature [12], with a higher risk of recurrence in the first 8 weeks (at 30 days in the control group and 38 days in the intervention group). We cannot say whether different results might have been obtained by prolonging telemonitoring-based follow-up beyond this risk period. Use of telemedicine services for follow-up of COPD patients has been evaluated in a number of studies, fundamentally for early detection of exacerbations during periods of disease stability. To date —as was also highlighted by our study— in no case has telemonitoring been shown to have decisively achieved greater efficacy in clinical

control than that achieved by close clinical follow-up with optimisation of treatment [13, 14, 15, 16].

Our study shows that protocolised telemonitoring-based home follow-up and control of patients admitted due to COPD exacerbation is more efficient than conventional protocols based on face-to-face visits. The telemonitoring protocol saves on home care visits without entailing any loss of efficacy (p=0.0001). The support of the telemonitoring protocol means that a home-visit planning agenda can be drawn up and managed in advance, thereby enhancing efficiency in the use of health resources and the hospital-at-home programme. Only such home visits are made as require face-to-face action by healthcare staff (detection of moderate or severe exacerbations), so that with a similar healthcare staff roster, it then becomes possible to increase the number of patients that could benefit from early discharge, hospital-at-home programmes. Other studies, such as those by Segrelles et al [17] and Cristobal Esteban et al [16], likewise highlight a significant decrease in the use of health resources, number of hospitalisations and hospital emergency visits, albeit in relation to patients with stable COPD subject to acute exacerbations. The Cochrane review conducted by MacLean [18] only showed a trend towards a decrease in the number of hospitalisations and hospital emergency visits. Continuing to focus on aspects of efficiency, according to data from the European Lung Foundation, the mean number of days of hospital admission due to COPD exacerbation stands at 10.9 [6]: using the telemonitoring protocol, this figure was reduced to less than half, with a low readmission rate (3%), something that has positive repercussions on cost-effectiveness.

Satisfaction with home care and the impact on wellbeing and daily life during the programme can be said to have been very high in both groups. In particular, patients attended via the telemonitoring service displayed good acceptance of new technologies, and felt equally well cared for despite receiving fewer home visits. Most of the patients reported the subjective feeling of reassurance that the telemonitoring service gave them (4,57), its ease of use (4,62), and their readiness to use the service again in future (4,70). Although all the patients had an informal carer at home, few needed help in carrying out the telemonitoring protocol (1,43).

Anxiety, quality of life and adherence to treatment were similar in both groups, with these improving as follow-up progressed. Other studies have similarly failed to observe any improvement in these variables, though this is not altogether comparable due to their having used other quality-of-life (SGRQ or SF-36v2) or anxiety-depression questionnaires (hospital anxiety-depression score) [13, 19, 20, 21]. Specifically, with respect to patients' adherence to the telemonitoring protocol, compliance with the two daily transmissions can be said to have been complete, even when some extra data-transfers were made at the request of the healthcare staff and others on the patients' own initiative.

As regards the decision-support system, its performance was robust and acceptable. The system triggered 28 alerts relating to the detection of decompensations in vital signs which might have been precursors of a moderate exacerbation. Nonetheless, a comprehensive analysis of the support system lay outside the study's stated objectives, since hospital-at-home conditions with a short-term (up to one week), highly intensive telemonitoring protocol such as the one proposed (2 telemonitoring sessions per day), do not provide a suitable context for conducting this type of evaluation. Studies undertaken to date report a very different methodology, ranging from sole reliance on telephone calls to monitoring of different vital signs,

maintaining a symptoms diary, and/or administering certain questionnaires [18], without sufficient scientific evidence being generated on which to base any recommendations in this respect. Accordingly, it still remains to decide which algorithm and set of biomedical parameters (vital signs and clinical symptoms) would be the best for predicting exacerbations telematically.

The telemonitoring platform performed robustly and data-transmission problems were caused by specific losses of GSM coverage at patients' homes. These problems were resolved by moving the monitor to another room in the home with greater coverage, in order to transmit the data.

Lastly, though the study was randomised, by virtue of its characteristics it involved a non-pharmacological intervention and could not be blinded. The patients selected were those whose intellectual and cognitive capacity or family support made it likely that they would able to operate the monitor, meaning that our results cannot be generalised to the whole COPD population.

2.6 CONCLUSION

Accepting the limitations imposed by the fact that the study has not yet been completed, one can nevertheless state that protocolised telemonitoring-based follow-up and control of vital signs, with medical and nursing supervision in early discharge, home hospitalisation of patients admitted due to COPD exacerbation, is as effective as conventional protocols based on face-to-face visits (without any differences in number of exacerbations, readmissions, or time to first exacerbation). The telemonitoring protocol yielded a more efficient use of staff resources (lower number of home visits and fewer days of admission), and among the patients themselves resulted in a degree of adherence, impact on wellbeing and daily life, anxiety-depression, and satisfaction similar to that of the conventional protocol.

The above-described study could encourage implementation of this type of follow-up at other hospitals, in an effort to improve healthcare by boosting self-care, enhancing adherence, and reducing in-hospital adverse events.

More quality studies are still needed in order to be able to draw up a series of recommendations with sufficient scientific evidence on the use of telemonitoring in patients with COPD exacerbations.

2.7 ACKNOWLEDGMENTS

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CHAPTER 3

SERVICIO ARAGONÉS DE SALUD: RESULTS OF THE "PITES ISA T-CUIDAENCASA: PLATFORM OF INNOVATION IN HOME EHEALTH SERVICES" PROJECT

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Index terms: *Terms: Health and social attention, chronic, health innovation, e-salud, innovation platform, palliative care, interoperability, archetypes, reference models.*

ABSTRACT

PITES-ISA is a coordinated project of a 7 nodes network, as second phase of PITES project, an innovation platform in telemedicine and e-health (PI09-90110 project and coordinated). PITES main goal was the technological innovation, based in clinical units for the development of an application environment, tools and ICT infrastructure, based on open standards, secure and accessible and interoperables; with the specific goals of developing personal mobile telemedicine and e-health solutions that support new assistant models for chronic patients and dependent people. PITES-ISA is one of this network projects of the "PITES ISA (PI12-00508) and keeps same principal goal focusing in specific goals as the definition, design and development of tools in three strategic domains: interoperability, patient security and decision support.

Objective: This article will present how the PITES ISA T-CUIDAENCASA's project promotes the collaboration among professionals on the provision of integrated care in palliative care in patients who can adapt to home hospitalization, having an attention of high quality and maintaining their clinical security, and at the same time, providing all professionals with the necessary tools to share clinical data to provide this type of assistance.

Methods and Procedures: Through the creation of a new unit for palliative care, and settling the basis for interoperable platforms to share clinical information.

Results: The Palliative Care unit has managed in 2015 130 episodes, with an average of 11 new episodes per month, 90% of the episodes belonging to patients over 65 years old. An application for the transformation of clinical discharge reports to fit the Reference Model UNE-EN ISO 13606 was developed, and successful tests were performed to send those clinical reports with the ISCIII interoperability platform.

Conclusions: Implement home hospitalization care models supported on ICT is a challenge not yet resolved by the care organizations. The need of technologies mature and secure, achieve the cooperation of actors and use of collaboration platforms, data sharing and optimum use of resources are key values that need to

be aligned to foster the sustainable home care models. There is a need to work on the interoperability of the information systems of the different care stakeholders, outside the SALUD network, in order to guarantee the continuity of the provision of the care plans.

3.1 INTRODUCTION

Population ageing and changes in lifestyle are central factors in explaining the increasing prevalence of chronic disorders, a trend that it is expected to continue over the coming decades, challenging the sustainability of health care systems worldwide. The toll that Non-Communicable Diseases (NCDs) represents for health care systems in Europe is close to 70% of the total burden and these conditions also have a dominant impact on both mortality and disabilities [1-3].

There is evidence indicating that current fragmentation of care generates avoidable inefficiencies at system level [4], perpetuates a reductionist approach to chronic disorders that precludes management of co-morbidities [5] and does not facilitate future predictive and personalized medicine.

Thus, there is an urgent need to introduce substantial changes in the way we approach delivery of care for chronic patients, as well as its articulation with social support services. This need led the World Health Organization (WHO), in 2002, to launch the Innovative Care for Chronic Conditions initiative (ICCC) [3, 6] formulating basic principles and strategies to enhance management of chronic patients.

The project was conceived to develop the practicalities of the ICCC-WHO [3, 6] acknowledging that Integrated Care Services supported by Information and Communication Technologies (ICS-ICT) [7], as enabling tools, are two core components in the new scenario.

Well-articulated innovative ICS-ICTs are proposed as a more cost-effective solution on the hypothesis that they can improve the care experiences and outcomes for patients by coordinating their care better and simultaneously promote cost-effectiveness through preventing the unnecessary use of complex care services [8-12].

The main objective of the project was to identify proper strategies for future extensive regional deployment and adoption of ICS-ICT aiming at transferring complexity from hospital to primary care and to patient home with a proper integration with community services. The intended service-focused approach adopted in the project has important implications on deployment strategies.

All four ICS-ICTs considered in the project, namely: Wellness and Rehabilitation, Enhanced Care for frail patients, Home Hospitalization and early discharge and Remote Support to primary care for diagnosis and therapy, had been previously assessed through small pilots [13-15]. The four ICS-ICTs cover a wide spectrum of care coordination with a strong focus on prevention and modulation of the disease progress.

The project was designed to explore the five factors classically recognized as barriers for deployment of ICS-ICT, namely: lack of evidence of clinical benefits, technological issues, service reimbursement, regulatory and ethical aspects and organizational factors. A systematic assessment of the results has been carried out following the methodological approach proposed in MAST [16].

In summary, the core hypothesis was that deployment of ICS-ICT may generate efficiencies at health system level that facilitate adoption and sustainability of the services. Finally, the project has contributed to generate specific strategies for extensive deployment of ICS-ICT at regional level, facilitating the generalization of the lessons learnt and contributing to the reshaping of the health systems to successfully face the challenge of chronic conditions.

3.2 METHODS AND PROCEDURES

3.2.1 Starting point: Resources available

The resources available for the palliative attention are those from the SALUD, a unit for Socio-Sanitaire Attention (UVSS), and a team for home-help (ESAD) that can act as assessment, consultancy or care unit. A psychologist of the Asociación Española Contra el Cáncer is involved for the attention of relatives of oncological patients, and the Aragon Ethical Committee for clinical research (CEICA).

Two external hospitals are involved, for admissions for palliative treatments, although without an adequate classification of the demands. Same happens on primary care resources, 061 (emergency) or the Emergency Rooms at Barbastro's Hospital, where palliative patients attend on a limit situation.

Nevertheless this amount of resources, there was no training programs oriented to professionals or relatives. There is a lack of coordination plans, or lack of organization of the demand. Additional support on psychological attention and clinical and social care was required, to create a functional group of palliative care.

Technical media was also required to deploy a program of detection of patients, with IT support to build an specific common collaborative platform, accessible by all staff at SALUD and care providers involved, and integrated with the already existing information systems.

The first step was the creation of a working group, to enhance the palliative care provided by Barbastro's Hospital, with the challenge to design a system for early detect palliative care patients and that permits the organization of rationale patients flows.

Then, the priority was to identify patients with criteria suggestive of terminal disease. In this sense, this working group began to develop a system of detection alarms on the sector, using computerized procedures, based on several criteria on oncological patients, organ diseases, dementia, AIDS, and paediatric patients.

Afterwards, a more detailed evaluation is carried out by the SocioSanitaire Attention Unit (UVSS) at the hospital level or by ESAD in Primary Care. In this sense, there are already early ICT solutions in the hospital and Primary Care related to the dependent patient –although not integrated into the SALUD IT infrastructure– that needed to be adapted before its use to register this population group.

Based on this, the personalized integrated care plan would be organized in terms of objectives, necessary resources, more adequate place of provision of services and education for families with unification of criteria regardless of the level of care.

3.2.2 Method

The first step is to establish clear and unified criteria for the consideration of patients in advanced disease situation.

Second, the Sector Palliative Care Committee was created, that works in a network and acts in a coordinated way is composed of UVSS, ESAD, a reference figure for each of the hospital services/health centers involved, with possibility of immediate telephone and telematic communication. Two coordinators for this team were appointed, one for the hospital and another for Primary Care, with management and executive capacity over decisions and resources.

Thirdly, implement care plans and an interdisciplinary work methodology without interlevel differences.

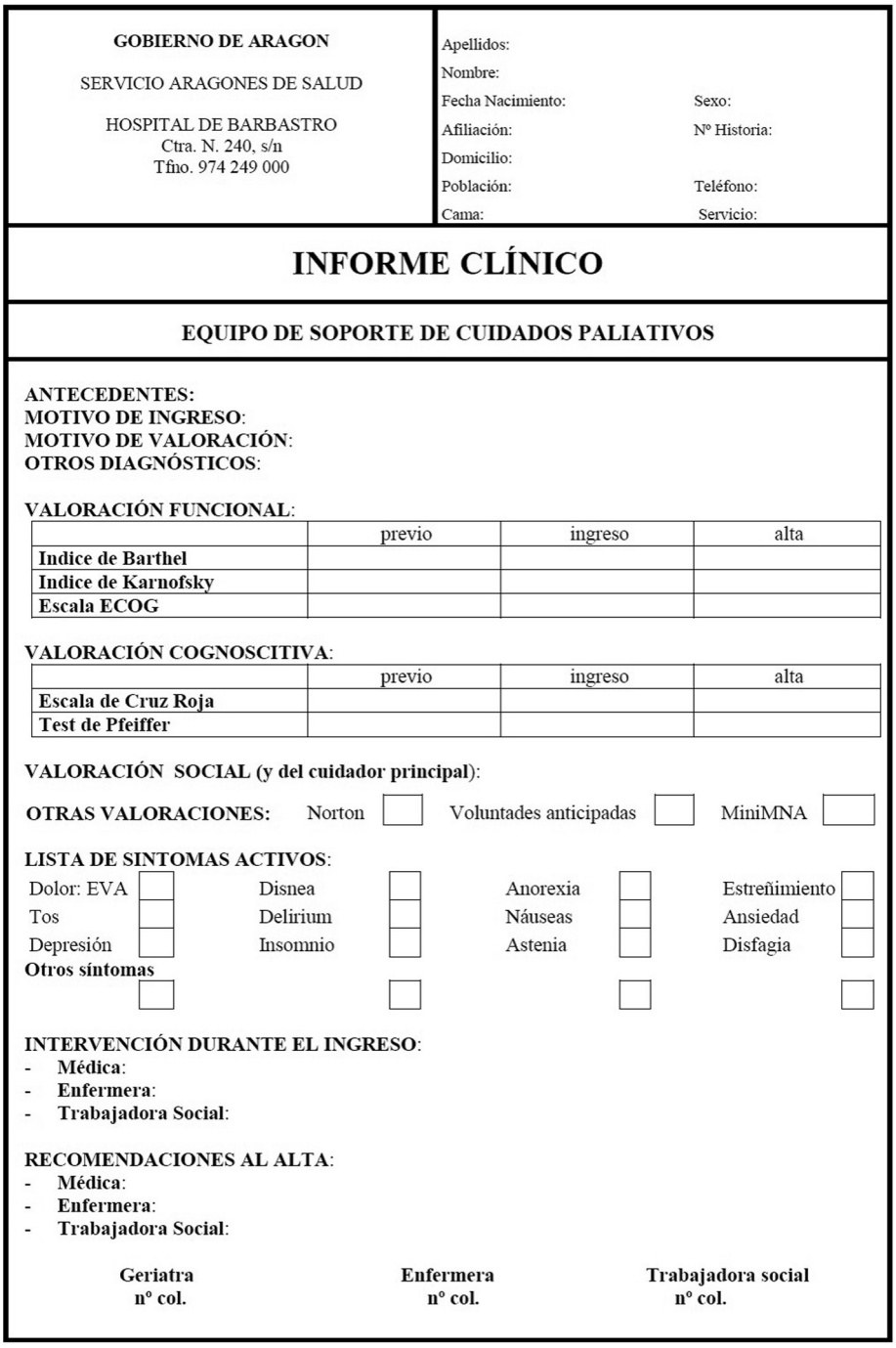
A solution was designed for the automatic detection of patients that would potentially need palliative care; based on agreed criteria between professionals of different attention levels. Moreover to this solution, an alert system and a common database accessible to the whole Health Sector in all care levels was also designed.

The initial assessment will be performed by the usual care team. Then, the harmonization of the communication and collaboration between the groups (UVSS / ESAD) and the patient responsible service, for the advanced assessment of the patients' needs.

At this step, the patient will be registered on the system as patient who meets criteria suggestive of terminal illness with complex needs, and a care plan will be created together with the care agenda. The collaborative platform gives access to the care plan and reports for all professionals (Figure 1), patient and family, by sharing the information that will permit the assurance of the continuity of the proposed measures and objectives.

A periodic review of cases and methodology will be performed by the Sector Palliative Care Committee.

Figure 1. Report from the Palliative Care Team



GOBIERNO DE ARAGON

SERVICIO ARAGONES DE SALUD

HOSPITAL DE BARBASTRO
Ctra. N. 240, s/n
Tfno. 974 249 000

Apellidos:
Nombre:
Fecha Nacimiento: Sexo:
Afiliación: Nº Historia:
Domicilio:
Población: Teléfono:
Cama: Servicio:

INFORME CLÍNICO

EQUIPO DE SOPORTE DE CUIDADOS PALIATIVOS

ANTECEDENTES:
MOTIVO DE INGRESO:
MOTIVO DE VALORACIÓN:
OTROS DIAGNÓSTICOS:

VALORACIÓN FUNCIONAL:

	previo	ingreso	alta
Indice de Barthel			
Indice de Karnofsky			
Escala ECOG			

VALORACIÓN COGNOSCITIVA:

	previo	ingreso	alta
Escala de Cruz Roja			
Test de Pfeiffer			

VALORACIÓN SOCIAL (y del cuidador principal):

OTRAS VALORACIONES: Norton ☐ Voluntades anticipadas ☐ MiniMNA ☐

LISTA DE SINTOMAS ACTIVOS:

Dolor: EVA ☐	Disnea ☐	Anorexia ☐	Estreñimiento ☐
Tos ☐	Delirium ☐	Náuseas ☐	Ansiedad ☐
Depresión ☐	Insomnio ☐	Astenia ☐	Disfagia ☐

Otros síntomas ☐ ☐ ☐ ☐

INTERVENCIÓN DURANTE EL INGRESO:
- **Médica:**
- **Enfermera:**
- **Trabajadora Social:**

RECOMENDACIONES AL ALTA:
- **Médica:**
- **Enfermera:**
- **Trabajadora Social:**

Geriatra nº col. **Enfermera nº col.** **Trabajadora social nº col.**

Finally, the dissemination of the methodology and process by specialized personnel to train other health professionals, patients and relatives of the same clinical assistance.

In order to ensure the continuity of assistance between the assistance levels, the interoperability of systems was identify as a challenge to achieve for a proper provision of home care. As a first step, Servicio Aragonés de Salud and the Palliative Care Unit identified the necessity to start the interoperability with the discharge reports.

Servicio Aragonés de Salud is aligned with the implementation of the Electronic Health Record driven by the National Health System (HCDSNS) and therefore, has

adopted the strategy of interoperability of the National Administration for the sharing of clinical information. Initials tests were performed sending the discharge reports throughout with the National Interoperability platform developed by the Institute of Health Carlos III (ISCIII), according to its double model, separating the information from the knowledge, using the Reference Model UNE-EN ISO 13606.

In this regard a first analysis of the normative, reference models and archetypes was performed. Next, SALUD adapted the discharge reports to be compliant with the normative, by modelling the information on the discharge report, into a) data structure, following the reference models, and b) the clinical data, throughout the use of the archetypes. In some case already existing archetypes —created by ISCIII— were used; some others had to be created to fit the SALUD discharge report (see Figure 2).

Figure 2. Discharge report

New archetypes were defined in ADL language (Language for the Definition of Archetypes) using the LinkEHR program and following the reference models UNE-EN ISO 13606 and ISO 21090, that would enable the sharing of information between the Barbastro Hospital with Instituto de Salud Carlos III.

These were among other:

- CEN-EN13606-COMPOSITION.AltaUrgencias (see Figure 3)
- CEN-EN13606-ENTRY.Episodio.v1
- CEN-EN13606-ENTRY.Evolucion.v1
- CEN-EN13606-SECTION.ConstantesAlta.v1
- CEN-EN13606-ENTRY.PresionSanguinea.v1

- CEN-EN13606-ENTRY.FrecuenciaCardiaca.v1
- CEN-EN13606-ENTRY.FrecuenciaRespiratoria.v1
- CEN-EN13606-ENTRY.SaturacionOxigeno.v1
- CEN-EN13606-ENTRY.Temperatura.v1
- CEN-EN13606-ENTRY.GlucosaSangre.v1
- CEN-EN13606-SECTION.AnaliticaAlta.v1
- CEN-EN13606-ENTRY.GasometriaBasal.v1
- CEN-EN13606-ENTRY.Cultivo.v1
- CEN-EN13606-SECTION.PlanificacionTratamiento.v1
- CEN-EN13606-ENTRY.Inhalador.v1
- CEN-EN13606-ENTRY.Antibiotico.v1
- CEN-EN13606-ENTRY.Antitermico.v1
- CEN-EN13606-ENTRY.Objetivo.v1
- EpisodioAltaUrgencias.xml

Figure 3. Archetype CEN-EN13606-COMPOSITION.AltaUrgencias.v1.adl

```
archetype (adl_version=1.4)
    CEN-EN13606-COMPOSITION.AltaUrgencias.v1

concept

language

description
    original_author = <
    >
    lifecycle_state = <"Draft">
    details = <
        ["es"] = <
            language = <[ISO_639-1::es]>
            purpose = <"Informe 1:  Alta de urgencias">
        >
    >

definition
    COMPOSITION[at0000] occurrences matches {1..1} matches {  -- AltaUrgencias
        content existence matches {0..1} cardinality matches {0..*; unordered; unique} matches {
        }
    }

ontology
    term_definitions = <
        ["es"] = <
            items = <
                ["at0000"] = <
                    text = <"AltaUrgencias">
                    description = <"AltaUrgencias">
                >
                ["at0001"] = <
                    text = <"Datos Episodio">
                    description = <"Datos Episodio">
                >
                ["at0002"] = <
                    text = <"Episodio">
                    description = <"Episodio">
                >
                ["at0003"] = <
                    text = <"Informe alta de urgencias">
                    description = <"Informe alta de urgencias">
                >
                ["at0004"] = <
                    text = <"Información al alta">
                    description = <"Información al alta">
                >
                ["at0005"] = <
                    text = <"Evolución">
                    description = <"Evolución">
                >
                ["at0006"] = <
                    text = <"Constantes al Alta">
                    description = <"Constantes al Alta">
                >
                ["at0007"] = <
                    text = <"Analítica al alta">
                    description = <"Analítica al alta">
                >
```

Modelling the report permitted the formal representation of the clinical concepts (both semantic and syntactic), and transfer the information, maintaining its meaning and context. Once it was done, tests were run to send that information through the ISCIII Interoperability platform.

3.3 RESULTS

The results achieved during the work performed were the creation of the Palliative Care Committee, and a protocol for home integrated care provision. The Palliative Care Unit has managed in 2015 130 episodes, with an average of 11 new episodes per month. 90% of the episodes belonging to patients over 65 years old with a resulting of 374 visits at home held and 805 phone calls.

An application for the transformation of clinical discharge reports to fit the Reference Model UNE-EN ISO 13606 was developed, and successful tests were performed to send those clinical reports with the ISCIII interoperability platform.

3.4 DISCUSSION

Implement home hospitalization care models supported on ICT is a challenge not yet resolved by the care organizations. The need of technologies mature and secure, achieve the cooperation of actors and use of collaboration platforms, data sharing and optimum use of resources are key values that need to be aligned to foster the sustainable home care models.

There is a need to work on the interoperability of the information systems of the different care stakeholders, outside the SALUD network, in order to guarantee the continuity of the provision of the care plans.

3.5 CONCLUSIONS

During the period of the project, the SALUD has achieved a double objective. On one hand enhancing the collaboration among clinical and social agents from different attention levels for the provision of integrated care at home, through the creation of a Palliative Care Unit and providing it with a collaboration platform that would fit the home care model.

On the other hand, settle the basis for the adaptation of the current platforms to transform them into interoperable systems capable to share clinical data according to the nationally-proposed standards (UNE-EN ISO 13606).

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CHAPTER 4

PITES-ISA IN ANDALUSIA: CLINICAL DECISION SUPPORT SYSTEM FOR THE PRESCRIPTION OF GENETIC TESTING IN THE GYNECOLOGICAL CANCER RISK AND SCREENING THE RISK OF THROMBOEMBOLISM DURING HOSPITALIZATION

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Index terms: *gynecological cancer, thromboembolism, Clinical Decision Support System.*

ABSTRACT

As part of the PITeS-ISA project, Virgen del Rocio University Hospital has developed a set of generic tools and services for clinical decision support based on the combination of Service Oriented Architectures and technological standards. The implemented infrastructure allowed to pilot new technological approaches that bring increased capabilities for management of medical knowledge in large healthcare providers based in a processable format. These services are based on methodologies for modeling clinical processes and decision rules that are executed through decision support engines. The project applied opensource software specialized in Decision support and the HL7 virtual Medical Record standard. This project was focused on two clinical scenarios: i) patients with the aim of standardizing the criteria for prescribing BRCA1 and BRCA2 genetic testing; ii) to calculate risk factor punctuation to monitor the risk of venous thromboembolism evolution. The combination of this infrastructure with clinical and genomic patient information from internal medicine and oncology fields were able to identify the possible benefits for patient care that will be able to incorporate personalized medicine paradigm to daily practice.

4.1 INTRODUCTION

Andalusia, a southern region of Spain, has a population of more than 8.3 million inhabitants with the Andalusian Health Public System (AHPS) as main healthcare provider. The Virgen del Rocío University Hospital (VRUH) is one of the biggest hospitals in Spain and the largest complex of the AHPS. The hospital includes a complete service portfolio to assist a basic population of more than half a million inhabitants in the Province of Seville. The hospital is a regional and national reference center for the most complex specialties and procedures, having the institutional recognition of the Andalusian and Spanish Ministries of Health. This hospital has an Electronic Health Record System with more than 1.5 million patients and more than 18 million encounters. Also, the Biomedical Informatics Group has experience in

Health Informatics Standards, Clinical Information Modelling, Interoperability, Telemedicine, Decision Support Systems and Natural Language Processing.

PITES-ISA project starts from the results of PITeS project. PITeS has allowed the effective development of a framework for the design and implementation of telemedicine services, identifying the organizational needs of the AHPS for implementation of interventions based on telemedicine for the monitoring and control of chronic patients.

Under this line of work, PITES-ISA project has contributed to the use of advanced standards about Service Oriented Architecture (SOA) in health, semantic interoperability of genomic and clinical information, and modeling of decision rules and processes, facilitating the development of clinical decision support applications. In addition, this project also seeks to demonstrate the capacity to support new delivery models of eServices by combining advanced medical informatics technologies for the representation of genomic and clinical information, the execution of clinical rules and processes, and the execution of artificial intelligence algorithms in a real care context.

According to these initial working hypotheses, PITES-ISA project has focused on developing an infrastructure based on a standard SOA architecture in health, in order to maximize scalability and flexibility. The resulting infrastructure is a generic platform to support the decision-making of clinical professionals from a set of modeling and execution of decision rules, processes and artificial intelligence electronic services. This infrastructure also includes:

A. A methodology for the modeling and implementation of rules, information and clinical processes capable of supporting the care process in any clinical domain, based on standards of representation and execution of the three entities (rules, information and processes).

B. Services of modeling, management and execution of decision rules and business processes through the Virtual Medical Record specifications of HL7 and BPMN. These services implement a knowledge base according to Evidence-Based Medicine.

C. Service of implementation of artificial intelligence algorithms that serve to establish a continuous analysis of the clinical activity through processes of Data Mining to propose new rules and to obtain a dynamic knowledge base that evolves over time.

D. Service of semantic interoperability with Electronic Health Record (EHR) and Genomic Information systems, through an intensive application of standards, to provide personalized medicine support to patients based on their genomic, clinical and family history information.

In addition, this infrastructure has been adapted and validated for the diagnosis, treatment and follow-up of patients within two clinical application scenarios:

I. Scenario 1: Screening the risk of thromboembolism during hospitalization.

II. Scenario 2: Hereditary Breast and Ovarian cancer risk integrated assessment.

Scenario 1: Screening the risk of thromboembolism during hospitalization

Clinical background: The prophylaxis of Venous Thromboembolism (VTE) in non-surgical patients is a problem that can be improved by a Clinical Practice Guideline (CPG), because of its frequency and severity, variability in clinical practice with a high level of uncertainty, high potential impact on patients, and high consumption of resources. VTE is considered responsible for 150,000 to 200,000 annual deaths in the USA, and despite the advances in its treatment, 10% deaths in the hospital environment are due to VTE, which in 75% of cases occurs in non-surgical patients. Most of these deaths are sudden or in the first two hours before treatment can be effectively instituted, so prophylaxis is the key action in this problem, which can affect both inpatients and outpatients.

The main expected benefit is the reduction of VTE and deaths in patients with non-surgical processes. A meta-analysis evaluating clinical trials on prophylaxis in medical patients estimates that is possible a relative reduction of 56% in deep venous thrombosis (DVT) and 52% in pulmonary embolism (PE) with the use of different heparins, without leading to a significant increase in the development of severe bleeding, which would be the main drawback of this intervention. The cost of prophylaxis with low-molecular-weight heparin in different studies in 2002 ranges from $1,248 to $3,088 for each avoided VTE, so it can be considered a cost-effective measure.

Nowadays, healthcare professionals from AHPS use a simple desktop application that calculates VTE risk factor without any integration with EHR system. This application is an electronic version of the National PRETEMED guideline [1] for thromboprophylaxis, a clinical practice guide based on the evidence, on the prevention of VTE in Medical Pathology.

Scenario 2: Hereditary Breast and Ovarian cancer risk integrated assessment

Clinical background: Currently, Breast Cancer (BC) is the most common tumor which affects to women in the western world, and Ovarian Cancer (OC) is the fifth. Besides, there are many difficulties in its diagnosis and its treatment which imply a high mortality, greater than 50% at 5 years since diagnosis. The International Agency for Research on Cancer estimated a worldwide incidence of 1.67 million new cases diagnosed per year in BC and over 0.23 million in OC [2]. Though the appearance of these tumors is usually sporadic, around 10-15% of diagnosed cases are heritable. BRCA1 and BRCA2 genes described germinal mutations which are inherited dominantly and with a high penetrance in 7% of BC and about in 11-15% of OC [3]. In fact, BRCA1 and BRCA2 mutations increase the risk of developing a BC and/or an OC. Concretely; people with BRCA1 mutations have a 57% risk of developing BC, and have more than 40% of developing OC. For BRCA2 mutations, the risk is 49% in BC, and of 18% in OC [4-6].

On the other hand, another significant element is its behavior pattern. Hereditary gynecologic cancer usually starts in younger people while this trend is not usual for sporadic cancer. Due to it, it is important for people with family history to know the risk of developing hereditary cancer because if the risk is unknown, it might increase anxiety and concern to our patients.

We should also point out that the treatment received by our patients depends on the BRCA1 and BRCA2 gene mutation. If the mutation is positive, patients will receive

monitoring or preventative measures. On the other hand, If the result is negative, it will decrease the anxiety level of our patient. In this sense, there are some studies which demonstrated that patients are benefited by the genetic testing results [7-9] because they found out a significant decrease in patient concern about developing this kind of cancer. However, these genetic tests have a high cost to the healthcare system. In addition, several studies in the literature indicate that performing these genetic tests to the population is not cost-efficient [10]. In this sense, we have to define criteria to identify patients with high risk for developing these mutations in order to prescribe them these genetic tests. For this purpose, there has to be a consensus between the scientific society and the official organization in the definition of these criteria [11]. Nowadays, genetic tests are only recommended for patients with previous family and personal history. We believe that provide to clinicians a Clinical Decision Support System (CDSS) to improve the performance of genetic testing is the key to optimize the prescription of this kind of tests.

Decision Support Systems: generally speaking, decision support systems (DSS) are computer systems used as support for the decision-making process which are chosen among different alternatives obtained from estimates of values. The main characteristic of DSS is the ability to multidimensional analysis that allows enhancing the information until to reach a high level of detail, to analyze the data from different perspectives, to make projections of information for future prognosis and to provide alternatives. During the last years, several rendering technologies such as GLIF, Guide, Asbru, GASTON, GLARE, HELEN, PROforma and SAGE as Electronic Clinical Guidelines (ECG) have been applied. A recent review of the state of the art emphasizes that these technologies must advance in the interaction of ECGs with the basic clinical knowledge to allow adaptation to the specific case of the patient in the management of their diseases [12].

The control and management of clinical knowledge applied to DSSs complementary to the EHR has been presented as a recommended strategy for large healthcare providers because it allows better management of clinical knowledge [13]. In addition, the new European directive for the certification of medical devices specifies that all software with algorithms or intelligence, whose objective is to facilitate the decision-making process in the clinical domain, must be certified [14]. From the point of view of the latest generation of computer architecture, SOA is proposed as a viable option to incorporate all clinical information complementary to the EHR to support personalized medicine [15].

In the USA, the Agency for Quality and Research has developed, among other projects, Health eDecision that has defined the technological infrastructure on which to implement DSS as a complement to EHR systems. This proposal is based on (i) the service-oriented architecture specification in Health defined by HL7 and OMG for the deployment of decision support services [16] and (ii) the Virtual Medical Record (VMR) standard from a rigorous analysis of the market for such tools [17]. These emerging standards are being materialized in the OpenCDS initiative [18]. In other areas, the topic is reviewed in depth [19] looking for new computational paradigms to represent, use and acquire biomedical knowledge [20].

Terminology: One of the large benefits obtained from introducing interoperability inside healthcare environments is the patient safety improvement. Interoperability also facilitates that information linked to the patient has not to be inspected manually

and reduces the number of times that the same information needs to be processed or recorded by different systems or professionals.

Incorporating Clinical Decision Support Systems within clinician workflows is one of the main strategies for preventing decision errors in healthcare environments e.g. prescription errors [21]. They help health professionals to be provided with clinical information and recommendations based on clinical practice guidelines and medical experience and evidence [22]. In order to maximise the benefits from the adoption of CDSS, it is recommended to include knowledge management strategies that support knowledge evolution on regular bases [23].

4.2 METHODS AND PROCEDURES

The preference for open source tools has been considered as a strategy, these are IT tools distributed throughout developers and users communities under the conditions described in the GNU, GPL1 and similar exploitation licenses. Under this perspective, the components that have been integrated within the PITeS-ISA platform were decided. This decision was in keeping to the strategy of the research group of developing technology built upon open source applications with the aim of not remain bound to proprietary solutions including paid licenses that could burden the mid- and long-term development of research-driven technological products from an economic point of view.

According to the literature, national initiatives for setting-up a Clinical Decision Support System able to provide clinicians with improved capacities for disease prevention, diagnosis and therapy planning have been developed [24]. According to this research, five main requirements must be met when designing and developing the technical infrastructure on a large scale:

- Availability of a centrally managed repository for hosting the computer-interpretable knowledge. This project has developed a Knowledge Repository (KR) which includes the Knowledge Modules (KM) or decision rules. This KR has been built upon the JBoss Drools Guvnor authoring management tool.
- Information needed for providing Clinical Decision Support must be standardized. In our case, information exchanged between the regional EHR and the PITeS_ISA platform is performed according to the HL7 v2 standard, including all the needed clinical information for executing the rules (clinical observations, problems, adverse reactions, active prescriptions, clinical consultations, diagnoses and procedures)
- Representation of patient information must also be standardized. EHR information has been harmonized according to the virtual Medical Record (vMR) standard. Furthermore, clinical information hosted in the EHR has been coded according to ICD-9, NANDA, and local terminologies.
- To standardize how to leverage computer-interpretable KRs and patient information in order to guide clinical decision-making. In this sense, the PITeS-ISA project made use of the OpenCDS [25] clinical decision support service aiming at evaluating vMR modeled patient data, thus generating patient-specific conclusions based on KMs within the frame provided by the KR. Connections and mappings between HL7 v2 messages and vMR standard has been carried out making use of the Mirth Connect [26] open source Enterprise Service Bus.

- Finally, a standardized strategy must drive the location and retrieval of patient data across different health information systems. According to this requirement, all the elements of the developed infrastructure have been integrated with the regional EHR system, thus allowing a seamless health information exchange from other health information systems in keeping with local security and privacy standards [27].

From a methodological point of view, to address the first scenario, several phases are required:

- Phase 1: Modeling the clinical process. For this purpose, a tool is used to model processes using the BPMN 2.0 standard language or an extension to BPMN 2.0.
- Phase 2: To identify the elements of the relevant information for feeding the rules. The possibility of modeling information either as archetypes or ontology, has been evaluated.
- Phase 3: To model clinical decision support rules and allow its access in the point of care, triggering alerts and recommendations as needed by the health professionals. The modeled process addresses this phase, integrating it in the clinical decision support system mentioned in phase 2.

Scenario 1: Screening the risk of thromboembolism during hospitalization

In this scenario, a clinical decision support system was developed based on a stratification of patient risk of suffering Venous Thromboembolic Disease (VTD).

Clinical description:

Target Population. - Patients discharged from any medical unit at the Hospital Universitario Virgen del Rocío in Seville.

Involved processes. -Translated from a process point of view, we should consider the following items:

- The scope of action: Specialized Care.
- Input Limit: Moment in which a subject is admitted to the hospital and has a high risk of thromboembolism.
- Output Limit: Subject with a thromboembolism medically and/or surgically treated.
- Marginal Limit: When one of the following conditions is met:
  - Discharged from hospital.
  - Moved to another unit.
  - The subject is deceased.

The Andalusian Health System provides several care processes to manage the thromboembolic pathology, such as the "Integrated pulmonary thromboembolism" care process.

Objectives and clinical impact:

Objectives:

- To analyze the impact of the implementation of an alert system to control the risk of VTD in hospitalized patients.

- To evaluate the effect on the incidence and mortality of hospital-acquired VTD.
- To analyze the variability on the indications of VTD in hospitalized patients.

Clinical Impact: Nowadays, VTD is the most frequent avoidable cause of death in hospitals. Thanks to the decision support system in this scenario, we improved the knowledge about the prevalence of risk factors for the development of VTD in non-surgical patients, the adequacy of the VTD indication, and the impact of a strategy of change in clinical practice based on the use of information and communication technologies. Thanks to this, specific actions of great impact could be further developed to reduce the morbidity and mortality associated with this disease and, therefore, continuously improve the safety and efficiency of hospital health services.

Scenario 2: Hereditary breast and ovarian cancer risk integrated assessment

Clinical overview: PITeS ISA project addresses the development and validation of specific decision support applications for diagnostic, treatment and follow-up of breast cancer patients.

Involved processes: These are the set of preventive, diagnostic and follow-up activities aiming to an integral management of subjects presenting health issues, symptoms and clinical findings through imaging diagnostic tests displaying lessons with suspected malignancy, as well as those subjects at high risk of developing breast cancer in the future, coming from any of the clinical areas: Primary Care, Specialised/ Hospital Care and/or Breast Cancer Early Detection Program.

Target population:

Inclusion criteria.

- Subjects attending primary care/gynecology consultations concerned about the risk of developing breast and/or hereditary ovarian cancer in the future given their personal and family background.
- Subjects suffering breast and/or ovarian cancer.
- Subjects considered by the physician in high risk of developing hereditary breast/ovarian cancer in the future, disregarding the health issue in consultation. A subject in high risk of developing this disease is considered when:
  - Previous breast biopsy and positive histopathological result for: atypical ductal hyperplasia, lobulillar neoplasia, papillary lesson or typical ductal hyperplasia in postmenopausal subjects.
  - Subjects with a background of chest radiation throughout the adolescence.
  - Subjects with a familial history of breast and/or ovarian cancer.

Objectives and clinical impact:

The main objective was to provide health professionals with an adequate support when making decisions regarding the diagnostic procedure, adding safety and quality to their performance. Moreover, the technological development of these tools has provided a set of personalized information that could also inform the patient during the shared decision-making process regarding the treatment procedures to be in keeping with their personal preferences in case several therapeutic options are available.

These validated decision support tools are endorsing the evidence about their daily utility in a healthcare environment in several domains: establishing novel

recommendations in the clinical practice, increasing patient's safety, avoiding clinical variability, optimizing the diagnostic process, supporting decision-making for professionals and patients, etc. As a result, improvements in healthcare quality and an optimization of resources and healthcare times were expected, thus implying economic savings and better health outcomes in the healthcare system. All the information generated is available for its exploitation oriented towards research, thus driving the discovery of new clinical knowledge.

Integrating these tools with patients' genomic information has allowed the application of the personalized medicine paradigm within the risk assessment domain. Artificial Intelligence (AI) technologies have been incorporated in order to set up new evidence regarding prognostic factors for the risk of suffering a disease, thus enabling the activation of adequate measures for each clinical case based on this new knowledge.

4.3 RESULTS

Scenario 1: Screening the risk of thromboembolism during hospitalization

In this scenario, we developed a semantic-interoperable Clinical Decision Support Infrastructure based on a computer-interpretable medical knowledge repository. We also analyzed the benefits of integrating a Terminology Server [28] and validated the system in a case study related to patients with thromboembolism. Besides, we measured the potential impact of this system in order to improve the patient safety.

The developed infrastructure includes the following components:

- A Clinical Decision Support (CDS) Knowledge Management Framework which allows us to define and manage decision support rules.
- A Clinical Decision Support engine which integrates the clinical information of the patients and executes the decision support rule in order to generate recommendations to the clinicians from a Knowledge Module.
- A Terminology Support Framework to maintain the content of medical vocabularies and the mappings from one vocabulary to another.

As part of the developed CDSS, we integrated a KM which stores a set of rules written according to the Clinical Guideline that determine patient's risk of VTE. Besides the risk score, the CDSS allows clinicians the access to the active patient prescription, diagnosis and procedures list. Our CDSS is integrated with some of the web services published by the regional EHR to collect information about patient's history. The information exchange with the regional EHR is based on HL7 v2 messages. To ensure the integration of this information within our CDSS infrastructure, we mapped the HL7 v2 records to the Virtual Medical Record (vMR) structure. Then, the new message is sent to the open source initiative known as OpenCDS. Though OpenCDS, we are able to execute the decision support rules through a set of web services to implement the communication interface between the different components of our infrastructure, we made use of an open source Enterprise Service Bus known as Mirth Connect.

We used a Knowledge Management Framework to define and create a Knowledge Repository. This framework is integrated with the CDS engine to evaluate decision support rules based on the information stored in this KR. A centrally managed repository of computer-processable knowledge was developed to integrate the

different knowledge modules, also known as rules. These rules were designed using the JBoss Drools Guvnor software, which provided us an easy interface to define the different decision support rules into a central Knowledge Repository. By means of the Guvnor software, we were able to translate the Clinical Knowledge into clinical decision support rules to be executed by the CDSS.

On the other hand, we also integrated a Terminology Management System (TMS) to use and maintain large standard (ICD-9, NANDA, etc.) and local terminologies (active ingredients, drugs, etc.). This system allows us to ease the mapping process between concepts identified into our regional EHR and associate them to the OpenCDS reference code system.

To implement this system, we chose the CTS open-source implementation study case, Apelon [29]. With the deployment of a local instance of Apelon inside our regional CDSS infrastructure we were able to:

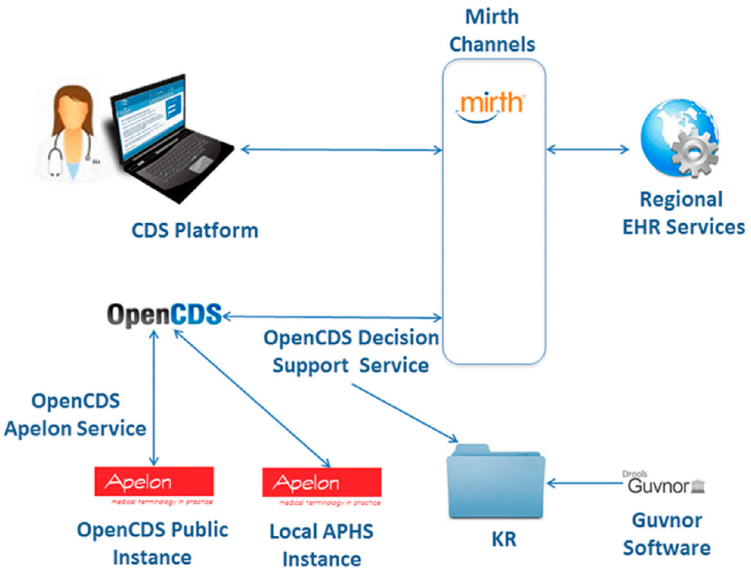
- Manage the concepts defined for the AHPS local terminology;
- Import standard terminologies such as ICD-9 and ICD-10;
- Define mappings between OpenCDS concept codes and other terminologies concept codes.

Clinical concepts included within the decision rules are also defined into a OpenCDS terminology, which is stored and maintained in a publicly accessible Apelon instance, an open source Terminology Server. We also include a local AHPS Apelon instance. Other code systems should be loaded inside the local Andalusian Health System Apelon instance to ease mappings between local set of codes and OpenCDS reference code system.

In Figure 1, it is shown the infrastructure of the CDSS developed for this scenario.

The evaluation results are shown to the clinicians through an user interface including additional information related to the patient such as problems, active prescriptions, diagnoses and procedures. On the other hand, this interface also includes information related to the model proposed in the inSPECt tool (Interactive Portal for Evaluating Surveillance Clinical decision support) [30].

Figure 1. Technological Architecture for the scenario 1



Scenario 2: Hereditary Breast and Ovarian cancer risk integrated assessment

The development of a Clinical Decisions Support System to evaluate hereditary breast and ovarian cancer risk provides support to clinicians about medical prescription of genetic testing for BRCA1 and BRCA2 mutations. As part of the PITES-ISA approach, the solution developed in this scenario is based on the integration of open source tools [31], promoting the use of a service-oriented architecture and interoperability standards defined by HL7 such as Virtual Medical Record (vMR)) and OMG [32]. There were designed the decision support rules needed to identify the level of risk of possible existence of BRCA1 or BRCA2 gene mutation and the minimum set of information for executing these rules. The system also generates additional documents with information about the evaluated patient and the final recommendation provided by the CDSS. According to the level of risk, we identify two different cases:

- Patients with low level of risk receive a document with general recommendations which are similar to the information provided to healthy population.
- Patients with high level of risk receive additional information associated with their risk to develop this kind of cancer, in addition to offer them the possibility to be derived to the hereditary familial Gynecological Pathology Consultation for proper genetic counseling and request a genetic test.

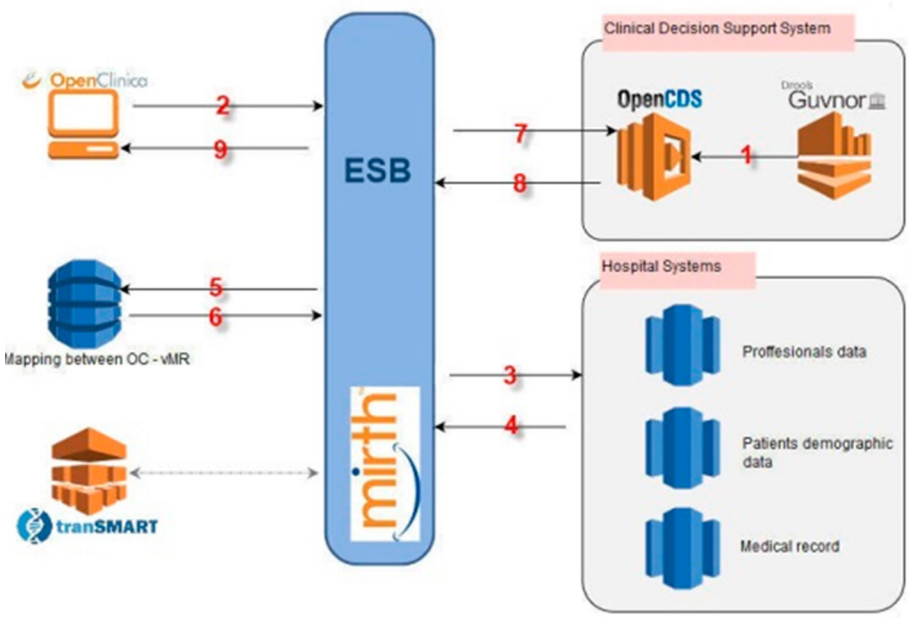
The minimum set of data and decision support rules integrated into the CDSS were designed taking into account the guideline defined by Spanish Society of Medical Oncology [33]. The rules designed in this scenario evaluates patient risk and recommends the performance of a genetic test according to the information registered by the clinicians joint with additional information gathered from the regional EHR. According to the SEOM guideline and the experience of the Gynecological Unit of the Virgen del Rocio University Hospital, we have implemented the following rules clustered in two groups:

- Patient with Breast Cancer (BC) or Ovarian Cancer (OC): Woman diagnosed with papillary serous OC of high grade; or woman diagnosed of BC before 30 years old; or woman diagnosed of BC and OC; or woman diagnosed with bilateral BC, when one of the tumor was before 40 years old; or woman diagnosed with triple negative BC before 50 years old; or men diagnosed with BC.
- Undiagnosed patient of cancer. Woman with 2 cases of cancer in first degree relatives and also: one of the tumors was diagnosed before 50 years old; or there was one relative with BC and OC; or there was one male relative with BC and there was another relative with BC or OC; or there were 3 or more relatives with BC were at least 2 of them were first-degree relatives.

In order to generation of new hypotheses and rules in the future, additional information is also registered in the CDSS such as age of diagnosis in case the patient has BC or OC, first and second degree relatives with BRCA1 or BRCA2 mutations (name and type of the mutation using Human Genome Variation Society) and relatives with any kind of tumors (type, age of diagnosis and kinship).

The technological infrastructure developed in this scenario follows an architecture similar to the figure 2.

Figure 2. Technological Architecture for the scenario 2



As is shown in the diagram, the central node of the infrastructure makes use of an Enterprise Service Bus (ESB). Through this ESB, which is based on the open source tool Mirth Connect, we implemented the communication layer between the different components included in the CDSS. Among these components, we highlight the following ones:

- A Clinical Trial Management System (CTMS) is included to provide the user interface to the health professionals. By means of this module, we are able to register clinical information about patients through electro forms. This system also provides the capability to launch the rule to be evaluated by the CDS engine and show the recommendation generated by the CDSS.
- A decision support engine, implemented by means of openCDS initiative, executes the different rules mentioned above and provides a recommendation associated with the level of risk calculated for a specific patient. To execute the rule in OpenCDS the call is automatically generated by Mirth Connect which gather all the information recorded in the CTMS and include additional information extracted from the Hospital Systems. With all this data, the ESB builds a message which follows the vMR reference model and calls an OpenCDS service to validate the rule.
- A rule modeler based on the JBoss Drools Guvnor software. This software imports the vMR schema and allows us to design and model decision support rules. Once these rules are defined, they are accessible through OpenCDS.
- A biomedical research datawarehouse (tranSMART), a unified database which integrates all the clinical information from different data sources such as the CTMS and the regional EHR. This software provides clinicians the capabilities to search, view, and analyze all data stored within.

In the figure 3, the user interface is presented to show how the information is registered in PITES-ISA system and how the recommendation is presented to the clinicians.

Once the user records all the information about the patient, it is possible to launch the CDSS in order to get a recommendation about medical prescription of genetic testing for BRCA1 and BRCA2 mutations. The following screenshot (see

figure 4) shows that the interface is divided in three different parts (from top to bottom): one for describing the different values for each rule implemented in the CDSS; another one to show the final result and the recommendation provided by the PITES-ISA system; and one more to register the final decision of the clinician where you can specify if you finally decide to derive or not the patient to the Genetic Unit.

Figure 3. User interface to register clinical data in the scenario 2

Figure 4. Screenshot with recommendation associated to the scenario 2

4.4 DISCUSSION

The project was able to design a CDSS for complex rules and found limitations in the existing open source initiatives such as OpenCDS and Guvnor. Based on the experience carried out in this project, it was possible to identify alternatives that were above the state of the art technological approaches presented in this field. We believe that an approach based on developing a rule engine through the Mirth Connect Enterprise Service Bus allowed further versatility than specific tools just focused on the implemented vMR standard. Likewise, this project was able to design and implement a set of services were designed focused on patient evaluation and communicating the patient results. This IT infrastructure is able to manage the clinical knowledge in a computable standard format to generate patient specific recommendations. The defined Service Oriented Architecture was able to allow the evolution of EHR systems and patient registries without being dependent of the decision support rules implemented. As it is described in the recommendations for national infrastructures proposed by Kawamoto (2009) this change of paradigm provides benefits for large healthcare providers.

The technological solution developed in this project was able to provide new capabilities that were not previously available in the Andalusian Health Service IT infrastructure. As a consequence, there existing infrastructure was not able to provide the required flexibility to cope with the medical knowledge evolution. Every year there are new releases of multiple integrated care plans specifying the recommended practices for providing coordinated care in the most relevant diseases, but IT systems were not able to incorporate new requirements defined as essential for patient care in a reasonable period. The low flexibility provided by the existing EHR systems represented a problem that made highly expensive to satisfy the required changes in patient care. The presented research allowed developing multiple generic components that will be able to be applied for the design and implementation of Decision Support Systems. As a result, it is expected that the developed infrastructure will allow reducing the cost associated with the implementation of rules and algorithms that ensure the evaluation of patients according to the recommended best practice.

The inclusion of a terminology server as part of the IT infrastructure provides the benefit for consistent management of concepts between multiple systems applied in large healthcare organizations. Through the designed federated architecture multiple systems will be able to update the definition of concepts applicable in our organization. our TS offers benefits to existing terminology management services such as better management of mappings from one vocabulary to another, support the transition from one terminology version to an updated one and to provide a standardized interface for the usage and management of terminologies.

Thanks to the integration of the CDSS in an EHR infrastructure, patient information doesn't need to be rewritten. Moreover, the CDSS implemented gives more context information providing a better decision to the physician. The project was able to demonstrate how this architecture could be applied to calculate risk factor punctuation to monitor the risk of VTE evolution throughout the time and the early detection of breast and ovarian cancer.

The OpenCDS initiative was based on the vMR specification for modeling the decision support rules. As part of this project, there were identified limitations in vMR to cover all the necessary concepts and entities in a health scenario. It was

identified that vMR is presented in an abstract way that, although it is very interesting in a conceptual point of view, it might be difficult to manage. As a consequence, the rule modeling process for a real scenario using vMR and a mapping process between OpenClinica and vMR format have been very hard tasks. The performed research is expected to be continued with the incorporation of new technological standards. The Health Level Seven International Foundation has recently approved the Fast Healthcare Interoperability Resources (FHIR) standard [34] as a new communication specification that aimed to provide standardized resources for healthcare communication. Based on the multiple tools developed this standard got a high support from EHR and eHealth vendors. Although this initiative has designed a set of FHIR resources for clinical decision support they are still are in a low maturity level. It is expected that new open source initiatives like CDSHooks [35] will guide the evolution of how this standard will be defined in the near future. As a result, it is expected that the methodology applied for implementing the PITeS-ISA platform will continue to be applicable.

4.5 CONCLUSIONS

This project was able to implement an IT infrastructure focused on implementing CDSS based on the management of decision rules and clinical concepts through the combination of terminology server and CDS Engine. The identified limitations from the existing technological standards could lead to new international collaborations for defining new technological approaches that incorporate tools for implementing them. The project was piloted with a sample of patients with the aim of standardizing the criteria for prescribing BRCA1 and BRCA2 genetic testing.

4.6 ACKNOWLEDGMENTS

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CHAPTER 5

PITES-ISA IN CATALONIA: INNOVATION IN INTEGRATED CARE SERVICES FOR CHRONIC PATIENTS

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Index terms: Coordinated Care, Chronic Diseases, Co-morbidity, Physical Activity, eHealth, Adaptive Case Management.

ABSTRACT

Objectives: The PITES-ISA node in Catalonia focuses on integrated care services for chronic patients with a personalized medicine foundation and a three-fold objective: i) Regional deployment of healthcare services; ii) Catalan test-bed for international leadership as 4-star EIP-AHA reference site; and iii) Transfer and exploitation of new products and services, which generate return value to the healthcare sector.

Methods and Procedures: PITES-ISA in Catalonia operates through five main strategic actions, among which three focus on implementing regional level innovative care services: A1) Collaborative lung function testing for early diagnosis of chronic diseases in primary care; A2) Self-management empowerment for healthy lifestyles; and, A3) Collaborative management of complex chronic patients. The other two strategic actions develop functionalities for: A4) Technological and organizational support following an adaptive case management approach, and A5) Comprehensive clinically-applicable and subject-specific health risk assessment for patient stratification. The project follows a co-design approach to ensure fit-for-purpose solutions.

Results: Major project results are: (i) Regional implementation of enhanced quality and accessibility of lung function testing across the health system; (ii) A randomized controlled trial on a pre-habilitation intervention in high risk candidates for major surgery has demonstrated efficacy. The program, as well as its extension to lower risk patients, is being deployed as mainstream services for candidate patients to assess cost-effectiveness; (iii) Implementation science strategies have been designed to assess adoption of integrated care interventions for community-based management of complex chronic patients, including transitional care and long-term care, and for patients under long-term oxygen therapy; (iv) Adaptations of technologies facilitating the transition toward Adaptive Case Management in existing healthcare systems and the evolution of the regional patient gateway as a self-management tool; and finally (v) The regional population-based health risk assessment tool, Adjusted Morbidity Grouper (GMA), has demonstrated high discriminative power on predicting target events (i.e., mortality, hospitalizations, multiple admissions, and on yearly healthcare

costs per patient) of patients with Chronic Obstructive Pulmonary Disease, indicating the potential to enhance health risk assessment and stratification in the clinical arena.

Conclusions: PITES-ISA has successfully executed implementation research in a real-world setting of its five main strategic areas (A1-A5), generating efficiencies at health system level while facilitating investments on innovation in integrated care services with no further increases in total healthcare costs.

5.1 INTRODUCTION

PITES-ISA is a coordinated Project that includes 7 different Spanish nodes (PI12-00508, PI12-00673, PI12-01241, PI12-01305, PI12-01415, PI12-01433, PI12-01571), all of them aligned with the main aims of the 'Health, demographic change and wellbeing' program of the Spanish Strategy for Science, Technology and Innovation. Hence, the principal objective of PITES-ISA is to support development of application environments, tools and technological infrastructures, based on open standards, safe, accessible and interoperable, for the creation of innovative telemedicine and e-Health solutions for chronic care management.

Is it widely accepted that the epidemics of non-communicable diseases and the need for cost-containment are triggering factors for a profound reshaping of the way we approach delivery of care for chronic patients [1]. In this new scenario, conventional disease-oriented approaches, centred on the management of clinical episodes, are being replaced by novel patient-centred integrated care services, which requires cooperation among health and social care providers across healthcare tiers. Such a transition has proven successful in areas wherein one organization is providing care [2-4] but extensive deployment of case management services in settings with heterogeneous healthcare providers is still a challenge.

The two major barriers for adoption of patient-centred integrated care [5] are: i) Organisational interoperability among professional teams, from different providers and healthcare tiers, working around the patient; and, ii) Technological interoperability among heterogeneous healthcare information systems.

With respect to organisational interoperability there is an urgent need for current health and social care systems to overcome organisational barriers by developing an approach that better co-ordinates and integrates services around the needs of patients and service users of all ages with chronic, medically complex and disabling conditions. This is where the potential of Adaptive Case Management (ACM) for planning, coordinating and reviewing the care of an individual is greatest. From an ACM perspective, patient-centred case management is defined as a set of well-standardized tasks to be carried out with patients based on their health condition and social circumstances to achieve target objectives, aligned with their comprehensive treatment plan. ACM provides the infrastructure for knowledge-based work (e.g. case management) that conventional systems cannot support because processes are too dynamic, variable and unstructured. The overarching goal of the ACM approach is to enable the case manager to face new cases reusing structured experiences with previous cases. Over time, the case manager should be able to adapt the system to his or her own style of working without needing the help of any technology specialist.

With respect to technological interoperability, Information and communication technologies (ICT) have a major role in facilitating health information sharing among heterogeneous providers, each one using proprietary health information systems. Moreover, the use of appropriate ICT has been shown to be essential to support continuity of care through collaborative tools, facilitating accessibility of citizens and patients to healthcare and generating a disruptive scenario in terms of information management. Successful cases addressing the technological requirements associated with the deployment of case management services within a given health information network exist [3,6]. However, this issue remains a major challenge in those healthcare sectors with heterogeneous providers each one using proprietary hospital information systems and with a lack of operational strategies for health information sharing.

Contributing to the principal objective of PITES-ISA, its node in Catalonia (PI12-01241) operates through 5 main strategic actions for regional deployment (Catalonia) of selected innovative care services: A1) Collaborative lung function testing for early diagnosis of chronic diseases in primary care; A2) Empowerment for self-management of healthy lifestyles; and, A3) Collaborative management of complex chronic patients. Complementary strategic actions focus on the development of A4) Technological and organizational support to implement such innovative care services; and, A5) Comprehensive health risk assessment for patient stratification and service selection.

In order to maximize the capacity of the project to progress with these 5 strategic actions, PITES-ISA in Catalonia operates within the NEXTCARE project (www.nextcarecat.cat) of the regional (Catalan) smart specialization strategy for healthcare. Ultimately, addressing NEXTCARE innovation objectives, PITES-ISA aims to establish a favourable environment for I+D+i, helping to vertebrate the future social and economic developments of healthcare innovation.

5.2 MATERIALS AND METHODS

The site

In 2010-13, the strategic plan of the Hospital Clínic of Barcelona introduced a strategy for "Digitalization of Clinical Processes". Multiple committees [7,8] have been working to reengineer key processes (e.g., electronic prescription, patient portals) and areas (e.g., intensive care, emergency room, surgery, etc.) of the hospital, with an integrated vision within the Barcelona-Esquerra healthcare district and, most importantly, around the needs of the patients.

To this end, health information exchange systems have been developed as part of the interoperability framework of Barcelona-Esquerra healthcare district [7] and the regional tools for interoperability at healthcare level (i.e., the Catalan IS3 program). Although there is agreement at conceptual level on the need for technological support for an effective deployment of novel collaborative and integrated care processes, current tools are not enough to fully support adaptive case management.

The project is being developed in close coordination with the Department of Health through TIC-SALUT and the Catalan Agency for Health Information, Assessment and Quality (AIAQS) among several other companies and entities actively supporting the Catalan 4-star EIP-AHA reference site.

Strategic Actions

A1 – Transfer of specialized diagnostic tools to primary care: forced spirometry as use case

The Forced Spirometry (FS) program [9] emerges from a series of studies reporting on articulated applications covering unmet needs for collaborative FS testing. The studies were initiated within the EU project NEXES [10] and specific parts of the overall setting have already been successfully evaluated in the Basque Country. The FS program has been designed as part of the regional deployment of integrated care services in Catalonia. It consists of the two lines of activity ultimately aiming at regional adoption of the FS program and generalization of the approach to other areas, as well as to other testing procedures. The underlying hypothesis is that the proposed FS program facilitates the transference of diagnostic testing from specialized care to the community, which should generate significant healthcare efficiencies and provide valuable information on longitudinal changes of lung function either spontaneously or due to interventions.

A2 – Pre-habilitation intervention in high risk candidates for major surgery

This strategic action encompasses a portfolio with customized self-management services aiming at promoting daily physical activity in chronic patients. The aims are to increase accessibility, cost-effectiveness and sustainability of effects of rehabilitation programs. It targets three layers of candidates proposing different modular services in each of them: (i) citizens at risk and patients with mild disease; (ii) community-based program for clinically stable chronic patients; and, (iii) pre-habilitation program for candidates to high-risk surgery.

The latter will be extended to a general program for prevention of surgical complications currently being implemented at Hospital Clinic. In the context of the perisurgical treatment, being unfit increases the risk of death and complications after major surgery. To this end, a trimodal prehabilitation (supervised endurance training, nutritional counseling and mindfulness) is an intervention performed in the preoperative period aimed to the preoperative optimization of the surgical patient with the objective of reducing perioperative complications, especially in patients with higher risk. The program is also focused on improving the patient's healthy lifestyles after the immediate postoperative period.

A3 – Collaborative management of complex chronic patients

The action addresses core aspects of the management of Complex Chronic Patients (CCP) across the healthcare tiers: (i) Implementation of clinical processes resulting in integrated care interventions for two use cases, community-based management of CCP including transitional care and long-term care, and Integrated care for patients under long-term oxygen therapy; (ii) Adoption of collaborative and adaptive case management (ACM) [11] for the two use cases indicated above; (iii) Evaluation of the impact of enhanced clinical health risk assessment and stratification [12] and, (iv) Innovative assessment of healthcare value generation of the services, both during the deployment phase and after regional scale-up of the novel services.

A4 – Technological and organizational support

The project intends to overcome previous pilots at Regional, National and International level, which we have been promoting and leading. To reach real world extensive deployment and trials, we have assumed that integration with current management systems using existing interoperability frameworks is a must. Consequently, self-management tools for patients will be integrated to the Catalan Personal Health Folder (i.e., Cat@Salut La Meva Salut) to enable secure access, authentication, and take advantage of underlying management features. Similarly, we are assuming that the collaborative and adaptive case management tools for professionals will be integrated to the IS3 Interoperability framework for process exchange and to the Shared Electronic Health Record of Catalonia (HC3) for data sharing.

A5 – Clinical risk stratification and prediction

This action will further develop the GMA (Adjusted Morbidity Groups) population-health risk prediction tool [12,13]. GMA serves for commissioning of healthcare services, as well as to identify highly vulnerable patients allocated at the tip of the risk pyramid (case finding). Comprehensive clinically applicable subject-specific health risk assessment constitutes a necessary step for patient stratification aiming at generating healthcare efficiencies. The current GMA version covers four key requirements: (i) a population health approach using the entire source population of 7.5 million inhabitants of the region, with a bi-annual update of the risk pyramid distribution; (ii) publicly owned by the Catalan ministry of health without licensing constraints; (iii) open source computational algorithms; and, iv) the GMA morbidity grouper relies only on statistical criteria, without expert-based criteria, thus facilitating quick adaptation to different populations.

Co-design of solutions for the strategic actions

The project follows a co-design approach using iterative Plan, Do, Study, Act (PDSA) cycles [14] to understand and improve the project strategic actions (A1-A5). PDSA cycles consist of a systematic series of steps for gaining valuable learning and knowledge for the continual improvement of a product or process. Briefly, the "plan" stage aims to identify potential changes for improvement of a given system; in the "do" stage the proposed changes are implemented and tested; afterwards, the success of the changes are evaluated in the "study" stage; and finally, the "act" stage identifies adaptations and plans for next steps to inform a new cycle. The pragmatic nature of PDSA provides flexibility to develop interventions according to stakeholder's feedback ensuring fit-for-purpose solutions, while providing the opportunity to build evidence for change, engaging stakeholders as confidence in the intervention increases.

Ethical and Regulatory Issues

Ethical and legal aspects associated with the deployment of ICS-ICT, including ethical challenges and the lawfulness of the proposed service models, were identified and analysed. The impact of regulatory issues on equipment was not the focus of the project because our choice was to use commercially available equipment. In contrast, ethical and legal issues, particularly those related to concerns about privacy, consent, responsibility of care and liability related to novel technologies, information sharing, transmission or decentralization of clinical procedures, were considered a core area of activity during the project. We have taken this orientation because privacy becomes

a central issue, particularly when considering enhancing health-risk assessment and patient stratification combining determinants of health from formal care, informal care, biomedical research and population health.

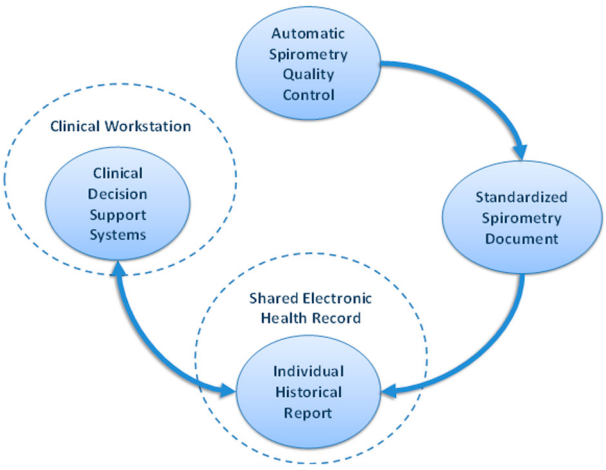
5.3 RESULTS

Regional deployment of the innovative care services

Main summary results of the innovative care services (A1-A3) carried out in the project are described below:

Transfer of specialized diagnostic tools to primary care: forced spirometry as use case (A1) - The regional deployment program of enhanced quality and accessibility of lung function testing across the health system have been published in [9]. The four core components of the program (Figure 1) are: (i) Enhanced automatic FS quality assessment; (ii) Accessibility to standardized (and quality-labelled) FS testing across healthcare tiers; (iii) Generation of an individual FS report including historical information from a given patient; and, iv) Clinical decision support systems (CDSS) in the clinical workstation of primary care professionals, facilitating accessibility to the patient FS historical report, as well as access to off-line remote support by specialized professionals, upon request. A clinical pilot has been done in one primary care unit in Barcelona with a threefold aim: (i) to assess functionality of the entire circuit; (ii) to perform a new clinical validation of the algorithm; and, (iii) to evaluate acceptability of key performance indicators of large scale deployment. The clinical pilot has allowed to elaborate (i) Recommendations to the Catalan Government to achieve full consolidation of the FS program; and, (ii) Proposals to European and international respiratory societies (ERS/ATS) of an update of current FS standardization document.

Figure 1. Four pivotal components needed for regional deployment in Catalonia (7.5 million inhabitants) of a collaborative forced spirometry program across healthcare tiers

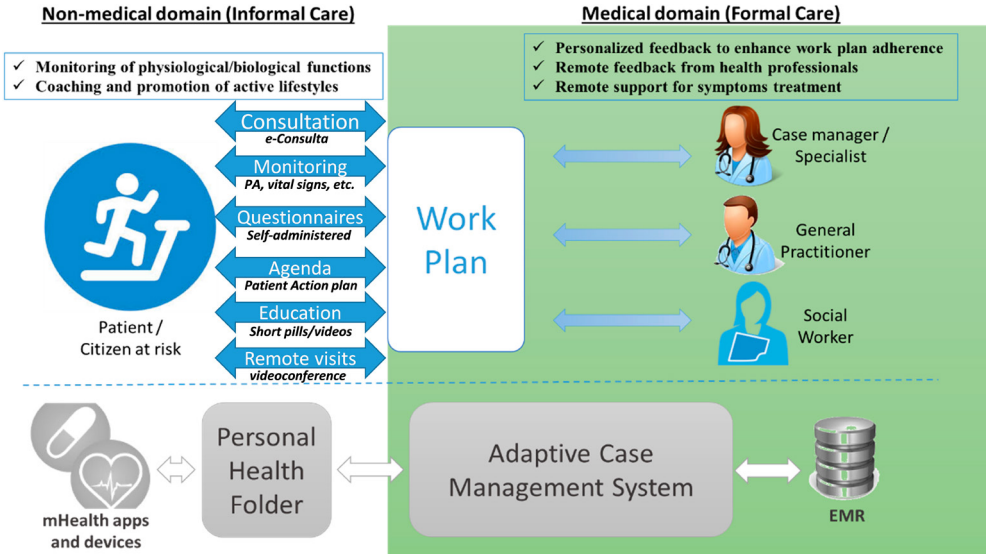


Pre-habilitation intervention in high risk candidates for major surgery (A2) - A recent randomized controlled trial on a pre-habilitation intervention in high-risk candidates for elective major abdominal surgery has demonstrated efficacy [15] by enhancing aerobic capacity, reducing the number of patients with postoperative complications by 51% and the overall rate of complications. The program, as well as

its extension to lower risk patients, is being deployed as mainstream services of Hospital Clinic of Barcelona (>1,000 patients/year) and will be extended to a general program for prevention of surgical complications currently being implemented at Hospital Clinic.

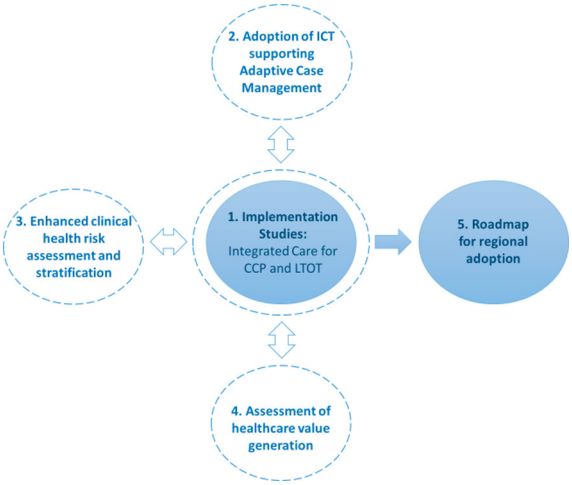
The setting at Hospital Clinic aims to solve current practical limitations for extensive deployment of the service(s), namely: i) accessibility, ii) behavioural change component; and, iii) financial sustainability; so that the service(s) can become operational as a standard of care intervention. From a technological point of view, Figure 2 depicts the different tools that are envisaged as facilitators both at the medical (right hand-side) and the informal care (left hand-side) domains.

Figure 2. Depiction of main actors and technological support to the peri-surgical intervention



Collaborative management of complex chronic patients (A3) - Proven efficacy of integrated care interventions assessed through randomized controlled trials may not translate into effectiveness at health system level [16]. In this respect, preparation of the workforce and enhanced clinical stratification have been identified as two key limiting factors for successful deployment of integrated care. Both factors are taken into account in a protocol that have been designed [17] to assess adoption of the two target use cases: Community-based management of complex chronic patients, including transitional care and long-term care, and for patients under long-term oxygen therapy. The protocol relies on the hypothesis that implementation of: (i) structured, but flexible service workflows; that is, a collaborative and adaptive case management approach [11] and (ii) enhanced patient health risk assessment and stratification [12], can overcome current limitations of multi-morbidity management. The protocol aims to assess this hypothesis considering five pivotal aims (Figure 3) for evaluation of the regional deployment of the two target use cases. Assessment will be carried out following a Triple Aim approach [18,19] considering pre-defined outcome variables for: (i) health and well-being, (ii) experience with care, and (iii) costs, and combining empirical questionnaire data collection, information from electronic medical records and registry data. The main study outcome will be twofold: (i) demonstration of cost-effectiveness of the interventions; and, (ii) identification of factors that modulate success of large scale deployment.

Figure 3. Five pivotal aims two achieve successful regional adoption of the community-based protocol for collaborative management of complex chronic patients across health-care tiers

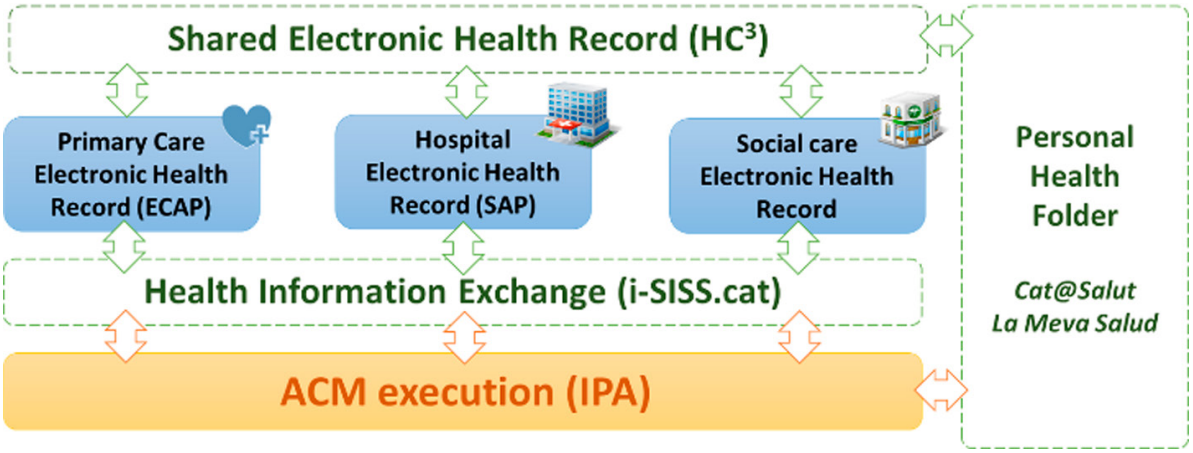


Technological support

Adoption of adaptive case management [11,20] to support collaborative work constitutes an emergent approach that facilitates case managers to adapt well-structured service workflows to the continuously evolving needs of the patients. This implies selection and scheduling of specific tasks during case management and ad-hoc collaboration with other professionals across healthcare and social support tiers, which facilitates collaborative decisions triggered by expected and unexpected events.

Therefore, the innovative care services (A1-A3) carried out in the project will be supported by a software platform that will allow the execution of well-structured but adaptable clinical workflows. This platform will be open source and built-up on top of the current health information systems of the different healthcare providers and using existing regional interoperability infrastructures (Figure 4). In order to support both patient collaborative work and self-management, the personal health folder already deployed in the region is currently being adapted for the purposes of the project as a key component of the Catalan Digital Health Framework [21].

Figure 4. Depiction of main components of the Catalan Digital Health Framework

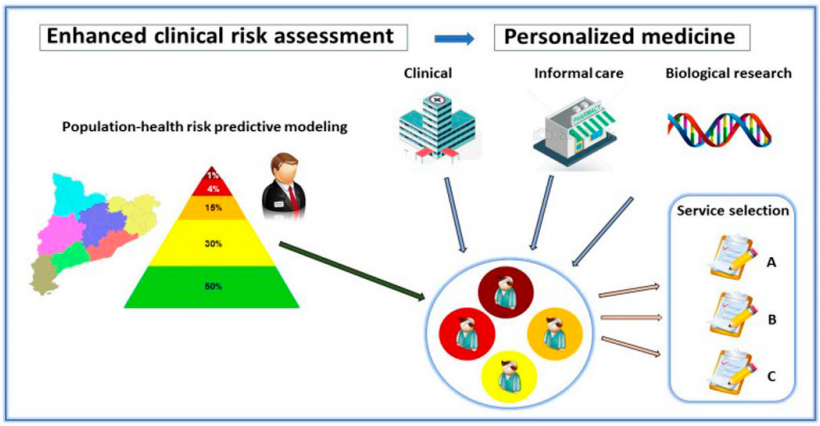


Enhanced clinical risk stratification and prediction

Current patient-based health risk predictive models are essentially using clinical variables only. However, three categories of covariates have been identified to show potential for inclusion into patient-based health risk predictive models, as displayed in Figure 5: (i) input from enhanced case finding tools; that is, population-health risk predictive models such as the GMA; (ii) individual clinical, physiological and biological information relevant to the medical problem being assessed; and (iii) subject-specific informal care data including lifestyle, adherence profile, socioeconomic status, requirements in terms of social support and environmental factors. It is hypothesized that inclusion of all these covariates influencing patient health may markedly increase the predictive accuracy and facilitate clinical decision-making based on sound estimates of the prognosis of an individual.

The three categories of covariates shall be dynamically captured from different sources, respectively: (i) population-health risk predictive models; (ii) articulated healthcare and biomedical research knowledge (integration of clinical, physiological and biological/molecular information); and, (iii) in-place personal health folders (lifestyle, adherence profile, socioeconomic status, social support and environmental factors). The implementation of this holistic approach generates novel requirements to be adopted by the field. Main identified barriers and opportunities to enable the required potential for Big Data analytics in health applications have been identified and recently reported in [22].

Figure 5. Four categories of covariates that have been identified to show potential for inclusion into patient-based health risk predictive models



5.4 DISCUSSION

PITES-ISA in Catalonia articulated lessons learnt [10] in previous experiences carried out and validated in Catalonia during the last years in order to generate a collaborative ecosystem with high potential for transferability to other geographical areas. To this end, it is crucial the implication of the main stakeholders in the process (staff and patients) in order to capture the feed-back of all actors of the integrated care process. Ultimately, the outcomes of the project will help to generate guidelines for large scale deployment of novel patient-centered care, including transferability analysis, facilitating adoption of integrated care services for management of multi-morbidity with a personalized medicine foundation [23].

As with all scientific methods, documentation of each stage of large scale deployment is important to support scientific quality, local learning and reflection and to ensure knowledge is captured to support organizational memory and transferability of learning to other settings. To this end, the field of implementation science [24] promotes the adoption and integration of evidence-based practices, interventions and policies into routine health care and public health settings. Implementation research plays an important role in PITES-ISA to identify barriers to, and enablers of, effective large scale deployment of innovative care services. To this end, Implementation strategies need to be developed iteratively to adapt to the local context and respond to unforeseen obstacles and unintended effects. Therefore, the keys for the success of large scale deployment includes appropriate documentation, testing of change, initial small-scale testing and use of co-design strategies over time.

From the technological standpoint, the project promotes Adaptive case management (ACM) as a new paradigm to support flexibility for healthcare professionals during the continuously evolving process of patient-centered care. Cases vary so much that case managers are constantly striving for innovative approaches to meet the needs of new cases. Therefore, case managers are involved not only in picking a predefined action from a set of well-standardized tasks to be carried out to a patient in alignment with his/her comprehensive treatment plan, but also in helping to improve the actions that can be taken during the process of case management.

In the ACM paradigm, patients' empowerment through patient gateways, should allow patients access to their optional and scheduled tasks, to review their follow-up, to check educational information, to share and discuss with other healthcare professionals and to establish remote monitoring of their clinical variables, such as heart rate, blood pressure, weight, oxygen saturation, physical activity, etc. However, this require enhanced dynamic communication among Informal Care, Health Care and Biomedical Research through multilevel/multi-scale heterogeneous data integration into a Digital Health Framework [21].

In addition, it is expected that such Digital Health Frameworks will allow enhanced applicability and integration of powerful data analytics, including risk predictive modelling, into clinical practice. In this regard, the development of novel clinical decision support systems, supported by advanced visual analytics, facilitating representation of patient information for effective clinical management of time-varying individualized data is a real, yet unmet need, to facilitate clinical judgment for decision-making.

This novel healthcare scenario reveals new emerging needs regarding highly relevant non-solved ethical issues. These are related to privacy, security of data transfer, as well as risks associated with healthcare decisions that rely on inadequate risk predictive models. The complexities involved in some of these aspects can only be addressed through a democratic debate; openness and transparency of the healthcare governance; as well as a timely and appropriate evolution of legal frames.

5.5 CONCLUSIONS

In summary, PITES-ISA has successfully executed implementation research in real-world settings of its five strategic actions (A1-A5), generating efficiencies at

health system level while facilitating investments on innovation in integrated care services with no further increases in total healthcare costs.

5.6 ACKNOWLEDGEMENTS

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CHAPTER 6

DEVELOPMENT OF A TELEMEDICINE SYSTEM FOR RHEUMATOLOGY PATIENTS

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Index terms: *Interoperability, Mobile applications, Patient monitoring, Telemedicine, Web site.*

ABSTRACT

Objective: The development of a telemedicine system for rheumatological patients that can solve the existent deficiencies nowadays: lack of health care continuity, excessive therapeutic expenses, failures using the existent clinical guides and a high number of adverse events during treatment.

Methods and Procedures: After the interviews with the clinicians of the rheumatology service at University Hospital Complex of A Coruña, we identified the scope of the work (all rheumatic pathologies) and the questionnaires and information needed for patient monitoring. We developed both a web and a mobile application to allow patients to visualize information and answer questionnaires. The questionnaire answers are stored as ISO 13606 extracts into a repository that allows flexible querying. Also, we built a web application for clinicians to query and edit patient information. Lastly, we developed an alarm system that detects events during patient treatments and notifies clinicians.

Results: A telemedicine system composed by web and mobile applications for rheumatological patients, a web application for clinicians, an alarm system and an ISO 13606 extract repository.

Conclusions: We can conclude that this work allows facing the main problems of rheumatology patient treatment and monitoring. Thanks to the effort put into reusability, any clinical area can benefit from the results of this work.

5.1 INTRODUCTION

Rheumatic diseases are those conditions that acutely or chronically compromise the functions of both the skeletal and the muscular system. They are characterized mainly by being chronic and producing high morbidity, disability, loss of quality of life and a high social, institutional and individual cost.

Nowadays, the main deficiencies in rheumatologic patients care are, fundamentally, lack of continuity of care, excessive therapeutic expenses, non-compliance with clinical guidelines and a high number of adverse events during treatments.

All these problems in the treatment can be approached with the use of telematic solutions, and this is the objective of the work presented in this chapter.

The telemedicine system we propose consists of web and mobile applications for patients, an administration web application for clinicians and an alarm system to detect incidents during the treatment.

To achieve interoperability we created the required ISO 13606 archetypes, in addition to an implementation of the ISO 13606 standard and a repository of clinical extracts.

The functionality of this application revolves around patient questionnaires. This is because the clinical approach to rheumatic diseases is completely different, in several important aspects, from the one that is followed in the case of other chronic diseases such as hypertension or diabetes, in which there is a reference criterion for its measurement (like blood pressure or blood sugar). In rheumatic diseases, on the other hand, the content of a patient's anamnesis is more important for decision-making.

In addition, patients with hypertension or diabetes are often unaware of their condition in the absence of objective test data (blood pressure or blood sugar). On the other hand, patients with rheumatic diseases are generally aware of the symptoms, and information from the anamnesis is more important than analysis results, image tests or the physical examination itself when making clinical decisions.

The results of self-administered patient questionnaires are generally more significant for predicting severe consequences of these diseases like incapacity for work, costs and mortality. Its use is effective for detecting changes in a patient's situation, evaluating the response, improving the quality of care and guiding the treatment.

By being self-administered, these questionnaires are susceptible to be carried out telematically, resulting in web or mobile applications that the patient can use without the help of health personnel.

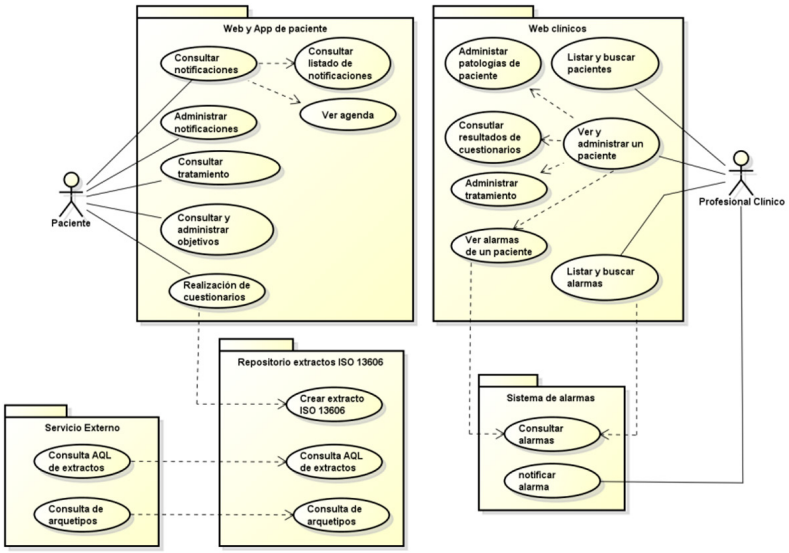
5.2 USE CASES

After the interviews with the health personnel of the University Hospital Complex of A Coruña (CHUAC) rheumatology service, we identified the scope of the work, which spans all chronic rheumatologic pathologies, and all the necessary information and questionnaires for monitoring the rheumatologic patients.

Figure 1 shows the use case diagram of the system. Patients and clinical professionals are the actors. The diagram shows both the web and the mobile patient applications in the same box because they share all use cases: everything that can be done from the web can also be done from the mobile application.

Another aspect to comment about the diagram is the appearance of an external service that queries the ISO 13606 extract repository. This is only to show that the extract repository has been made independent of the rest of the system components (that is, it can be used from any application) and extracts can be consulted by any allowed external service in the future.

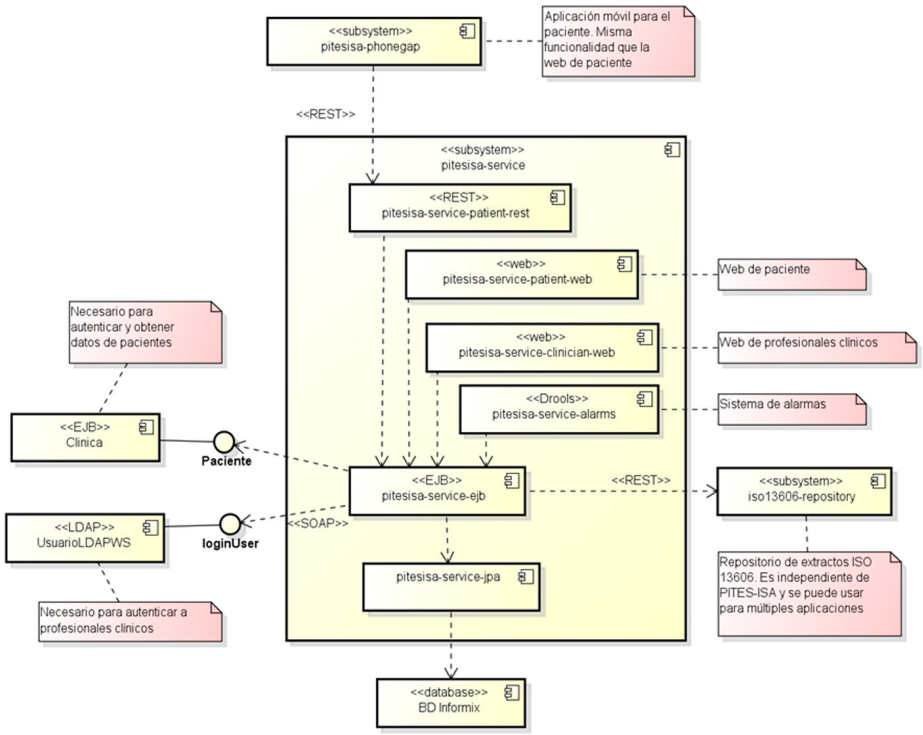
Figure 1. Use case diagram of the whole system



5.3 ARCHITECTURE

Figure 2 shows the components that make up the system technical architecture and the technologies used for its intercommunication. At a technical level, the system consists of three units: a mobile patient application, a Java EE enterprise application and an ISO 13606 clinical extract repository. This section contains an overview of the architecture, as the specific details of each component will be described in their corresponding sections.

Figure 2. Component diagram of the system



A. Mobile patient application

The multiplatform mobile patient application (pitesisa-phonegap) uses Phonegap technology. The mobile application communicates with the enterprise application through REST web services to retrieve and save the information.

B. Java EE enterprise application

The Java EE enterprise application (pitesisa-service) is deployed to an IBM WebSphere Application Server. This application includes patient and clinical professional websites (implemented using JSF), the REST web service (using JAX-RS) for the mobile application, the alarm system (using Jboss Drools), the business logic (using EJB) and database persistence (using JPA). It should be noted that business logic is responsible for communicating with external services required to authenticate patients and clinical professionals.

C. Clinical extract repository

The ISO 13606 clinical extract repository (iso13606-repository) is implemented as a Java EE application also deployed to an IBM WebSphere Application Server. It provides the enterprise application (and any other application in the future) with the possibility of storing and querying ISO 13606 clinical extracts through REST services. Currently, the PITES-ISA enterprise application is used to create and store responses from patient questionnaires in the form of ISO 13606 extracts. The repository application stores the data in a MongoDB database, as will be detailed in its corresponding section.

Finally, it should be indicated that the rest of the data is stored in an Informix database.

5.4 PATIENT WEB APPLICATION

The patient web application allows patients to monitor their diseases from anywhere, identifying themselves through the health card data. We will go deeper in each of its functionalities.

A. Notifications query

The patient can view the notifications that he has established as well as the automatic notifications of the system (i.e. warnings about questionnaires that patients must answer).

The display of the information is available in two sections: a list sorted by date (which is the home page of the website) and an agenda that shows the notifications in a calendar.

B. Notification management

The patient can set his own notifications about medication intake (so that he will be reminded in the future what to take and how much) and medical appointments.

C. Treatment query

The patient can view the information regarding his treatment: medication (including medicament, shots and start and end dates of the treatment), diet and exercise.

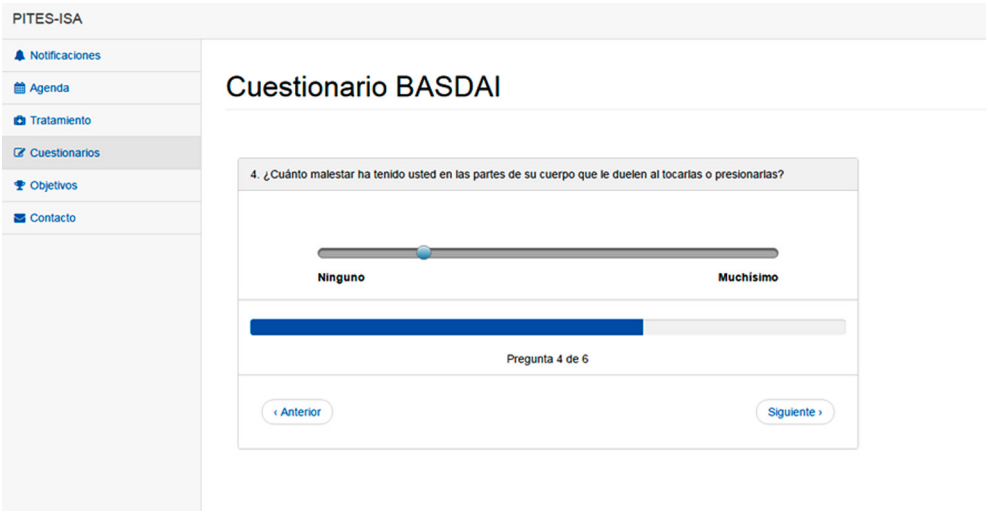
D. Questionnaire completion

The patient is shown a list of questionnaires that he must answer, storing that information for later visualization by the clinical staff or the alarm system. Questionnaires consist of multiple types of questions. Figure 3 shows an example of analogical visual scale question.

E. Goal review and management

The patient can create and manage any suggested goal (e.g. stop smoking, reduce weight, etc.) as well as add updates on their progress.

Figure 3. Analogical visual scale question within a questionnaire on the patient website



5.5 PATIENT MOBILE APPLICATION

In addition to the web application, we also developed a multi-platform mobile application for patients, which allow the monitoring of rheumatological diseases from the patient's home. Authentication, as in the patient web application, is performed through the data of the health card.

A. Notifications and management query

Patients can view lists of pending notifications (about questionnaires that must be answered) and upcoming notifications (medication intake, medical appointments and upcoming questionnaires). In addition to the lists, notifications are received on the device even if the application is closed.

B. Treatment query

Like in the web application, the patient can review his treatment, including medication and recommendations on diet and exercise.

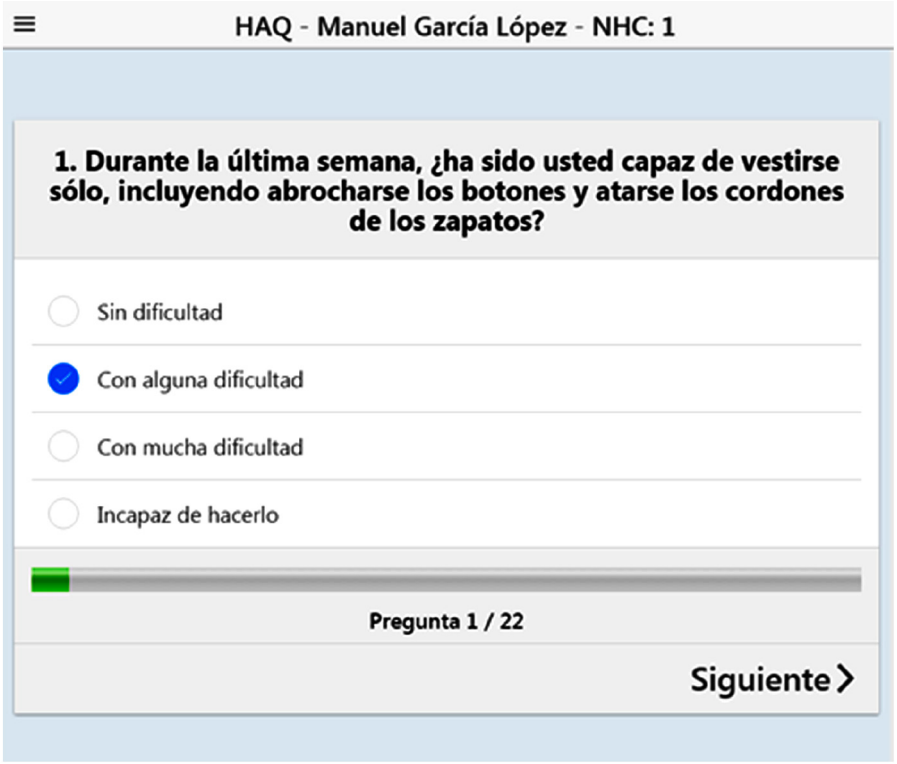
C. Questionnaire completion

All questionnaires can be answered through the app, in a similar way to the web application. Figure 4 shows an example of a simple selection type question.

D. Goal review and management

As in the web application, the patient can visualize, manage and update (adding new activity) goals that have been set.

Figure 4. Example of simple selection question in the mobile patient application



5.6 CLINICIAN WEB APPLICATION

The website for clinical staff allows them to view and edit patient and alarm information generated by the alarm system. Below we will see in more detail the main functionalities provided by the web application.

A. Patient's pathologies management

The clinician can view and edit the pathologies assigned to the patient.

B. Patient's questionnaires query

The health staff can view a list with all the questionnaires completed by the patient, being able to perform searches and to order by different criteria (name of the questionnaire, date of completion and final result) and visualize the answers to each question.

As shown in Figure 5, graphs of the progress of the results can be visualized for each questionnaire in that patient, in order to visualize their evolution over time.

C. Patient's treatment management

The clinician can manage the patient's treatment (which may include medication, diet and exercise). Such treatment can, subsequently, be reviewed by the patient from the web or mobile applications.

D. Alarm searching and listing

It is possible to query a list with all the generated alarms for a specific patient, besides ordering and searching by different attributes (alarm type and date of detection). In addition to a specific patient, the web allows to view and filter the generated alarms for all patients, and can sort and filter by different fields (patient, type of alarm and detection date). This information is queried from the alarm system.

Figure 5. Results of a patient's questionnaires on the clinical staff website

5.7 BACKEND

Besides the patient and clinical staff websites, the Java EE enterprise application, deployed on the application server, implements the required operations to support these webs (through EJBs) and the patient mobile application (through REST web services).

This includes:

1. The data persistence layer to the Informix database (using JPA). Patient data, questionnaires, treatments, notifications, alarm system rules and alarms are stored.
2. Business logic layer (using EJB), which implements all the required operations to support the web and mobile applications. As part of these operations, communication with the repository of ISO 13606 extracts (through REST services) is included for the clinical extract storage of the completed questionnaires. In addition, it communicates with the hospital's internal services to manage the patient and healthcare professional access.
3. An alarm system (using Jboss Drools [1]), integrated within the telemedicine service, capable of detecting any type of situation based on a patient's data and notifying the suitable clinician. In addition, authorized professionals can filter and review these alarms in multiple ways through the tools developed as part of the telemedicine service. This way the alarm system allows detecting and reacting to any situation of a patient, serving, therefore, as a tool to aid clinical decision.

5.8 INTEROPERABILITY

The use of the ISO 13606 standard provides us with the semantic interoperability of clinical information, making possible the continuity of care of the rheumatologic patient. This objective has been completed by the development of archetypes, the implementation of ISO 13606 standard, the generation of a clinical extract repository and the integration of all this with the rest of the PITES-ISA platform.

A. Archetype generation

In order to achieve semantic interoperability, ISO 13606 [2] archetypes have been developed. These archetypes are necessary for the analysis and complete monitoring of a rheumatologic patient.

After several interviews with specialists in the area of rheumatology of the CHUAC, it has been concluded that remote monitoring of all rheumatologic pathologies (16 in total) can be performed and that the questionnaires completed by the patient are much more important than the physical examination and analysis tests.

Therefore, the archetypes for each questionnaire have been created, both for general questionnaires (common to multiple pathologies) and for those particular to specific pathologies. Archetypes have also been created for physical measurements.

For the archetype creation, the recommendations have been followed [3], trying to obtain the quality criteria in its elaboration [4]. As part of these indications, we have created (as far as possible) the subsets of SNOMED-CT [5] terms necessary to represent the medical concepts of archetypes.

B. ISO 13606 standard implementation

The creation of archetypes is not enough to achieve interoperability, since they are simply representations of domain concepts. It is also necessary that the clinical

extracts generated by the system (results of questionnaires and physical measurements) are coded according to a standard, which in our case is ISO 13606.

To do so, we have developed a Java implementation of the UNE-EN ISO 13606 standard, which allows reading, writing and validating both archetypes and extracts. This implementation hides the complexity of the standard and is reusable in any project.

Specifically, it allows to:

1. Read and write archetypes using ADL 1.4 format [6], the one recommended in part 2 of the ISO 13606 standard. The archetypes are automatically validated to check their conformity with the ISO 13606 reference model.
2. Read and create clinical extracts in XML format following part 1 of the ISO 13606 standard. In addition, we have implemented the semantic validation of extracts, that is, the verification that each node of the extract complies with the corresponding constraints in the archetype.
3. Generate an extract easily by specifying only the essential information, hiding as much as possible the complexity of ISO 13606. This is possible because most of the information included in an extract can be obtained from the corresponding archetype

C. Clinical extract repository

The ISO 13606 clinical extract repository is the system in charge of semantic interoperability of information. Generates and stores ISO 13606 clinical extracts corresponding to questionnaires to allow their querying by an external service, using the Java implementation of ISO 13606 created for this task. It is important to note that it has been designed to be used by multiple applications (not just PITES-ISA) and for any type of archetyped information (not just questionnaires).

It provides the following features:

1. Extract creation: the system automatically receives the questionnaires completed by the patients and generates (and stores) the corresponding ISO 13606 extracts.
2. AQL extract query: the system provides a service to other external systems to query ISO 13606 extracts, following the official specification of the AQL (Archetype Query Language) [7] language. We have chosen AQL for this purpose as it is flexible enough to query information included within extracts.
3. Archetype querying: the system provides a service to other external systems to query the ISO 13606 archetypes used to generate clinical extracts.

It is important to indicate that the storage of ISO 13606 extracts in relational database systems presents important problems, mainly because it consists of hierarchical information with a variable structure, unknown beforehand. This has forced us to evaluate different solutions and we have concluded that a NoSQL document system, like MongoDB, is the right one for this situation, mainly because the data model is adjusted to the structure of the information.

MongoDB stores documents with variable structure, and the conversion of XML ISO 13606 extracts to this type of documents and vice versa is practically automatic.

Therefore, at the time of the storage of extracts in the repository we have chosen MongoDB.

It is necessary to show that the rest of the information of the application (patients, treatments, events, etc.) is stored in a relational database system, because, in this case, its use is appropriate.

D. Integration in the PITES-ISA project

The aim of semantic interoperability is to allow automatic communication of clinical extracts among different computer systems. For this reason, the developed archetypes (and the extracts generated from all questionnaires completed by patients) have been integrated into a central repository belonging to the UITeS (Telemedicine and eHealth Research Unit) of the Carlos III Health Institute, framed within the overall objective of the project.

5.4 CONCLUSION

The initial objective of the project was to provide a solution to alleviate the current existing deficiencies in the care of rheumatologic patients: lack of continuity of care, excessive therapeutic expenditure, failure to comply with clinical guidelines and a high number of adverse events during treatment.

The lack of continuity of care has been addressed through the work done in the field of interoperability of clinical extracts. This allows the automatic communication of data among different health information systems, which makes possible the patient's continuity of care.

Regarding the excessive therapeutic expenditure and failure to comply with clinical guidelines, the telemedicine system partially solves these problems. We have calculated that, due to the digital format of the patient questionnaires and their automatic integration, the health staff in the area of rheumatology manages to save approximately 10 hours per month in the consultations, therefore this time can be dedicated to take care of patients in more detail. Besides, increasing the agility in the process of conducting questionnaires makes it feasible to increase the number of completed questionnaires up to approximately double, so clinical professionals (and the alarm system) have more data available in the decision making process about the treatment. Another added benefit is the elimination of the potential human error risk present when manually dumping paper questionnaires into computer systems.

The impact of the high number of adverse events in the treatment can be reduced partly thanks to the alarm system which, together with the increase in the number and frequency of performed questionnaires per patient, allows a much earlier detection of adverse situations during treatment.

Therefore, we can conclude that the developed system allows addressing the main problems in the treatment of rheumatologic patients, which was the objective of the work.

Given the focus on reusability, which can be seen in the implementation of the ISO 13606 standard and in the extract storage and query system, the work presented in this paper sets a basis and opens the way to new interoperable telemedicine applications. With this, the scope and influence of the work ended up being much

greater than simply the rheumatic pathologies, since any medical area could benefit from the results obtained in the work presented in this article.

5.6 ACKNOWLEDGEMENTS

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