



C3-Cloud

“A Federated Collaborative Care Cure Cloud Architecture for Addressing the Needs of Multi-morbidity and Managing Poly-pharmacy”

PRIORITY Objective H2020-PHC-25-2015 - Advanced ICT systems and services for integrated care

D3.1 Survey of the State of the Art Research, Technologies and Architectures

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EXECUTIVE SUMMARY

Introduction

The C3-Cloud project “**A Federated Collaborative Care Cure Cloud Architecture for Addressing the Needs of Multi-morbidity and Managing Poly-pharmacy**” will establish an ICT infrastructure enabling a collaborative care and cure cloud to enable continuous coordination of patient-centred care activities by a multidisciplinary care team and patients/informal care givers. A Personalised Care Plan Development Platform will allow, for the first time, collaborative creation and execution of personalised care plans for multimorbid patients through systematic and semi-automatic reconciliation of clinical guidelines, with the help of Decision Support Modules for risk prediction and stratification, recommendation reconciliation, poly-pharmacy management and goal setting.

In the Work Package 3 “**Design of C3-Cloud System Architecture**”, the Task 3.1 “Survey of the State of the Art” addresses a survey of the technologies and architectures in the research areas of C3-Cloud. Within the scope of this task, a comprehensible survey will be performed in the related research areas addressed by C3-Cloud project at the beginning of the project in order to be able to decide on approaches, identify the research results and technologies that can be re-used, extended, or inspired in C3-Cloud. The available technology solutions and the results of the previous EC supported projects will also be explored.

Objective of the deliverable

The objective of **D3.1 Survey of the State of the Art – Research, Technologies and Architectures** is to provide a comprehensive survey of currently available standards, technologies and architectures in the field of advanced ICT systems and services for integrated care, that could support the design of the C3-Cloud architecture.

The survey gathers partners’ experience and expertise, as well as broader sources of information, such as academic literature knowledge and results of the previous Commission supported projects. Existing solutions are also explored to better understand the benefits they bring and assess their limitations. In C3-Cloud, we aim to address some of those limitations while we work towards an integrated care solution for multiborbidity.

Outline of the deliverable

Chapter 1 describes the context, the purpose and the methodology of the deliverable and a list of definitions of key acronyms used in the deliverable.

Chapter 2 introduces **integrated care and standards in the care plan management** domain, and describes relevant work in this area, reviewing related standards and existing approaches.

Chapter 3 focus on **clinical decision support** topics and **multimorbidity**, reviewing related standards and existing approaches.

Chapter 4 considers **patient empowerment** approaches, reviewing related standards and existing approaches.

Chapter 5 presents 5 **technical and semantic interoperability** challenges, reviewing related standards and existing approaches.

Chapter 6 covers the fields of **security and privacy** related to the project, , reviewing related standards and existing approaches.

Chapter 7 provides the conclusive statements of the deliverable.

Chapter 8 lists all references used in the deliverable.

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1 SURVEY OVERVIEW

1.1 Context of the survey: The C3-Cloud Project

The C3-Cloud project will establish an ICT infrastructure enabling a collaborative care and cure cloud to enable continuous coordination of patient-centred care activities by a multidisciplinary care team and patients/informal care givers. A Personalised Care Plan Development Platform will allow, for the first time, collaborative creation and execution of personalised care plans for multimorbid patients through systematic and semi-automatic reconciliation of clinical guidelines, with the help of Decision Support Modules for risk prediction and stratification, recommendation reconciliation, poly-pharmacy management and goal setting. Fusion of multimodal patient and provider data will be achieved via C3-Cloud Interoperability Middleware for seamless integration with existing information systems. An Integrated Terminology Server with advanced semantic functions will enable meaningful analysis of multimodal data and clinical rules. Active patient involvement and treatment adherence will be achieved through a Patient Empowerment Platform ensuring patient needs are respected in decision making and taking into account preferences and psychosocial aspects. Co-design and 4-layered multi-method multi-stakeholder evaluation will lead to a user friendly solution. To demonstrate feasibility, pilot studies will focus on diabetes, heart failure, renal failure, depression in different comorbidity combinations. Pilots will operate for 15 months in 3 European regions with diverse health and social care systems and ICT landscape, which will allow for strengthening the evidence base on health outcomes and efficiency gains. C3-Cloud adaptive patient pathways and organisational models validated by patient organisations and a clinical reference group, change management and training guidelines will be shared with the European community. Commercial exploitation of C3-Cloud integrated care solutions will be facilitated through an Industry Vendor Forum and commercial EHR/PHR products of 3 leading SMEs.

1.1.1 Background and Challenges

A growing share of the population in OECD countries is age 65 and over: 15% in 2010, and expected to reach 22% by 2030. Life expectancy of elderly has also increased significantly in the last 50 years. People at age 65 in OECD countries will expect to live for 21 years on average for women and 17 years for men, which is an almost 40% increase since 1960. However, older age is associated with an increased accumulation of multiple chronic conditions: multi-morbidity, including a growing number of functional and cognitive impairments.

Multi-morbidity creates diverse and sometimes contradictory needs which challenge patients and the delivery of health services. The clinical management of patients with multi-morbidity is much more complex and time-consuming than those with single diseases. WHO Europe reports that while the number of older people living alone is increasing, the availability of informal care by family members is declining due to greater distances between the members and increased rates of divorce. There is consequently a growing demand for health care services to handle multiple chronic conditions, and for social care services to enable such patients perform everyday activities, supported by informal carer or home / community care services. Currently those with chronic conditions and long-term care needs experience shortcomings and gaps in care provision. This is particularly prominent at the interfaces within and between health and social care delivery organisations. Achieving good quality integrated care is an acknowledged difficulty in many health systems. Unfortunately, current European medical models (e.g. as directed by clinical guidelines) focus primarily on short and medium term interventions on the basis of single conditions, failing to integrate care planning well across providers and often overlooking the interconnected basis of chronic diseases. The over-arching societal challenge addressed by C3-Cloud, and by this call topic is: **How can we effectively care for and support elderly patients with multi-morbidity needs?**

There are several challenges in providing integrated care to elderly patients with multi-morbid chronic conditions:

- *Challenge 1:* Traditionally, the adoption of clinical practice guidelines has been promoted for managing chronic conditions. However **clinical practice guidelines are currently single disease centred**, and often fall short to organise care for patients with multi-morbidity.
- *Challenge 2:* **Poly-pharmacy induced by multi-morbidity** itself is an important factor that leads to a significant cost in the health system affecting patients, as well as institutions / healthcare organisations.
- *Challenge 3:* Managing multi-morbidity, through the current treatment methods, results in **specialty silos** and **fragmented care**, involving multiple health and social care providers who are not effectively communicating and sharing information.
- *Challenge 4:* **Patients and their informal care givers** including family members often **do not have a voice** in the management of their own care.
- *Challenge 5:* Existing **organisational models and care pathways are inadequate** for integrated care delivery to the multimorbid elderly.
- *Challenge 6:* Currently, there exists **evidence base, biased towards patients with single diseases**, which limits the potential to develop the next-generation of multi-disease care pathways.

1.1.2 Objectives

To tackle these challenges, the specific objectives (SO) of C3-Cloud are:

- *SO1:* Enable the development of personalised care plans for multi-morbid conditions through systematic and semiautomatic reconciliation of digitally represented clinical guidelines for individual chronic conditions, by a group of collaborating health and social care givers, and with the informed participation of the patients and their informal care givers.
- *SO2:* Provide an innovative online platform through which multidisciplinary care team members (MDT) can collaboratively manage (execute, monitor, update) the integrated personalised care plans for patients with multi-morbid conditions.
- *SO3:* Provide Clinical Decision Support Modules to support personalised care plan development and execution by clinical guideline reconciliation, risk stratification, poly-pharmacy management and goal setting and monitoring.
- *SO4:* Ensure active participation of patients and their informal care givers to the management of their multi-morbid chronic conditions through a Patient Empowerment Platform to alleviate the non-adherence problem.
- *SO5:* Provide an Interoperability Middleware addressing technical, semantic and privacy/security interoperability challenges to seamlessly integrate with the existing health care, social care and home/community care information systems for enabling patient-centric interoperable care coordination in an informed manner with the involvement of all stakeholders.
- *SO6:* Demonstrate the applicability of C3-Cloud integrated care approach and supporting set of innovative ICT components in varying clinical, technological and organisational settings by piloting in three European regions (South Warwickshire, Basque Country and Region Jämtland Härjedalen) with quite different health and social care systems and ICT landscapes.
- *SO7:* Analyse the trajectories of C3-Cloud participants and their data to strengthen the evidence base in caring for patients with multiple conditions and to inform future development of more streamlined and optimised multi-morbidity care pathways.
- *SO8:* Develop, experiment and refine new adaptive models of integrated care and organisational change management guidelines for achieving the design and implementation of integrated care supported with ICT in diverse settings.

1.1.3 Overall C3-Cloud architecture and its Research Pillars

The overall architecture of the C3-Cloud project is provided in Figure 1.

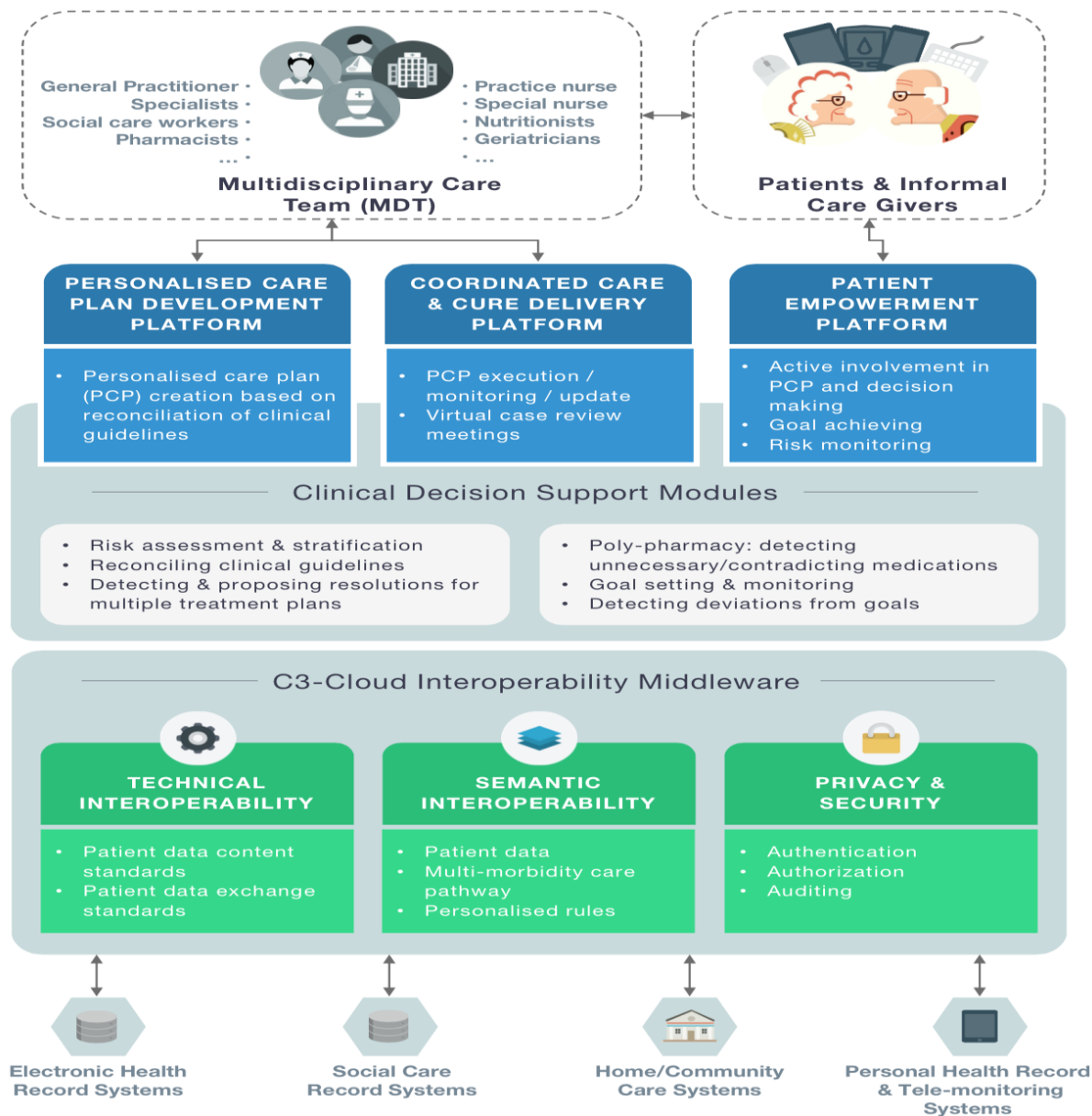


Figure 1 Overall C3-Cloud Architecture

The following research pillars are identified in C3-Cloud project in order to achieve the set objectives by realising the architecture above:

- **Research Pillar 1:** Developing the Personalised Care Plan Development Platform.
- **Research Pillar 2:** Developing the Coordinated Care and Cure Delivery Platform.
- **Research Pillar 3:** Developing the Decision Support Modules for reconciliation of multiple treatment plans and monitoring the execution of integrated care plan.
- **Research Pillar 4:** Developing the Patient Empowerment Platform to increase treatment adherence.
- **Research Pillar 5:** Developing the technical interoperability architecture.
- **Research Pillar 6:** Developing the semantic interoperability architecture.
- **Research Pillar 7:** Exploration of new patient pathways and organisational change models for improved coordination of care services.

1.2 Purpose

The purpose of Deliverable D3.1 is to provide a comprehensive survey of currently available standards, technologies and architectures in the field of advanced ICT systems and services for integrated care, that could support the design of the C3-Cloud architecture based on the research pillars. The available solutions and the results of the previous Commission supported projects are explored.

The fields covered by this survey include: Personalised Care Plan Development and Execution, Decision Support Modules for reconciliation of multiple treatment plans, Patient Empowerment Platform, Technical and semantic interoperability architecture and Security and Privacy.

The survey provided by this deliverable will be used together with the D8.1 deliverable (*Use Cases and Requirement Specifications of the Pilot Application*) and D3.2 deliverable (*Requirement Specification of the C3-Cloud Architecture*) as input to realize the *Conceptual Design of C3-Cloud Architecture* (D3.3).

1.3 Methodology

This survey is structured from the research pillars, the main research topics described in the C3-Cloud proposal. Based on the experience and expertise of the project partners, a statement of relevance of main subjects of each chapter with the C3-Cloud scope was established. Any relevant item identified provides a dedicated section within pillar chapters (presented in Section 1.1.3) and partners contributed to the content related with their relative experience and expertise. For each of concerned subjects, the present survey: 1) introduces the subject and its relevance with the C3-Cloud project, 2) lists the related existing projects, 3) lists the related existing standards. In a final section, the relevance and limitations of existing items in the scope of the C3-Cloud project is discussed.

In addition to gather partner experiences, the survey looks for broader sources of information, such as literature searches, green reports, reports from governments, NGOs etc, and offers a starting point to specific approaches that will be analysed in more depth in each individual task, such as in depth literature on clinical decision support. The partners were also consulted to suggest potential sources for material.

1.4 Definitions and Acronyms

Table 1 List of Abbreviations and Acronyms

Abbreviation/ Acronym	DEFINITION
CCOW	Clinical Context Management Specification
CDA	Clinical Document Architecture
C-CDA	Consolidated Clinical Document Architecture
CDS	Clinical decision support
CIG	Computer interpretable guidelines
CoAP	Constrained Application Protocol
CPG	Clinical practice guidelines
DSS	Decision Support Service
DSTU	Draft Standard for Trial Use
EHR	Electronic Health Record
FHIR	Fast Healthcare Interoperability Resources
HTTPS	Hyper Text Transfer Protocol Secure
ICT	Information and Communication Technology
IVR	Interactive voice response
LTPAC	Long Term and Post Acute Care
NICE	National Institute for Health and Clinical Excellence (UK government organization)
NGO	Non-Governmental Organization
OAuth	Open Authentication protocol
ONC	Office of the National Coordinator for Health Information Technology (United States Government Health and Human Services)
PHR	Personal Health Record
RS	Risk stratification
SAML	Security Assertion Markup Language
SMART-On-FHIR	Set of open specifications to integrate apps with Electronic Health Records, portals, Health Information Exchanges, and other Health IT systems.
SME	Small and Medium-Sized Enterprise
SOA	Service-Oriented Architecture
SSO	Single Sign-On
WHO	World Health Organization

2 PERSONALISED CARE PLAN DEVELOPMENT AND EXECUTION

2.1 Introduction

C3-Cloud will build a personalised care plan development and management platform for the use of multidisciplinary care team members in order to ensure integrated care for elderly patients with multi-morbid conditions. Relevant work in the area of integrated care and standards available in the care plan management domain are reviewed in the following sections.

2.2 Existing approaches on integrated care

The current section presents relevant European Union funded projects in the research area of integrated care.

2.2.1 SmartCare

The SmartCare project (wide deployment of integrated care services - 2013-2016), has been funded by the ICT PSP-2012-6 Competitiveness and Innovation Programme (CIP). The project deals with the

formalization of integrated care pathways in order to combat a series of threats to independent life commonly faced by the elderly [SmartCare]. The overall objective is to have service delivery supported by Information & Communication Technology in order to facilitate:

- Person-centred, co-ordinated care for individuals and their carers,
- Higher levels of self-care and self-management,
- Effective and efficient communication between all parties,
- Better use of resources and less duplication of effort.

The SmartCare approach has designed, delivered and deployed integrated care services following two care pathways for old persons with complex needs. The two Care Pathways developed are:

1. Integrated home support after a hospital discharge focusing on integrating all the processes, services, information, and communication required to ensure an individual has a safe, timely and smooth transition from their hospital stay back to their home, and receive appropriate rehabilitation and independent living enablement services.
2. Integrated long-term care support, designed to provide integrated and coordinated services for people living at home and who have complex needs that require a flexible approach to both health and social care support.

SmartCare services are innovative for they provide full support to cooperative delivery of care, integrated with self-care and across organisational silos. This was achieved through a comprehensive digital infrastructure of the integration building blocks that enabled effective care pathways. The pathways facilitate integrated care delivery across different care provision agencies including voluntary organisations, informal carers and self-care action. SmartCare Care Pathways are additionally supported by workflow tools, which activate the most appropriate resources across the entire spectrum of services available for older people both for scheduled and emergency care.

The integration building blocks focused on the challenges of data-sharing, coordination and communication:

- Integrated data access for care providers in different agencies and informal carers
- Design and execution of preplanned care pathways enabling temporal coordination between provision steps taken by care providers in different agencies, informal carers and cared for people.
- Access to the home: homebased systems (Telemonitoring and/or Telecare TM/TC) by care providers in different agencies and informal carers.
- Real-time communication between care providers in different agencies and informal carers, e.g. support to case conferences, and older people.
- Joint response to ad hoc requests by care providers in different agencies and informal carers.

The project supported the implementation and evaluation of SmartCare services in 9 European regions. 17 additional regions participated as committed regions, with 4 of these 17 regions acting as observers to learn from the experience. Indeed, SmartCare also developed a common framework suitable for application in other regions of Europe. Guidelines and specifications for procuring, organising and implementing the service building blocks were also included.

As a result, the SmartCare project has validated the role that ICT services and applications in integrated care (integration of health, social care and personal care) for complex life conditions, including topics such as dementia and mobility with health/deterioration. Moreover, it has allowed the unblocking of new services and value chains in active and healthy ageing, including the participation of new actors, that lead to the operational implementation of new care pathways and organisational models for integrated care.

2.2.2 BeyondSilos

BeyondSilos is a CIP Policy Support Programme (PSP) pilot (2014-2017) that aligns its care pathways with those of the SmartCare project: i) short-term home support for acute care, ii) long-term care. The

care pathways cut across organisational boundaries to activate and integrate all relevant actors to the patient's care.

The fundamental innovation of BeyondSilos is not the single technological components - although some of them are highly innovative in their own right, see list below,- but the fact that the various components are already or will be integrated with one another during the lifecycle of the project. The end result of this integration activity is a shared care platform that will enable the various formal and informal care providers who play a role in the support of the older people selected for the deployment of BeyondSilos to act in a coordinated way. This will help eliminating gaps and duplications in the continuum of care that older people living independently require.

The services available within the shared platform include:

- Collection and transmission of measurements and alarms coming from the medical devices
- Geo-positioning and geo-fencing
- Panic button
- Reminders
- Emergency calls
- Fall detection
- Collection and transmission of measurements and alarms coming from the environmental sensors
- Management of domotic (home automation) actuators
- Daily scheduler
- Serious games
- Questionnaires
- eInclusion services (videoconferencing, video clips, photos, etc.)

To the Consortium's knowledge, such a level of integration, apart from BeyondSilos, will only be achieved in SmartCare, of which BeyondSilos is the logical extension.

2.2.3 CareWell

The Carewell Project (CIP-ICT Policy Support Programme 2013-2017), funded by the European Commission, aims to design and implement new and cost-effective organizational models of Integrated Care for multi morbid patients. Carewell pathways mainly consist in two services: (i) integrated care coordination pathway to improve communication, coordination and information sharing between health care professionals and (ii) patient empowerment and home support pathways focused on keeping the patients at home maintaining, even improving their health.

The main innovation of CareWell project lies in combining a number of evidence-based components together to deliver a comprehensive, coordinated integrated care service. These components fall into the following broad areas:

- use cases, organizational models and care pathways underlining the importance of integrated care and how it can improve the patient experience as well as the health outcomes and efficiency of care,
- ICT tools focused on facilitating more timely communication and sharing information between the patient and healthcare professionals. Thus, gaps and duplications in care provision are minimized and a continuum of appropriate care services for patients is provided,
- ICT tools ensuring the tracking and follow-up together with effective support for self-care and self-management of patients,
- multidisciplinary organizational care service delivery models coordinated through the respective care pathways.

Thus, the CareWell project not only incorporates technological components, but also fosters the organizational and cultural changes needed for the provision of the integrated care. The latter ensures

continuity of care, improves patients' quality of life, as well as contributing to the sustainability of the healthcare system.

2.2.4 INTEGRATE

Benchmarking Integrated Care for better Management of Chronic and Age-related Conditions in Europe) is an FP7 HEALTH project (2012-2016) that aims at gaining valuable insights into how integrated care can be best deployed [INTEGRATE]. To achieve its goal, the INTEGRATE project is organised into three phases [INTEGRATE-BLOG]:

- **Phase 1** of the project, which was finalised in 2014, was based on the study of evidence on care delivery from four established EU integrated care practices: **COPD** (Hospital Clinic, Spain), **Diabetes** (Tilburg University, two care groups, the Netherlands), **Geriatric Care** (Charité Geriatric Center, Germany), and **Mental Conditions** (Karolinska Institute, Sweden). These four case studies, i.e. two diseases and two general conditions, represent the diversity of European health systems, two with tax-based and the other two with insurance-based healthcare systems. That allowed to gain understanding of integrated care in different settings and has added insights to the second phase of the project. Application of the common methodological framework to all four cases enabled distillation of key factors of good practice in integrated care.
- In **Phase 2**, the learnings from the first phase were taken up as basis of the five horizontal topics that looked into the (i) process design and service delivery, (ii) workforce changes, (iii) patient involvement, (iv) funding flows and regulatory conditions, while also analysing how the full potential of enabling (v) information technologies can be realised in better aligning the cure and care sectors. In each of these topics, the analysis is complemented by literature reviews and expert discussions. This phase was concluded by May 2015.
- **Phase 3** to be finalised by September 2016, the end of the project, is aimed to consolidate the evidence, compares it with international evidence and draws operational and policy recommendations. The project consortium has commenced an 'international check' that has brought together a comprehensive literature review, combined with the evidence from earlier phases in the project, to produce a framework that seeks to identify the most relevant factors influencing the progress of integrated care initiatives. The framework is intended to enable producing comparable descriptions of integrated care initiatives implemented in different contexts and settings across Europe in a user-friendly way for managers in charge of leading and implementing changes. The framework is currently at the validation stage with key experts in the field, and is further being 'road-tested' with the four case sites investigated in the first phase of the project and, additionally, across key informants from 16 case examples internationally. The purpose here is to refine the framework and hence develop a useful tool to support self-assessment.

INTEGRATE project has the potential to make a difference in understanding of integrated care, and contribute to better transfer of good practices and scaling up. It will also give insights in how integrated care enthusiasts can better design care process, identify needs of professional capacity building, involve patients in the care process, redefine financial flows and regulatory issues and see how IT can better support this innovative way of addressing the health systems most pressing issues: the increase in ageing and chronic conditions. The managerial and policy recommendations should provide guidelines for Member States and reform willing regions and institutions to successfully implement an innovative integrated care.

Building on the existing network of International Foundation of Integrated Care [IFIC], INTEGRATE is a very relevant umbrella project analysing best practices in varying settings, with the aim of developing guidelines on how integrated care can be delivered in the most effective way. These guidelines to address several aspects of integrated care challenges (e.g. organisational, technological, patient involvement) will be important sources of reference in the C3-Cloud project, especially in Task 4.2 - Development of New Organisational Models for Improved Delivery of Integrated Care, and Task 4.3 - Change Management for New Ways of Care Delivery. The timing between INTEGRATE and C3-

Cloud also helps a lot in this respect; we expect to have all final outcomes of the INTEGRATE project by September 2016, which provides us the opportunity to take all INTEGRATE experience into account in our work. Although the INTEGRATE project will soon be completed, we will contribute back our results and hands-on experience to the IFIC community. Yearly international conferences on integrated care organised by IFIC are valuable occasions for C3-Cloud presence.

2.2.5 ASSEHS

The ASSEHS project (Activation of Stratification Strategies and results of Interventions on frail patients of Healthcare Services) [ASSEHS], aims to activate stratification tools in the field and to evaluate the results of their implementation in different European health services, focussing on the use and value added to the provision of care to fragile elderly patients. The main goal of this project is to analyse valid, reproducible and transferable stratification strategies. To this end, it is important to identify the key elements, barriers and facilitators to defining, developing, implementing stratification tools and their impact on health systems. At the same time, the possible uses of stratification tools in health management, policies and clinical practice are being investigated. Their main expected results are: (i) the activation of the use of stratification tools in integrated care for fragile patients and (ii) the definition of a framework for implementing population-stratification tools.

Kronikgune, the coordinator of ASSEHS project, in close collaboration with Osakidetza (the Public Health System of the Basque Country), lead the work package dedicated to analysing the feasibility of implementing risk stratification strategies in health systems (WP5) and leads the Basque Country's participation as a region. Both partners participate by way of the stratification experiences launched.

2.2.5.1 Specific programmes of action: Integrated Intervention Programmes in Osakidetza

Risk stratification of the population intends to tag groups of patients who can benefit from proactive and preventive interventions. In fact, it can be a very useful tool in the care of patients with the same illness. The aim of stratifying is to identify and select target groups that may benefit from specific programmes of actions targeting specific conditions. Thus, Osakidetza has developed Personalized Plans for groups of patients suffering the same disease. These plans are called “Integrated Intervention Programmes (IIPs)”. Several have already been deployed in Osakidetza. The objective is to provide anticipatory and coordinated care to all patients identified through the risk stratification tool. Some chronic diseases such as heart failure, asthma, diabetes and COPD are the pathologies that may benefit from preventive interventions since there is evidence that interventions with preventive and self-care activities can positively influence patient health.

Currently, different Integrated Intervention Programmes are running:

- Multi-morbid
- COPD
- Heart Failure
- Diabetics with poor metabolic control (according to the values of glycated haemoglobin)

2.2.5.2 Multi-morbid Integrated Intervention Programme

The Integrated Intervention Programme for multi-morbid patients has been designed by managers and clinicians of the Hospitals and Primary Care Centres involved. In 2014, the population risk stratification process identified 683797 chronic patients as the target population. A clear design methodology of the new care pathway has been used: the analysis of current models, the detection of improvement areas, and the prioritization and definition of actions. The perspectives of all the stakeholders have been taken into account.

The new service model has improved “care as usual” in a number of ways: wider deployment of the reference internist and hospital liaison nurse into other hospitals in the region; follow-up phone calls by the GP practice nurse on a monthly basis to monitor the patient's health status; the use of eHealth Centre professionals in the care pathways; provision of symptom management questionnaires in the Personal Health Folder to further support self-management; rolling out the electronic prescription to additional healthcare professionals including pharmacists; the development of a structured and standard

empowerment programme for frail elderly patients and caregivers and provision of self-care and self-management educational material through the Personal Health Folder and Osakidetza web portal.

2.2.5.3 Inclusion criteria and / or identification of Multi-morbid IIPs in 2014

Over 13 years, chronic patient with at least one hospitalization in the year prior to the stratification. At least 2 of these three diseases: COPD, diabetes and heart failure, or 2 or more of the categories: “de Ollero”¹. Its predictive index is ≥ 95 percentile of the population identified as chronic (coded in Osabide Global by red triangle) and the patient does not have neoplasia, transplantation or dialysis. Clinicians may also include new multimorbid patients if they consider the stratification tool has not detected them.

In a second phase, the list of identified multimorbid patients is provided to each clinician for review, including or excluding patients according to the following criteria:

- Diagnostic coding errors
- Neoplasia in treatment
- Transplantation
- Dialysis
- Palliative Patients
- Institutionalized in assisted nursing homes with medical service
- Other

2.3 Related standards

The current section describes important standards related to the development and execution of Personalised Care Plan.

2.3.1 HL7 Care Plan Domain Analysis Model

HL7 Patient Care Workgroup (PCW) [HL7-PCW] has balloted the initial Care Plan model in 2007 as DSTU (Draft Standard for Trial Use). However, a number of ballot issues were not resolved satisfactorily and consequently the balloted contents did not reach DSTU status. Later, a new project plan was initiated in 2011 to develop a Domain Analysis Model (DAM) as a common reference to support the development of implementable care plan models. HL7 PCW worked together with various groups including HL7 Workgroups (e.g. EHR, Structured documents), IHE, NEHTA, Canada Health Infoway, and others. The Care Plan DAM project concluded in 2014 after complete resolution of informative ballot 2 comments [CarePlanDAM].

The care plan is a tool used by clinicians to plan and coordinate care for an individual patient. The care plan is known by several similar and often interchangeable names such as the plan of care and treatment plan. It is acknowledged that the use of these similar names and their associated meanings are context, organization and realm specific. The Care Plan DAM uses the concept care plan in the generic sense.

The purpose of the care plan as defined by HL7 Care Plan DAM is to:

- define the management action plans for the various conditions (for example problems, diagnosis, health concerns) identified for the target of care,
- organize a care plan and check for completion by all individual professions and/or responsible parties (including the patient, caregiver or family) for decision making, communication, and continuity and coordination,
- communicate explicitly by documenting and planning actions and goals,

¹ "de Ollero" refers to a definition of multimorbid patient. Ollero et al. [Ollero], in order to get a proper identification of multimorbid patients, have proposed grouping chronic diseases in clinical categories, considering the damage to the target organ and the functional impact generated. They identify as multimorbid patient the one with diseases in two or more the proposed categories.

- permit the monitoring, flagging, evaluating and feedback of the status of goals, actions, and outcomes such as completed, or unperformed activities and unmet goals and/or unmet outcomes for later follow up,
- manage risk related to effectuating the care plan,

Within the scope of Care Plan DAM project a number of storyboards have been defined as narrative descriptions of clinical scenarios where the care plan is created, accessed, updated or used during the provision of healthcare. The storyboards provide context to the information collected, retrieved, presented and reported in care plans. The following storyboards have been defined:

- Storyboard 1: Acute Care
- Storyboard 2: Chronic Conditions
- Storyboard 3: Home Care
- Storyboard 4: Pediatric Allergy
- Storyboard 5: Pediatric Immunization
- Storyboard 6 – Perinatology
- Storyboard 7 – Stay Healthy/Health Promotion
- Storyboard 8 – Case Management/Disease Management Care Coordination

Later by analyzing these storyboards, the Care Plan project team has developed a number of care plan model artifacts. A layered modeling approach was used which allows for separation of concerns by business requirements, information requirements and technical interoperability requirements, and to support forward and backward traceability through these layers. The first layer, the conceptual model level, identifies the business domain concepts and concept relationships necessary to define the scope of the domain semantics covered by the subsequent levels. The second layer, the logical information model, elaborates the conceptual model by adding attributes necessary to capture the data elements resulting from dynamic care planning interactions and required for capturing static point in time snapshots of the care plan. At the logical information level the model retains a one to one mapping of all the domain concepts except abstract data types such as String, Boolean and Code start to surface. The logical information model contributes intrinsic data properties necessary to specify a class model with sufficient detail to support interoperability information requirements. Care Plan DAM defined these two levels of abstractions. Realization of the third layer, the platform implementation model is handled by separate efforts as independent technical specifications such as CCDA (Consolidated Clinical Document Architecture) specification of the care plan and its exchange and SOA (Service-Oriented Architecture) specifications for coordination of care.

In this section a very brief overview of Care Plan DAM conceptual model is presented. Interested readers are invited to review Care Plan DAM specifications for detailed conceptual and logical models [CarePlanDAM].

2.3.1.1 Care Plan DAM Conceptual Model

The model consists of an abstract Plan which captures the shared components of collaborative, patient centered and holistic care. The Plan has associations to concepts for Health Concern, Health Goal, Health Risk, Care Barrier, Care Preference, Conversation, plan Activity (including interventions), Acceptance Review, Plan Review and key care team participations through time and space between the Patient, Provider(s), Care Giver(s) and other Supporting Member(s). Each is listed equally but it is the health concern, and the plan Activity that are directly driving the anticipated Health Goal (whether or not it is realistic). The Health Outcome(s) are tied to the health concern, goal and activity allowing evaluation of the progress of care towards the health goal(s). The high level relationships between Care Plan components is depicted in Figure 2.

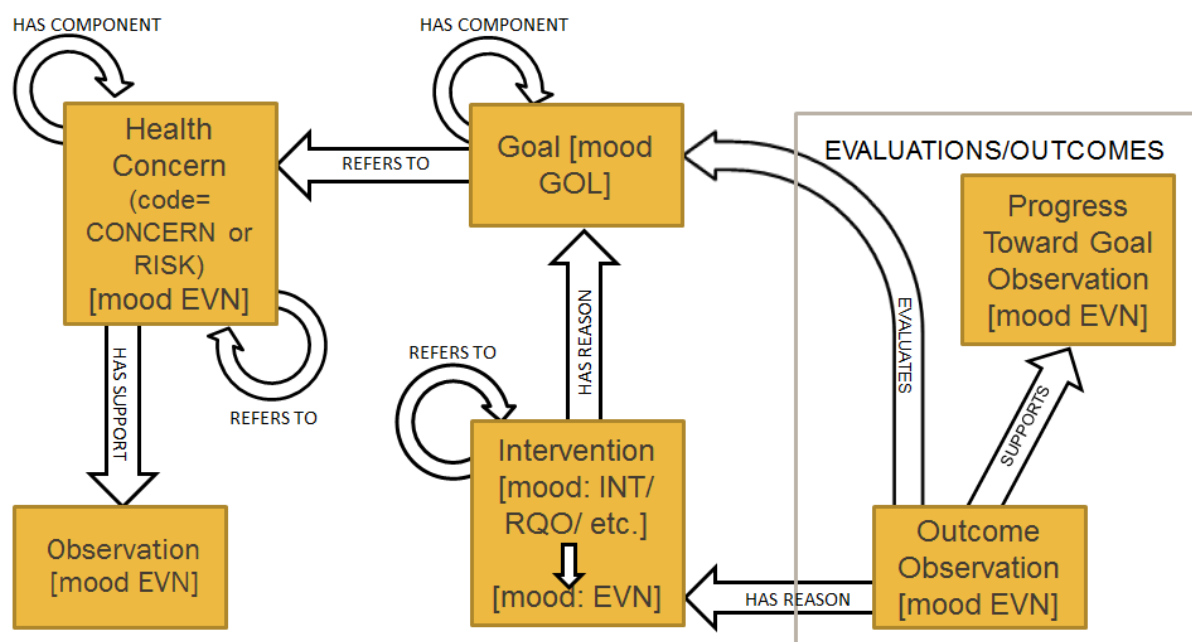


Figure 2 Care Plan Relationship Diagram [C-CDAR2]

The Plan and many of its associated classes support dynamic care team involvement. The Care Plan DAM has the capability to capture information about these participations. The details of the Plan result from the interactions of the Care Team consisting of the Patient and at least optional Providers, Care Givers or Supporting Members. A Plan is not intended to be static but continuously changing based on continual chatter, negotiation and interactions between the various care team members. The Care Plan by design is a collaborative, shared and dynamic structure with controlled Care Team involvement or participation. The Care Team is in many places, interactions span the continuum of care and time. Resolution of differences in opinion, correction of discrepancies and overall harmonization of the care plan requires raising awareness and visibility of care team Participations so that they are visible to all care team members (within the constraints of the circle of care which needs to know).

A Plan may come into being as a result of one or more patient Health Concerns or simply as a result of a patient Health Goal. For example, in the stay healthy use case, a health care consumer may not have a specific concern but simply a desire (i.e. goal) to improve some aspect of their health. In this case the patient may have a Plan entirely driven by Health Goals. The Plan is created with simply a goal in mind. For patients with some health conditions whether simple, chronic or complex, the Plan will reference one or more Health Concerns. The Health Concern specifies the reason for creating the Plan. In this case the Health Concern reason eventually leads to the definition of Health Goals as a result of conversations between the patient and his or her providers, care givers and supporting care team.

Certain individuals may have predisposition to certain Health Risk, which may or may not become health concern(s) over time. The model supports representation of these Health Risks to enable the care team to monitor them and have the awareness to implement mitigating actions if the need arises. An intervention, plan Activity, in turn may present certain Health Risks to the patient which must be closely monitored to prevent the manifestation of additional health concerns (e.g. the risk of administration of an immunosuppressant, surgery, etc.)

In Figure 3, a high level view of Plan conceptual model can be visualized.

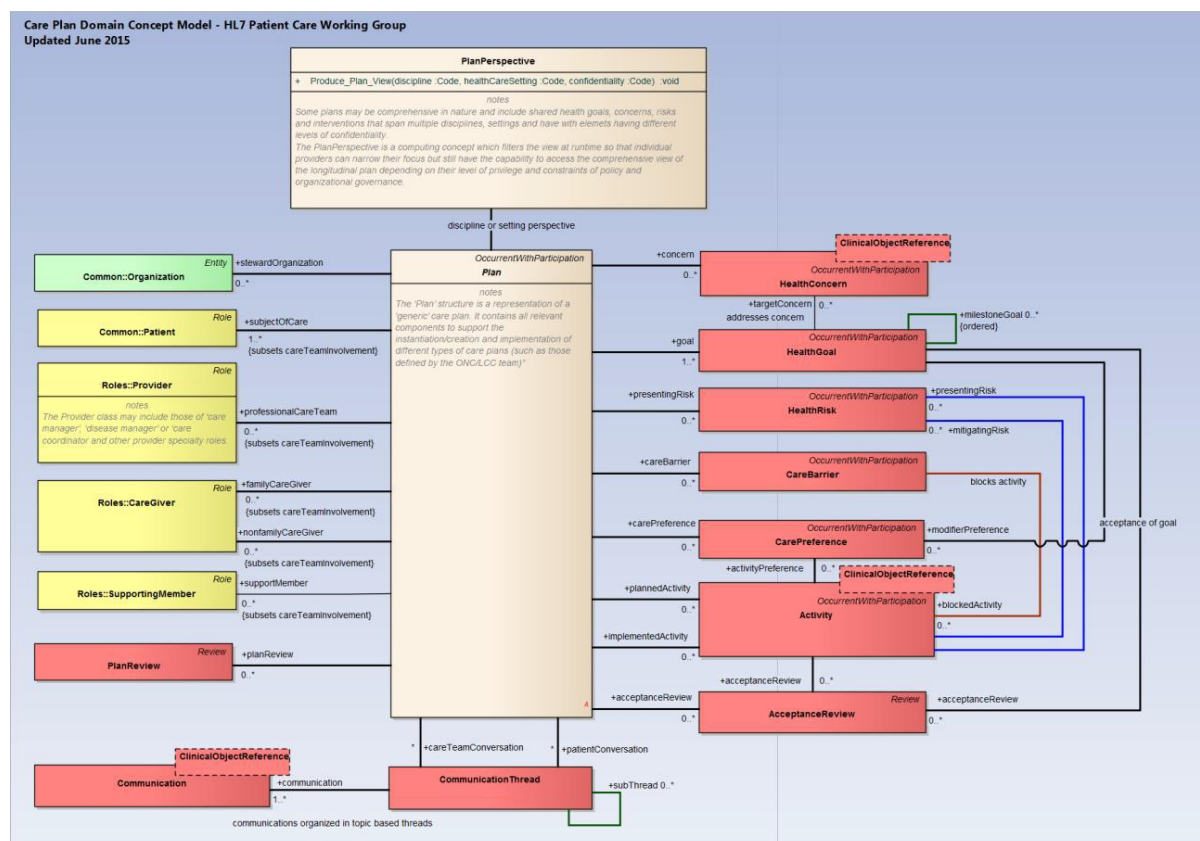


Figure 3 Plan Concept Model based on HL7 Care Plan DAM [CarePlanDAM]

Currently within the scope of HL7 Patient Care workgroup workplan two parallel activities are being coordinated for:

- Harmonization of the Care Plan model with FHIR care plan model (see section 2.3.3)
- Harmonization of the Care Plan model with C-CDA R2 care plan templates (see section 5.4.1)

These will be briefly discussed in the following sections.

2.3.2 ONC S&I Framework Longitudinal Coordination of Care Workgroup

The Longitudinal Coordination of Care (LCC) Initiative [LCC] has been initiated in October 2011 as a part of ONC Standard and Interoperability (S&I) Framework [S&I] with the aim of addressing the interoperability challenges in long-term, post-acute care (LTPAC) transitions. LCC initiative has been closed in September 2014, and in this period has delivered important outcomes by also collaborating closely with standardization organizations such as HL7 and IHE. The key deliverables produced by ONC LCC group are:

- LCC Transitions of Care Use Case 1.0
- Care Plan White Paper/Glossary
- LCC Care Plan Exchange Use Case 2.0
- C-CDA R2 Implementation Guidance

In the scope of Transitions of Care Use Case 1.0 document [LCC-ToC] published in June 2012, the functional requirements and technical specifications for Care Plan and Home Health Plan of Care exchange have been analyzed in detail. Several use cases have been studied to identify the requirements for transition of care from Acute Care Hospital units to LTPAC providers and patient/family and also from LTPAC providers to Acute Care Hospitals. The requirements for information exchange has been thoroughly analyzed and five new transition data sets have been identified as:

1. **Report from Outpatient testing**, treatment, or procedure
2. **Referral to Outpatient testing**, treatment, or procedure (including for transport)

3. **Shared Care Encounter Summary** (Office Visit, Consultation Summary, Return from the Emergency Department (ED) to the referring facility)
4. **Consultation Request** Clinical Summary (Referral to a consultant or the ED)
5. Permanent or long-term **Transfer of Care Summary** to a different facility or care team or Home Health Agency

As a result, the existing Transitions of Care (ToC) Data Set for Continuity of Care Documents (CCD) has been extended to include 325 data elements which were previously 175.

In parallel with this effort a Care Plan White Paper and an accompanying glossary [CarePlanWhitepaper] has been published in August 2012 where the content and functionality of care plans needed to support longitudinal coordination care for medically-complex and/or functionally impaired individuals is explored, and opportunities to support the interoperable exchange of care plans, including the home health plan of care (HH-POC) have been identified.

In July 2013, the Care Plan Exchange Use Case 2.0 [LCC-CPE] has been published where the functional requirements for EHR systems so that clinical and administrative information related to a patient's Care Plan or Plan of Care can be exchanged across multiple settings and disciplines have been identified.

As a continuation of these works, the LCC group, in collaboration with the Longitudinal Care Plan SWG, has worked for development and balloting of the HL7 Implementation Guide for CDA® Release 2: Consolidated CDA Templates for Clinical Notes (US Realm) Draft Standard for Trial Use, Release 2 (Sept 2013) [C-CDAR2] which provides new templates and requirements for the HL7 C-CDA standard for the exchange of data elements for consult note, summary note, transfer note and care plan/home health plan of care. Three new document types (Transfer Summary, Care Plan and Referral Note), six new sections and thirty new entry templates have been designed.

2.3.3 HL7 FHIR Care Plan Model

HL7 Fast Healthcare Interoperability Resources (FHIR, see also section 5.4.2) [FHIR] is an emerging standards framework created by HL7 which combines the features of HL7's v2, HL7 v3 and CDA product lines while leveraging the latest web standards (such as XML, JSON, HTTP, OAuth) and applying a tight focus on implementability. FHIR solutions are built from a set of modular components called "Resources". These resources can easily be assembled into working systems that solve real world clinical and administrative problems very quickly. FHIR is especially suitable for use in developing mobile phone apps, cloud communications, EHR-based data sharing, server communication in large institutional healthcare providers. FHIR has a direct support for RESTful architectures for managing the FHIR Resources.

The philosophy behind FHIR is to build a base set of resources that, either by themselves or when combined, satisfy the majority of common use cases. FHIR resources aim to define the information contents and structure for the core information set that is shared by most implementations. There is a built-in extension mechanism to cover the remaining content as needed.

The current FHIR standard published as a DSTU2 in October 2015, CarePlan concept is also designed as a Resource. The HL7 Patient Care workgroup, who has defined the most recent release of HL7 Care Plan DAM is actively participating to the activities to finalize CarePlan Resource as a part of FHIR. It is still an ongoing work where the constituting resources such as Care Team are still in development. In the following figures² a high level overview of HL7 FHIR CarePlan resource is depicted.

² <http://www.hl7.org/fhir/careplan.html>

Structure				
Structure				
Name	Flags	Card.	Type	Description & Constraints
CarePlan			DomainResource	Healthcare plan for patient or group
identifier	Σ	0..*	Identifier	External Ids for this plan
subject	Σ	0..1	Reference(Patient Group)	Who care plan is for
status	?! Σ	1..1	code	proposed draft active completed cancelled CarePlanStatus (Required)
context	Σ	0..1	Reference(Encounter EpisodeOfCare)	Created in context of
period	Σ	0..1	Period	Time period plan covers
author	Σ	0..*	Reference(Patient Practitioner RelatedPerson Organization)	Who is responsible for contents of the plan
modified	Σ	0..1	dateTime	When last updated
category	Σ	0..*	CodeableConcept	Type of plan Care Plan Category (Example)
description	Σ	0..1	string	Summary of nature of plan
addresses	Σ	0..*	Reference(Condition)	Health issues this plan addresses
support		0..*	Reference(Any)	Information considered as part of plan
relatedPlan		0..*	BackboneElement	Plans related to this one
code		0..1	code	includes replaces fulfills CarePlanRelationship (Required)
plan		1..1	Reference(CarePlan)	Plan relationship exists with
participant		0..*	BackboneElement	Who's involved in plan?
role		0..1	CodeableConcept	Type of involvement Participant Roles (Example)
member		0..1	Reference(Practitioner RelatedPerson Patient Organization)	Who is involved
goal		0..*	Reference(Goal)	Desired outcome of plan
activity	I	0..*	BackboneElement	Action to occur as part of plan <i>Provide a reference or detail, not both</i>
actionResulting		0..*	Reference(Any)	Appointments, orders, etc.
progress		0..*	Annotation	Comments about the activity status/progress

Figure 4 HL7 FHIR Care Plan Model Part -1

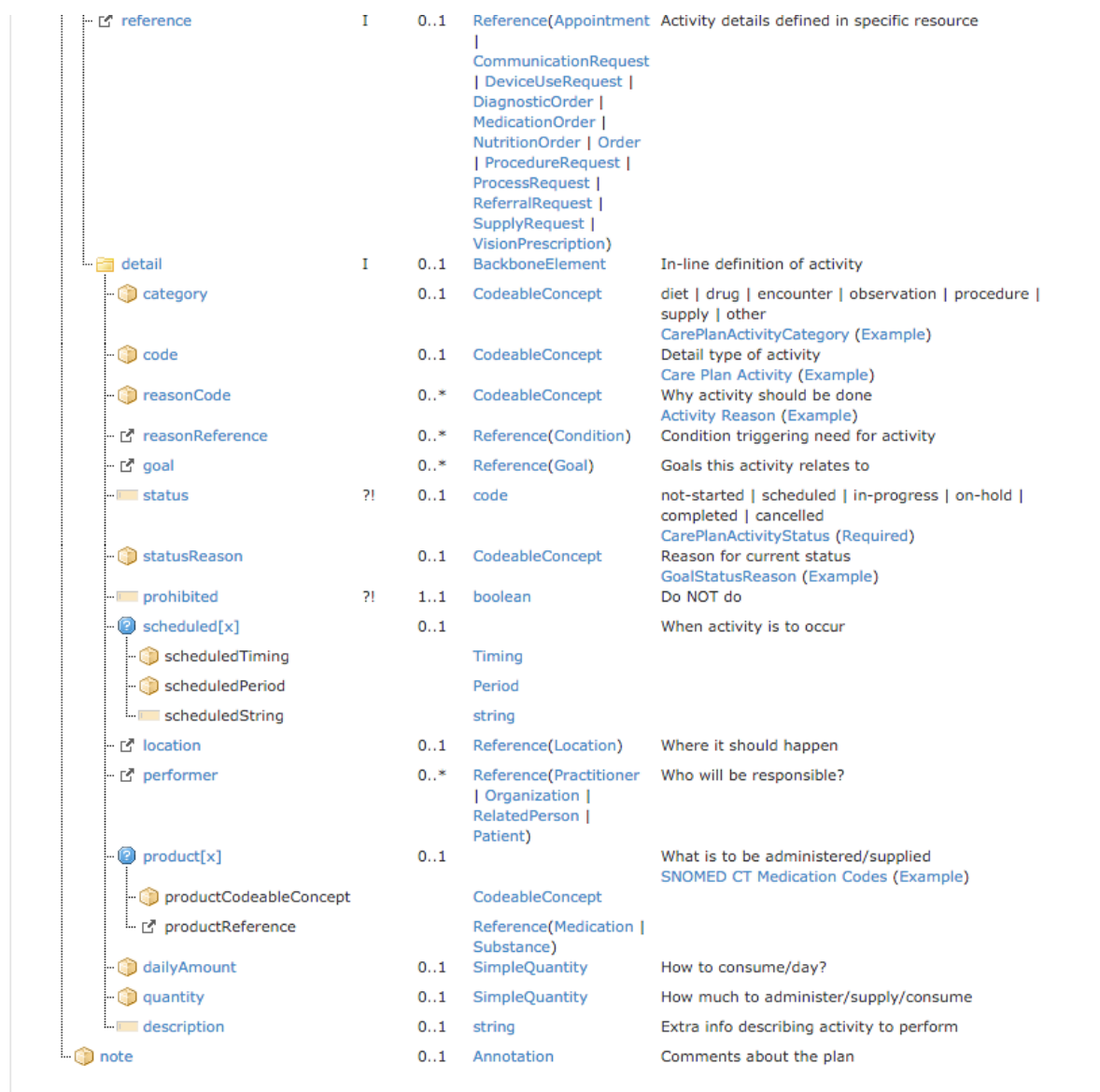


Figure 5 HL7 FHIR Care Plan Model Part -2

2.3.4 ISO 13940:2015 - A System of Concepts for the Continuity of Care (Contsys) Care Plan Model

As a part of ISO 13940:2015- Health informatics - System of concepts to support continuity of care, detailed description of concepts related to healthcare planning is provided [CONTSYS]. A model showing the associations between the concepts related to the use of clinical knowledge and decision

support in continuity of care and the other concepts defined in this International Standard is shown in

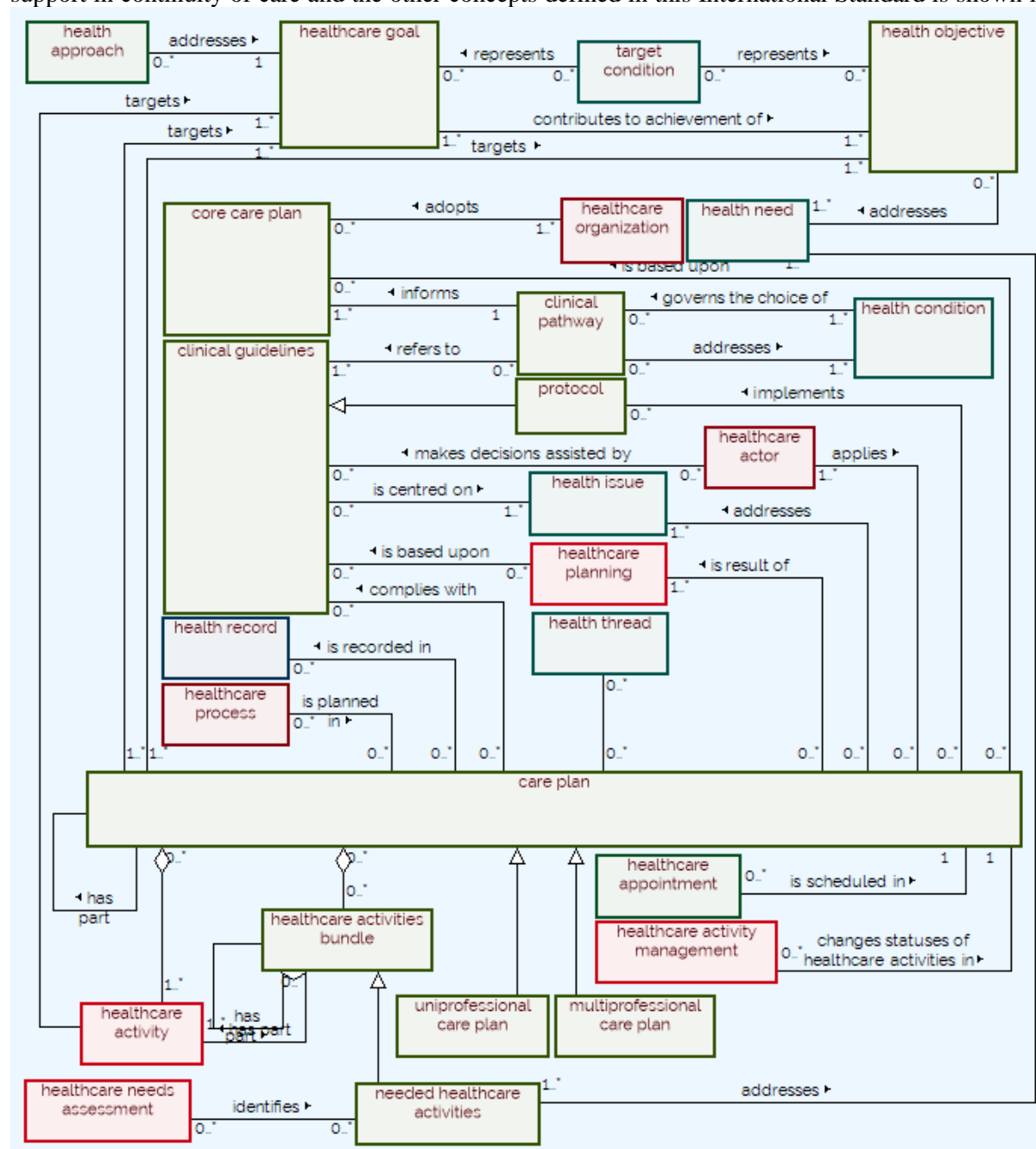


Figure 6.

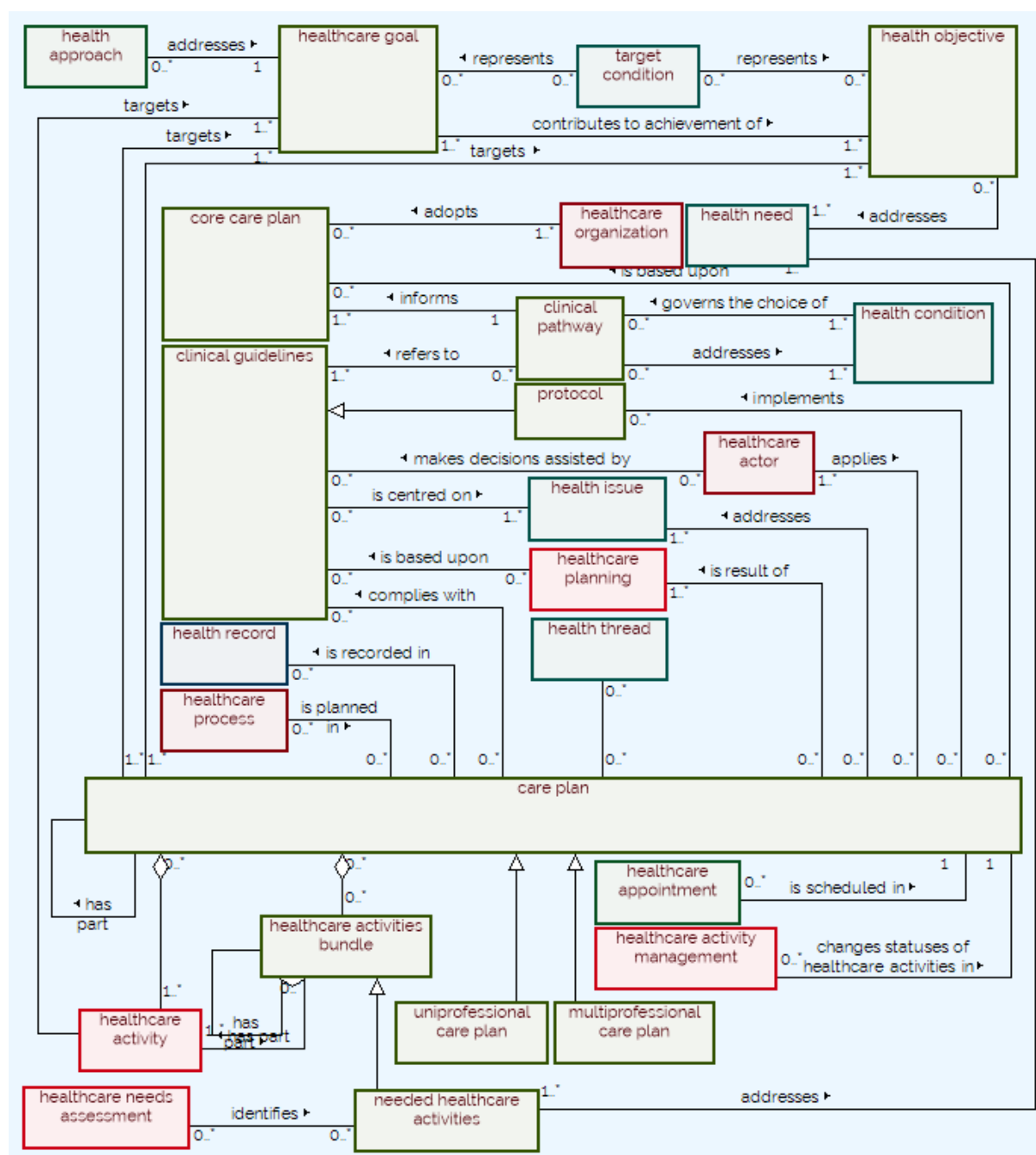


Figure 6 Comprehensive UML diagram of concepts related to healthcare planning from ISO 13940:2015 [UML-Health]

The core of this model, the “care plan” is defined as “dynamic, personalized plan including identified needed healthcare activity, health objectives and healthcare goals, relating to one or more specified health issues in a healthcare process”. Unlike HL7 Care Plan DAM, here we see that separate concepts for uniprofessional care plan (care plan limited to those healthcare provider activities performed by healthcare professionals having the same healthcare professional entitlement) and multi-professional care plan (care plan encompassing healthcare provider activities performed by healthcare professionals having different healthcare professional entitlements) are defined. An overview of the “care plan” concept in ISO 13940:2015 is depicted in Figure 7. In ISO 13940:2015 representation, a “care plan” is usually based upon knowledge in “clinical guidelines” (including “protocols”). “Clinical guidelines” are defined as “sets of systematically developed statements to assist the decisions made by healthcare actors about healthcare activities to be performed with regard to specified health issues”. “Care plans”

implement “protocols” which are customized clinical guidelines, often presented in a formal manner with respect to the expected behaviours and roles of healthcare actors.

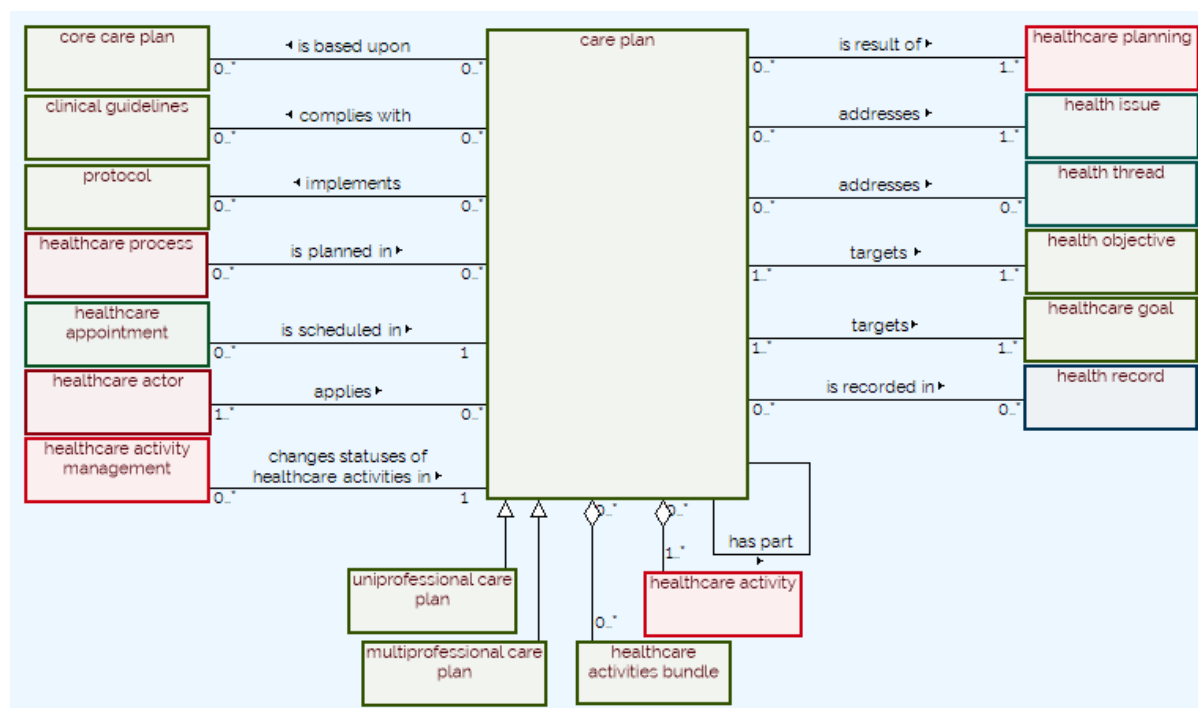


Figure 7 Care Plan UML Model in ISO 13940:2015 [UML-CarePlan]

“Clinical pathway” is defined as “pathway for the healthcare activities informing the content of core care plans”. Clinical pathways are designed to support healthcare administration and healthcare resource management. They provide detailed guidance for each stage in the management of a patient (treatments, interventions, etc.). “Care Plans” are designed to target “health objectives” (a.k.a intended outcome), which is defined as “desired ultimate achievement of a healthcare process addressing health needs”. A health objective could be expressed as one or several target conditions to be reached within a specified date and time. “healthcare goals” are desired achievements of one or more “healthcare activities”, considered as an intermediate operational step to reach a specific “health objective”.

2.3.5 IHE Patient Care Technical Committee Profiles

2.3.5.1 Patient Plan of Care (PPOC) Profile

The Patient Plan of Care (PPOC) profile [PPOC] provides a mechanism for electronic exchange of data related to creating and managing individualized patient care between and among health information technology systems. The PPOC, has a nursing focus, and aims at enabling the exchange of plan of care information in a standardized framework using the American Nurses Association (ANA) nursing process to evolve its information model. The PPOC focuses on the following six components in a clinical document defining care plan:

- Assessment
- Nursing Diagnosis
- Outcomes Identification
- Planning
- Implementation (Interventions)
- Evaluation

When a patient arrives for care (e.g., upon admission or transfer of care) they undergo an initial assessment. The care planning process includes diagnoses, outcomes identification (goals), and the planning of care with the patient or their advocate. The nursing process continues with the nurse

implementing actions to provide care for the patient based on the plan. Evaluation measures the current patient progress against the expected outcomes through subsequent assessments. Evaluations are used to adjust the nursing plan. These components are performed continuously through the care process. PPOC is a content profile that defines the implementation of an HL7 CDA document to represent the data elements needed for care planning during these processes, along with the IHE profile bindings to support the exchange of the information. The latest version of IHE PPOC Profile is dated October 2013, which is a Trial for Implementation.

2.3.5.2 Patient Care Plan Content Profile (PtCP)

Patient Care Plan is a content profile [PtCP] that defines a centralized patient care plan that will meet the needs of many stakeholders (providers and patients) and provide a method to reconcile and consolidate the many disparate care plans that can be attached to a patient. PtCP clearly defines the distinction between Treatment Plans, Plan of Care and Care Plan documents: *“A Care plan can contain multiple plans of care which are comprised of treatment plans and instructions”*. The following two figures clearly depicts these distinctions:



Figure 8 IHE PtCP- Structure of Patient Care Plan [PtCP]

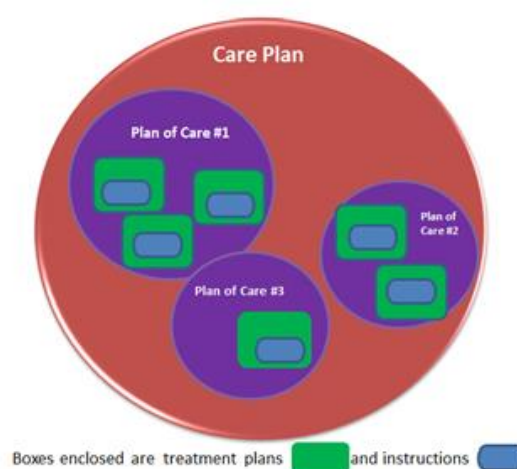


Figure 9 IHE PtCP- Contents of Patient Care Plan [PtCP]

The PtCP aims to support one overarching interdisciplinary plan of care where all disciplines that care for the patient are able to communicate their plan of care, treatment plan, problems, interventions and goals/outcomes, for the patient, and where these can be reconciled by also utilizing IHE PCC Reconciliation of Diagnoses, Allergies and Medications (RECON) Profile [RECON].

The PtCP Document is composed of several sections including a new Patient Care Plan Section. The new Patient Care Plan section contains subsections including Plans of Care, a Reconciled Plan of Care, Patient Goals, Reconciled Goals, Interventions, and Reconciled Interventions sections. The purpose of the Reconciled Plan of Care is to compile the data elements of the various Plans of Care. The Patient Goals subsection describes the patient's progress towards expectations for care and the Reconciled Goals subsection contains reconcile goals that have been completed and goals in progress. The Interventions subsection contains entries that display a holistic view of interventions and procedures (e.g., patient education, intravenous insertion) provided for patient care and the Reconciled Interventions subsection results from the reconciliation of all the various Intervention sections. Other sections in the PtCP document are used to provide a retrospective view of care provided to the patient and the patient response to care. An example is depicted below:

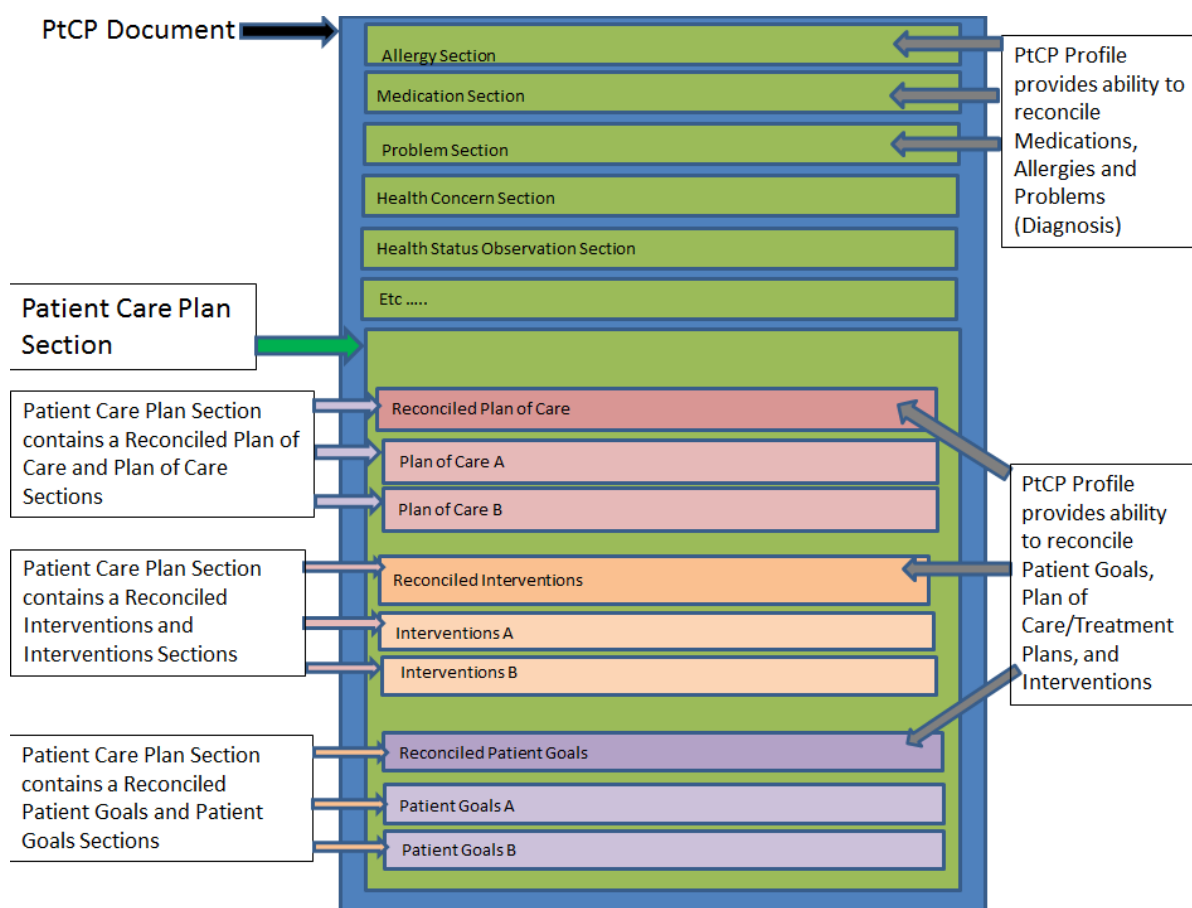


Figure 10 IHE PtCP Patient Care Plan Document [PtCP]

The latest version of IHE PtCP Profile is dated October 2013, which is a Trial for Implementation.

2.3.6 HL7 Coordination of Care Services Specification Project

Within the scope of HL7 CCS Specification Project [HL7-CCS], a Service Functional Model (SFM) has been defined to elaborate the functions or capabilities required for effective coordination of care systems. It includes illustrative story boards and care team collaboration illustrative models. This SFM defines the scope of the requirements for a subsequent phase of the project defining a technical services specification in cooperation with Object Management Group (OMG) [OMG] within the scope of The Healthcare Services Specification Project (HSSP) [HSSP].

The functional capabilities described as a part of SFM represent discrete steps in dynamic coordination of care interactions. They may be used in different combinations to help orchestrate the care coordination in collaborative care environments. The capabilities are described in terms of business level pre-conditions, inputs, outputs, exception conditions and post-conditions. The capabilities are grouped into related groups as follows:

- Care Team Membership Capabilities
- Care Team Communication Capabilities
- Care Team Availability/Scheduling Capabilities
- Care Plan Management Capabilities
- Plan Templates
- Plan Resource Support Capabilities
- Progress and Outcome Review Capabilities
- Observations and Supportive Content Capabilities

The current version of CCS Service Functional Model is dated May 2014 and is a Draft Standard for Trail Use (DSTU) Ballot [HL7-CCS-SFM].

3 DECISION SUPPORT MODULES FOR RECONCILIATION OF MULTIPLE TREATMENT PLANS

3.1 Introduction

In the C3-Cloud project, several clinical decision support modules will be developed to perform risk assessment and stratification of elderly people for inclusion in integrated care programmes; to reconcile clinical guidelines for individual diseases to develop personalised care plans; to detect and propose resolutions for guideline clashes; to detect duplicate, unnecessary or contraindicating medications; and to track deviations from the outcome goals set in the care plan.

A recent review by Fraccaro et al. [Fraccaro15] explored the extent of clinical decision support (CDS) adoption in multimorbidity from a technical/methodological perspective. The authors have used multimorbidity in a broad sense to infer comorbidity as well. Having more than one condition generates several issues including: interactions between pathologies; duplication of tests; non-adherence due to conflicting clinical practice guidelines; obstacles in continuity of care; confusing self-management information; and medication errors. Thus, clinical decision support systems need to be able to handle the complexity of multimorbidity and minimize iatrogenic risks. These relate to the possibility that a medical intervention causes iatrogenic disease, defined as “any onward or adverse consequence of a preventative, diagnostic or therapeutic regimen or procedure that causes impairment, handicap, disability or death” [Last85].

Knowledge-based systems

The review included 20 studies and the key aspects of clinical decision support. The most commonly used decision support method was knowledge-based systems, such as [Riaño12] and the COMET system [Abidi12]. Riaño et al. [Riaño12] propose an ontology for the health care of chronically ill patients at home. This ontology is extended with intervention plans for 10 chronic diseases and a method to personalize the ontology and the intervention plans is implemented. The clinical decision support system uses this personalized ontology to help clinicians to make decisions and tests have conformed the clinicians’ satisfaction of these tools in real settings. Another CDS system using a knowledge management solution is COMET [Abidi12], designed to address the knowledge needs of general practitioners by using semantic web technologies for knowledge representation and execution. Three patient scenarios can be handled by the system, for patient with Chronic Heart Failure (CHF), Atrial Fibrillation (AF) or a CHF-AF comorbidity. The system has been evaluated for handling single and comorbid case scenarios.

Medication

Medication was a main theme in the papers reviewed with prescription and medication review as topics. Example systems include the ATHENA-DSS system for guiding generalist practitioners through a list of patient information for a suggested optimal opioid treatment for chronic pain [Michel08]. Another system considers the clinical state of the patient and co-morbidities to suggest the most appropriate drug therapy for heart failure management, based on clinical practice guidelines [Dassen03]. Wit et al. [Wit13] present a system that monitors prescribed drugs of elderly patients in nursing homes. It processes extracts of clinical data from electronic prescribing systems and electronic health records and uses clinical rules to support health professionals to perform medication reviews.

Guideline interaction

Potential interaction between concurrent clinical practice guidelines in multimorbid patients is also a comorbid personalized guideline [JA13, Abidi12]. Some systems used constraint logic programming to identify and mitigate possible adverse interactions between clinical practice guidelines [Wilk11, Wilk13]. Other systems enable the sharing of decisions through a standard-based electronic health records and using social networking techniques to enhance continuity of care through a web platform [Martínez-García13]. The systems described simplify the analysis by considering only two concurrent clinical practice guidelines. In the C3-Cloud project, combinations of the four key conditions will be taken into account.

Comorbidity diagnosis

Some studies have used clinical decision support to address the diagnosis of comorbidities for patients with an index disease or condition. Natural language processing has been applied to clinical notes for diagnosing comorbidities in obese patients [Farkas09], whereas machine learning was used for the diagnosis of multiple concurrent neuropathies in Suojanen et al.[SAO01].

Summary

The review has found only a modest number of relevant articles addressing CDS and multimorbidity. Topics that are key to multimorbidity but had few or no relevant article include CDS self-management interventions, continuity of care, lack of patient-centred approaches, wider methodological considerations, technological interoperability; and rigorous evaluation of the CDS systems.

The following sections will focus on the clinical decision support topics that have been identified as key for the C3-Cloud project to address.

3.2 Risk Stratification

Currently governments and health organizations show a growing interest in developing new ways of health and social services provision to people with chronic diseases, strengthening action on social determinants and with a population approach. One of the initiatives to improve care for people with chronic diseases is based on the identification of high-risk patients that seeks to adapt the processes of care to their different needs.

Risk stratification is a tool to identify and / or group patients at higher risk of worsening or developing a new health problem, requiring more intense care and resources in the future. Thus, it serves to define early interventions that suit their future health care needs. There are different ways to identify and / or group patients according to their risk of future problems:

- Descriptive models:
 - Clinical judgment: Method based on the decision of health professional. It is based on their knowledge, instinct and experience to identify at-risk individuals who may benefit from early intervention.
 - Descriptive modeling: rule-based methods, thresholds or preset decision criteria that describe a high-risk patient. For example, over 65, chronic obstructive lung disease and a previous income.
- Predictive modeling: Based on predictive models that seek to establish relationships between sets of variables to predict future outcomes, using formulas and statistical methods. Most use regression models although currently there are many methods based on artificial intelligence. They have the advantage over clinical judgment or descriptive models that do not require direct contact between health professionals and patients, as it uses previously recorded data, which can be applied to large groups of people.

Risk stratification based on predictive models is a statistical process that determines the probability of occurrence of unwanted events / results. Risk stratification mainly uses data from patients recorded in health information systems. By grouping individuals according to the different risks; we can classify the population in different strata or segments. Therefore, these predictive models allow the stratification

of the population according to the increased risk of suffering the adverse events defined. This is the technique used in the known Kaiser Permanente Pyramid risk stratification.

Stratification allows a proactive population-based approach (i.e. including the entire population assigned to a service unit). It aims at recognizing in advance those who have a high probability to suffer an event or a problem in the near future. This trend to a "probable" future situation allows building proactive strategies (i.e., anticipating events) to avoid or lessen the impact of these events in both health and quality of life of people and consumption of resources.

Risk tools have two utilities:

- identifying patients who may benefit from interventions to prevent unwanted events (case finding). It allows anticipation of care over those groups of patients who are more likely to evolve positively with an early intervention,
- planning interventions and their funding. It allows better planning and efficient management of resources and better distribution of budget and funding. By means of adjusting the distribution of resources to risks, the burden of mobility is proportional to the respective population.

Thus, stratify the population offers the opportunity to be proactive, designing appropriate specific health care interventions according to the level of need of the different groups of people.

Predictive risk stratification models are composed of the mathematical algorithm that calculates the risk for each patient. The algorithm is generally based on multiple regression models, although neural networks or decision trees are also used. The mathematical algorithm that is used will depend on the available information (input) and what is wanted to predict (output). Clinical data from administrative databases such as electronic health records and interconnection of records from different healthcare and social fields have facilitated the exploitation of clinical information of the patient. The availability of information and the reliability of this are key elements. Examples of variables to be used in the model are: demographic (age, sex, etc.), previous use of resources, pharmacy, morbidity, Health, quality of life and health care and social and economic variables. One of the results ("output") is the expected cost. The expected consumption of health resources as "output" allows comparisons between morbidities and patients with very different needs attention. The aim of stratifying by consumption of healthcare resources is expected to identify and select target populations that may benefit from specific programs of action.

Clearly, the quality of data used will impact the quality of the predictions made. Similarly, as predictive models are built by extracting data from different sources, if there is a systematic error within a database, the result of the stratification will not be valid. The realization of stratification involves the next steps: extraction, purification and validation of information, and the uploading of results into electronic health records or established systems. This process may also have errors and takes time. However, it is worth to mention that the use of risk stratification can improve and optimize the quality of clinical and administrative data and this in turn should increase the validity of the prediction.

Among the best known instruments of predictive modelling are Adjusted Clinical Groups Predictive Model (ACG-PM), Diagnostic Cost Groups (DCG) and Clinical Risk Groups (CRG). They were designed in the US and are robust systems from a statistical point of view and versatile for applications. Their usefulness has been proven in public and private health organizations for several years. These models explain a significant portion of the variability in the use of health services of a population and offer, for each individual, an estimation of the volume of health resources that will require the following year.

In their most recent versions they combine information from diagnoses, prescriptions, and previous cost, diagnostic information, among others and have replaced previous models with less power prediction based only on demographic data or use of services. Some European experiences focus on making predictions about hospitalizations or avoidable hospitalizations, including: PARR, Sparra and CARS. Please find complete information on different tools in the Appraisal Standard of ASSEHS project (described in section 2.2.5) [ASSEHS].

3.2.1 Risk Stratification Tool Deployed in the Basque Country

3.2.1.1 Overview

- Region name: Basque Country.
- Health care system: National Health Service.
- Size of target population: Approximately 2 million, all patients in the region are targeted by the risk stratification tool.
- Aim: case finding for appropriate interventions and optimization of healthcare resources.
- Risk Stratification (RS) output: next year's healthcare costs.

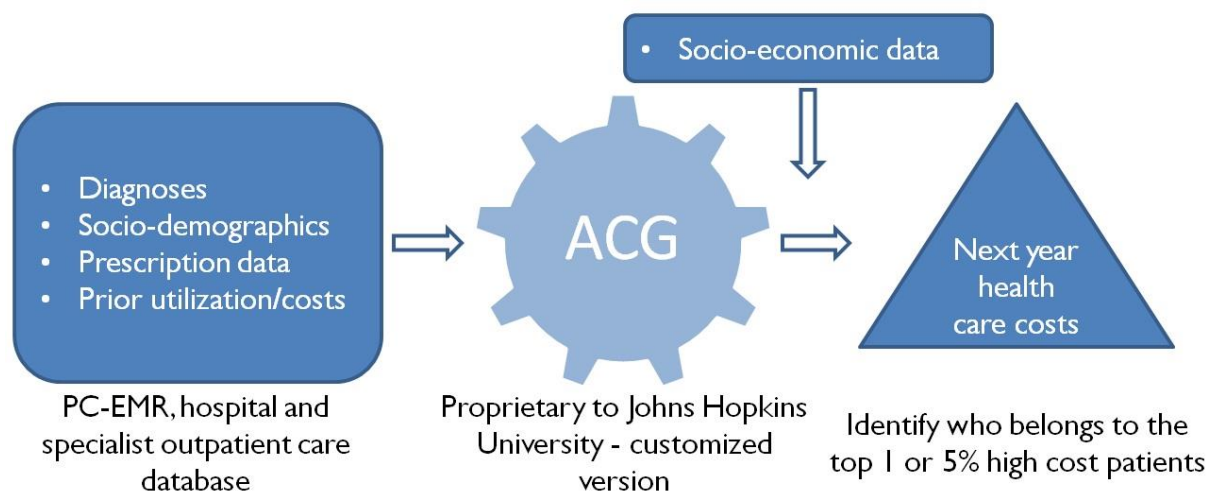


Figure 11 The diagram provides an overview of the data input, risk stratification model selected and model's outcome in the Basque Country

3.2.1.2 The risk stratification (RS) model

Within the Basque Country healthcare system, a customized version of the Adjusted Clinical Groups Predictive Model (ACG-PM) has been in use since October 2015. The ACG case-mix system was developed at Johns Hopkins University and the Department of Health and Consumer Affairs of the Basque Government has purchased a license via IASIST. The above-mentioned RS is applied in all the districts of the Basque Country: namely, Álava (capital: Vitoria-Gasteiz), Biscay (capital: Bilbao) and Gipuzkoa (capital: Donostia-San Sebastián).

The implementation and successive deployment of risk stratification in the Basque Country had two main aims:

- case finding,
- risk adjustment and capitative payment.

Despite the fact that the RS has already been deployed for case finding purposes, some research activities are currently being performed in order to improve the final outcome of the procedure. The use of RS for risk adjustment and capitative payment has been investigated but not yet deployed.

The outcome (dependent variable) generated by the Basque Country RS is the predicted next year healthcare costs. Then population is classified in four groups according to the presence or not of a chronic disease, 95th percentile of healthcare costs is used and only for chronic population. Two different thresholds are being considered for next year's healthcare expenditures, which will involve dividing the population into low- and high-cost patients: 95th and 99th percentiles of healthcare costs. This was used only to assess the goodness of the tool, but actually only 95th percentile is used and only for chronic population. The RS is based on predictive modelling using regression techniques, and both the calibration and internal validation of the model have been performed using the data (standardized costs of admissions, visits and procedures provided to each patient) recorded in 2008 and 2009 from more

than 2 million patients from the Basque Country. Additionally, the development, validation and related results are described in a peer-reviewed article [ONM13].

3.2.1.3 Deployment and maintenance

The RS is deployed to stratify the entire population of the Basque Country with a special focus on the top 5% high-cost chronic patients with respect to next year's health costs. The risk score provided by the RS is meant to be deployed in emergency room visits, hospital admission and general practitioner visits.

The RS tool is deployed at a regional level where the entire population of the patients (approximately 2 million) is stratified every two years to identify the top 5% high-risk patients for appropriate programmes. Concurrently, the research team performs periodic evaluation and optimization of the RS model. In that respect, the model is recalibrated (i.e., the parameters of the predictive model are recalculated) and slight changes are introduced in the set of independent variables used as input to the RS model. Those activities are performed during refinement of the stratification strategy and associated programmes in the region.

ACG-PM software [ACG-PM] is employed to assign each patient to one of 34 mutually exclusive categories. The final logistic regression model, which receives as input the ACG category, previous cost, socio-economic and demographic variables, was developed and evaluated using SAS software (SAS Institute Inc., Cary, NC, USA) [SAS] up to 2012 and, as from then, using SPSS software (SPSS Inc., Chicago, IL, USA) [SPSS]. Currently, it is still undecided if the RS tool which was developed and validated in the Basque Country will be available to other healthcare organizations or institutions.

The implementation and deployment of a RS model in the Basque Country provided the basis for the design of interventions targeting the subpopulation identified by the RS model. Additionally, the linkage between different data sources (please see following section) not only increased the predictive performance of the model but also gave rise to other opportunities (e.g. epidemiological research, economic evaluation of programmes, etc.) within the healthcare system of the Basque Country.

3.2.1.4 Input data for the stratification tool

The RS in the Basque Country uses data retrieved from primary care electronic medical records (PC-EMR) as well as from hospital and specialist outpatient care databases. More specifically, the RS model is based on the following categories of data used at different levels in the risk generation process:

- diagnoses (from each contact with primary care, hospital admissions and day hospitals),
- socio-demographics (age, sex),
- pharmacy data (prescription data from PC-EMR),
- prior utilization obtained directly from PC-EMR, hospital admissions and specialist outpatient care information databases,
- socio-economic data (census area of residence/deprivation index from MEDEA project).

The patients' data confidentiality is ensured via the use of an opaque identifier inside the Basque Country population stratification programme (PREST) database.

3.2.1.5 Description of Basque Country region and programme

There are 2.2 million inhabitants in the Basque Country, of which the over 65s represent 20.8%. The Health and Care expenditure in 2015 was 3400M€, and it is estimated that 80% was used for chronic patients. It is projected that in 20 years, 26% of the Basque population will be older than 65 years. This epidemiological pattern requires the improvement of the management of chronic diseases. In order to address the challenge of chronicity, ageing and dependency, the Basque Country has deployed a global approach in which all key stakeholders play a significant role. The Strategy on Chronicity from 2010 [BC-CC] and The Strategic Guidelines 2013-2016 [OsakiSLAP] of the Healthcare service, Osakidetza, reinforced and extended an integrated approach. The Basque Healthcare model aims to enhance patient centred and seamless care by improving the coordination and continuity of care between service levels and by adapting care to patient needs.

The prospective stratification of all the population assigned to Osakidetza was performed for the first time using the Johns Hopkins Adjusted Clinical Groups predictive model (ACG-PM). The stratification

process in the Basque Country classifies more than two million citizens according to the resources that they will require during the following twelve months. The data come from Osakidetza and the Department of Health, based on the previous use of health resources, demographic, socioeconomic and clinical variables. The expected use of health resources, the “output”, is a proxy of patient morbidity and severity with different needs of care. The aim of stratifying is to identify and select target groups that may benefit from specific programmes of action. Consequently, Integrated Intervention Programmes for multi-morbid and specific diseases patient groups (e.g. for diabetes, COPD, etc.) have been deployed. The objective is to provide anticipatory care and coordinated care to all patients identified through the risk stratification tool.

Stratification of patients uses the population pyramid model Kaiser. Patients are classified in each stratum based on their Predictive Index. For each stratum, differentiated interventions are designed. In Basque Country several stratifications have been performed: 2011, 2013, 2014 and 2015. The latest data available are those from 2014 stratification (Figure 12). The Risk score is displayed in Osabide Global, the Electronic Health Record (EHR) from Osakidetza (Figure 13).

- The case management layer includes 5% of population with chronic predictive index higher resources consumption. It is represented by a red triangle in Osabide Global, which would correspond to high-risk users requiring complex interventions or case management.
- The stage of care management groups 15% of the population with chronic predictive index of intermediate consumption resources. It is represented by an orange triangle in Osabide Global. They would be people with chronic conditions that require medical attention constantly, and those whose lifestyle makes them relatively heavy users of the system.
- Self-management stratum groups 80% of the population with chronic predictive index lower resources consumption. It is represented by a yellow triangle in Osabide Global. They would be patients with chronic disease but with good health.
- In stratum Promotion and Prevention, the entire population is grouped without chronic disease. It is represented by a green triangle in Osabide Global.

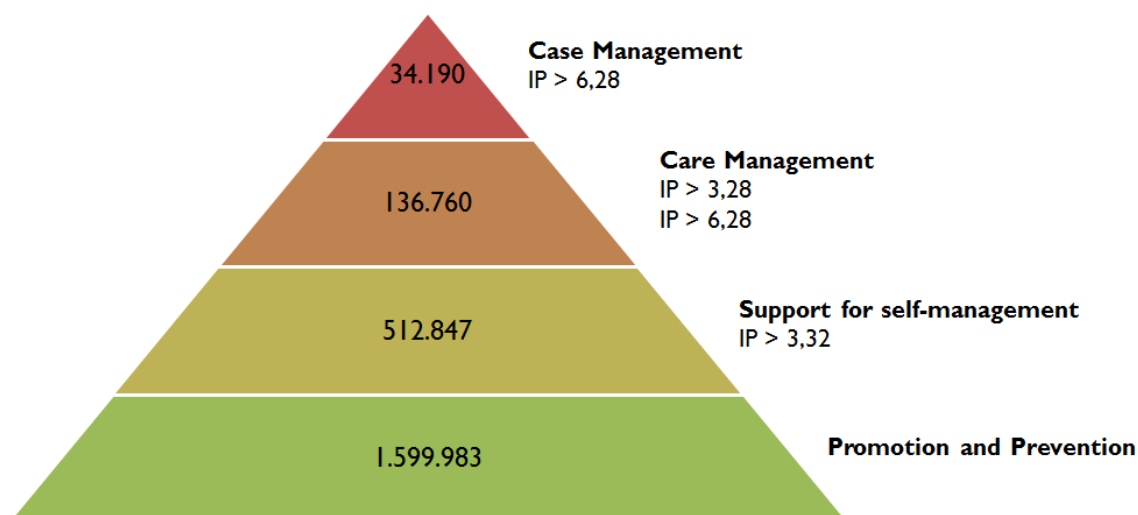


Figure 12 Risk stratification in 2014

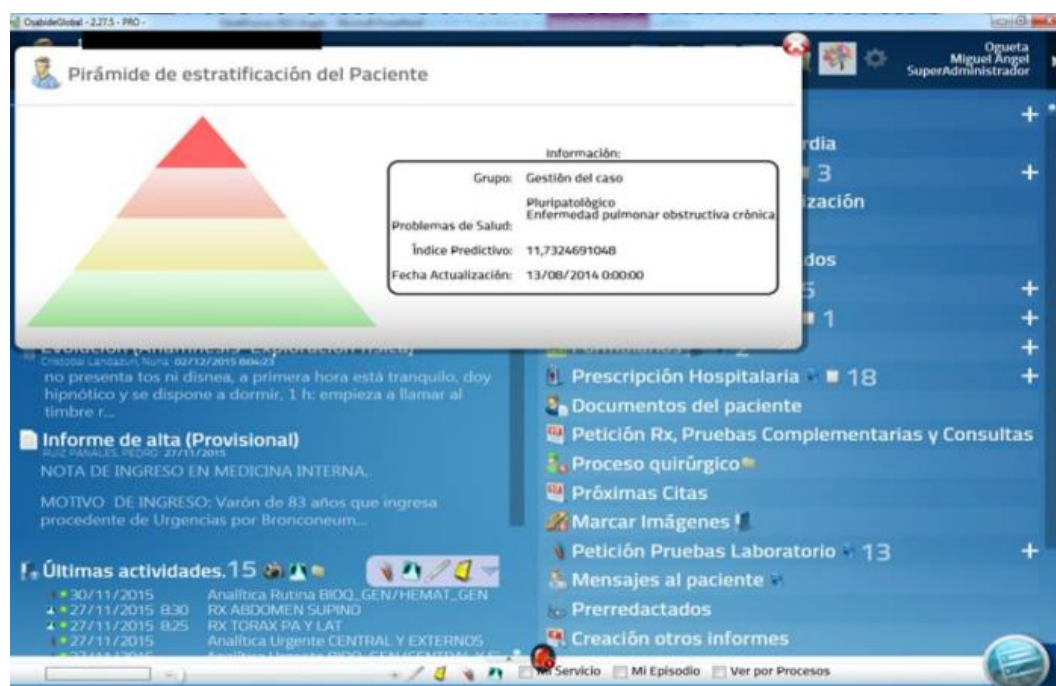


Figure 13 Risk score display in Osabide Global

3.3 Polypharmacy Management

The use of multiple medications, particularly prevalent among the elderly population, leads to complex drug regimens and rises the risk of further complications. If polypharmacy is typically defined as the concurrent use of multiple drugs by the same patient, it is however more complex than just the number of drugs that a patient takes. Polypharmacy increases the possibility of drug-drug and drug-disease interactions. Polypharmacy more commonly has a negative connotation, but sometimes it is necessary and can be beneficial in treating certain medical conditions. Polypharmacy can be categorized into 2 major classes [Swine08]:

- **Therapeutic Polypharmacy**

This type occurs when multiple drug regimens are carefully monitored by clinicians and are necessary for the treatment of conditions and for achieving a therapeutic goal. An example of therapeutic polypharmacy is the multiple agents used in the management of congestive heart failure, such as digoxin, angiotensin-converting enzyme inhibitors, and a diuretic.

- **Contratherapeutic Polypharmacy**

This type of polypharmacy occurs when an individual experiences unanticipated or unintentional adverse effects while he or she is on a drug regimen and is not monitored. Polypharmacy is particularly detrimental when an individual takes multiple pharmacologic agents for an extended period of time, particularly at high doses, without being monitored.

The major concern for all cases of polypharmacy is the prospect of adverse drug reactions and serious drug-drug interactions. In some instances, it is therapeutically necessary to use multiple agents to treat certain conditions. It is the responsibility of pharmacists to assess patients with multiple medication regimens and to make recommendations when necessary.

3.3.1 Polypharmacy Management experience in C3-Cloud

Osakidetza, partner in the C3-Cloud project, has a long established experience in polypharmacy management. The team includes Arritxu Etxeberria Aguirre and Rafael Rotaache del Campo, who have published many academic papers and chapter books on the matter, e.g. [Bernabeu14], [Etxeberria2011]. Both are members of the multidisciplinary working group about "Wise use and Polymedication" in Osakidetza. The group aims to promote the wise medication prescription addressing the phenomenon of polypharmacy with initiatives to encourage deprescription. Their latest initiatives are two prospective studies on polypharmacy with elderly patients over 80 (completed studies) and safety in patients over 65 years taking more than five drugs (ongoing study). Arritxu Etxeberria is also a member of the editorial board of the INFAC, a monthly newsletter aimed at updating knowledge in pharmacotherapy of health professionals in the Basque Country. She has published several articles on polypharmacy, including [INFAC15], [INFAC13], [INFAC12a], [INFAC12b].

3.3.2 Decision Support Tools and Methods for Polypharmacy Management

3.3.2.1 Introduction

The context: Ageing people, several chronic diseases, polymedication

Seniors are especially sensitive to medications with decreased drug elimination capabilities. In addition to that, senior citizens are the largest pharmaceutical consumer group due to the fact that they sometimes accumulate chronic diseases. Depending on definitions, 25-50 % of patients aged 75 years or older are exposed to at least five drugs often prescribed by various physicians [Sönnichsen16]. Then, pharmacotherapy in old age needs to be appraised in the context of ageing, taking into account the importance of multimorbidity, disability, frailty, and changing care goals [Azermail6].

The impact: When medication becomes the illness...

The phenomena, known as polypharmacy, of senior citizens consuming vast amounts of medications, prescribed over the years by various physicians, is well-known among the medical community. The usual issues associated with polypharmacy include underprescribing, overtreatment and decreased drug adherence [Meulendijk15a]. For the latter, patients that are on many medications are often non-compliant due to the complexity of the set of medications and this can have poor medical outcomes [FG13]. As an example of a consequence, for elderly patients, who constitute half of all chronically ill polypharmacy patients in The Netherlands, the percentage of all acute hospital admissions due to medication-related causes is twice as high of the percentage in the whole population [Meulendijk15a].

Multiple medications are not per se undesirable or even unavoidable but they necessitate a reinforced control. An important impact of polypharmacy and complexity of medications is the compliance rate in the elderly population [FG13]. Moreover, inappropriate polypharmacy occurs when more medicines are prescribed than are clinically indicated or when medicines are inappropriately continued [Young16].

The current situation

Polypharmacy increases the complexity of primary care interactions and makes high quality medicines review more difficult to achieve within available consultation timeframes [Young16].

Very often in looking for solutions, the problem of polypharmacy is associated with an increased risk for medication errors and adverse drug effects [Azermail6]. Then, during the last decade, efforts to lower the bad effects of polypharmacy focussed on reducing the 'inappropriate polypharmacy' from patients' medication regimen [Young16].

Use of a simple interdisciplinary medication review has been shown to lead to the reduction of inappropriate prescribing and costs, but there was no effect on clinically relevant patient outcomes, possibly due to a lack of power and insufficient observation time [Azermail6]. Indeed, a multitude of initiatives has been developed to assess the appropriateness of drugs prescribed for individual patients. Some measures have been adopted, like for instance Garfinkel algorithm, and some authors suggest a "process of deprescribing," prioritizing drugs in a patient with polypharmacy according to each drug's risk/benefit ratio. However, evidence showing a benefit of these measures regarding clinically relevant

endpoints is scarce [Sönnichsen16]. Among the explicit methods are the Beers Criteria and the Screening Tool to Alert to Right Treatment (START) and Screening Tool of Older People's Prescriptions (STOPP) criteria, while the implicit methods include the Medication Appropriateness Index and the pharmacotherapy review focused on drugs' use, indication, safety and effectiveness [Meulendijk15a]. The implementation of explicit measures is supported by the development of decision support systems.

3.3.2.2 PRIMA-EDS

In the following, we present some relevant work on the design of Clinical Decision Support for Polypharmacy Management.

Polypharmacy in chronic diseases: Reduction of Inappropriate medication and Adverse drug events in elderly populations by electronic Decision Support (PRIMA-EDS) [PRIMA-eDS] is an European FP7 project that will gather the best available evidence to develop recommendations to optimise treatment of polymorbid elderly. An electronic decision support tool will also be developed to incorporate these recommendations to be applied in primary care. While several approaches have been proposed to reduce polypharmacy and inappropriate prescribing, there is little evidence showing a benefit regarding clinically relevant endpoints.

The PRIMA-EDS tool analyses the patient's diagnoses, current medication, symptoms, biometric measurements and laboratory results and performs an electronic comprehensive medication review, and returns recommendations for drug discontinuation or modification based on the European list of inappropriate medications for older people [RMT15], 45 rules and recommendations based on systematic reviews and guidelines, 95 rules and recommendations from the Evidence-Based Medicine electronic Decision Support (EBMeDS)-database [EBMeDS], SFINX-database of interactions [Böttiger09], the PHARAO-database on adverse effects [PHARAO], and the RENBASE-database on renal dosing [Renbase]. The tool is being evaluated in a cluster-randomised controlled trial, with general practitioners in the intervention group using the PRIMA-EDS tool, while in the control group, general practitioners will treat according to current guidelines without the tool [Sönnichsen16]. Because of its modular design, comprehensiveness and easy integration with EHRs and case-report forms, EBMeDS [Koskela16, Nyberg12] was selected as the platform for developing the PRIMA-eDS tool. EBMeDS analyses only structure and coded patient data and provides patient-specific clinical recommendations or warnings in the form of reminders and links to guidelines.

3.3.2.3 STRIP Assistant

Systematic Tool to Reduce Inappropriate Prescribing (STRIP) is an all-encompassing drug optimisation process in primary care, that focusses on both pharmacotherapeutic analysis but also patients' medication histories and preferences [Meulendijk15b]. It combines the Polypharmacy Optimization Model (POM) [Maanen12], Gebruik Indicatie Veiligheid Effectiviteit (GIVE) – a pharmacotherapy review focused on drugs' use, indication, safety and effectiveness, and START and STOPP criteria [Gallagher08]. The tool has been included as part of a Dutch multidisciplinary guideline on polypharmacy in elderly patients [DCGP12]. The five steps of STRIP method includes (1) drug history; (2) analysis of drugs; (3) treatment plan; (4) patient preferences; (5) follow-up and monitoring.

The STRIP Assistant is a stand-alone web application aimed at assisting GPs and pharmacists with pharmacotherapeutic analysis of patients' medical records. The application generates context-specific advice based on the patients' records and decisions of GPs and pharmacists during medication review [Meulendijk15a]. The system uses a decision engine using Drools. In terms of semantic interoperability, the system uses the MEDOVD health exchange format used on all Dutch computerised physician order entry systems. However, to allow for use of different ontologies, conversion rules need to be implemented for mapping purposes.

Although its usability was tested, the STRIP Assistant tool needs to be further evaluated, especially on clinicians reviewing their own patients. In terms of clinical relevance, the study confirms the results of previous studies that structured methods for medication review significantly improve the medication appropriateness of prescriptions.

3.3.2.4 Ontological approach to polypharmacy

Polypharmacy contributes to the complexity of medication regimen, often resulting in non-adherence, therapeutic failure and adverse drug reactions [Muir01]. One approach to address this issue is to reduce the complexity. Grando, Farrish and colleagues have developed a drug ontology for safe prescription [Grando12]. This ontology was tested with patient records using an ontology-based prototype tool [FG13]. The tool aimed to (i) map prescription medication in the Epic electronic medical record system into the drug ontology; (ii) calculate the complexity of prescriptions and recommend changes to the regimen to decrease complexity; and (iii) evaluate the cost of current and proposed medication regimen and present the information to providers.

The Web Ontology Language (OWL) is used to represent the ontology and the Semantic Web Rule Language (SWRL) is used for the decision support rules. The tool is a Java application that accesses the ontology through SWRL queries. The complexity of drug prescription follows the Medication Regimen Complexity Index by George et al. [George04], which has been clinically validated by Hirsch et al. [Hirsch14]. SWRL rules were implemented based on evidence in the literature. In this work, not all the rules identified were implemented and areas of potential future work have been identified, such as the modelling of combination drug switching.

3.3.2.5 TRIM

The Tool to Reduce Inappropriate Medications (TRIM) is a clinical decision support system that has been developed to improve medication prescribing in older adults [Niehoff16]. The system has been developed to be used with the Veterans Affairs EHR – VistA. It has two components: an EHR data extraction program, and a medication evaluation program. The first application is used to identify patients based on the EHR data, in particular their medications, chronic conditions, age and gender. It also takes into account patients with upcoming primary care appointments.

The second application has three components. The first component is an interface for the chart review (body mass index, creatinine clearance, haemoglobin A_{1c}, blood pressure) and telephone assessment (e.g. self-reported medications, medication adherence, functional status, executive function). The second component is the evaluation of medication appropriateness, where manual medication reconciliation and automated clinical algorithms are used to look for markers of potentially inappropriate medications and potentially inappropriate regimen, and corresponding feedback to clinicians if the marker is present. The third component is the patient-specific medication management feedback report to the clinician. Initial evaluation of TRIM demonstrated to identify potentially problematic medications and regimens and further evaluations are required to see the effects on medication regimen and patient outcomes.

3.3.2.6 Discussion

The trial for the PRIMA-EDS tool is still underway and no results have been published so far. The main focus for this project is the polypharmacy management in primary care, whereas in C3-Cloud, due to the focus on integrated care, our focus is polypharmacy across health provision domains. One of the limitations of the study in PRIMA-EDS is that of potentially incomplete electronic health records, especially of GPs in primary care and where they may not know all medications prescribed by specialists. The TRIM system was shown to potentially be able to identify problematic medications and regimen using data from EHR and using clinical algorithms derived from clinical practice guidelines and evidence-based sources.

From the ontological work in this area, limitations of current work include the modelling of more complex prescription information and ways to combine patient record with guidelines and evidence across multiple health providers.

3.4 Clinical Guidelines

3.4.1 Clinical Guidelines for the Disease Groups in the Project

This section aims to provide the reader with an overview and links to resources for clinical guidelines regarding the four major disease groups that are part of the project. These guidelines will be the source

and background for the development of the Clinical Decision Support Modules, which will support the Personalised Care Plan Development Platform and the Coordinated Care and Cure Delivery Platform. There are a variety of different guidelines from different sources that contain convergent, but also sometimes differing recommendations for the diagnoses and management of the four diseases. These differences between guidelines reflect the different interpretations of the available clinical evidence, the difference in the date and place of issuance.

3.4.1.1 Diabetes guidelines

Guidelines of American Diabetes Association (ADA) for the standards of care in diabetes mellitus were published latest in January 2016 [GADA]. Previous ADA guidelines become endorsed by European Association for the Study of Diabetes (EASD), which issued a patient-centered update [GEASD] that was published later last year. These guidelines are complex in their nature and also cover the issue of diabetes management in the elderly, comorbid population. Summary of recommendations and guidelines that can serve as base for computerized decision support considering the diagnosis and treatment of diabetes mellitus type 2 are summarized in tables [GADATables] in a chart-convertible format.

3.4.1.2 Heart failure

The latest clinical guidelines for the management of heart failure has been recently published in the European Heart Journal [GHF]. Heart failure management guidelines issued by the American organizations of American College of Cardiology (ACC), the American Heart Association (AHA) and the Heart Failure Society of America (HFSA) in 2013 received an update in May this year published in the Journal of Cardiac Failure [JCF]. Translation of the complex recommendations from these guidelines to computer-based decision support might require collaboration between cardiologists and IT experts.

3.4.1.3 Chronic kidney disease

European Renal Best Practice (ERBP) is a European initiative that publishes guidelines in Europe about the management of chronic kidney disease. These guidelines address specific segments of renal failure management and some are independent guidelines but others are statements about and endorsement of previously issued guidelines from the Kidney Disease Improving Global Outcomes (KDIGO). Full list of the currently available guidelines from ERBP is available at: <http://www.european-renal-best-practice.org/content/erbp-documents-topic>.

The Renal Association in the UK published its guideline about chronic kidney disease management in 2011 [GCKDM] and updates were due in 2015 but not been published yet. The Renal Association has also issued specific recommendations regarding the management bone disorders associated with chronic renal failure and other specific aspects of chronic kidney disease management with interest for nephrologists (see list here: [GCKDMlist]).

In the United States Kidney Disease Outcomes Quality Initiative (KDOQI) and KDIGO published the Clinical Practice Guideline for the Evaluation and Management in 2012 [KDOQI] with general updates [KDOQIupdate1] and update about hemodialysis [KDOQIupdate2] from 2014 and 2015, respectively. KDOQI has published several specified guidelines and commentaries regarding the optimal management of patients with chronic kidney disease and a variety of frequently occurring comorbid conditions (see the full list: [KDOQIlist]).

3.4.1.4 Depression

Similarly to heart failure, renal failure and diabetes, different medical organizations have issued guidelines regarding the clinical management of depression. The Annals of Internal Medicine issued the latest guideline [GDepACP] from the American College of Physicians in March 2016. American Psychiatry Association (APA) published its latest guideline about the treatment of patients with major depressive disorder in 2011 [GDepAPA] and its shortened summary form as quick reference guide [MDDG] in 2011. The latest update of the NICE guideline in the UK is also available [GDepNICE].

The Institute of Clinical Systems Improvement (ICSI) comes up with an own guideline about depression focusing on the primary care management of these patients [GDepICSI]. The full list of available guidelines for the management of depression includes further recommendations by other medical organizations as well [GDeplist].

Careful evaluation of these guidelines by expert psychiatrists will be necessary to form the medical base that can be subject of computer-aided clinical decision support for the project.

3.4.2 Computer Interpretable Guidelines

Clinical practice guidelines (CPGs), as defined by the Institute of Medicine, are “statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options” [IM11]. The formalization of clinical guidelines as computer-interpretable guidelines (CIGs) is key to enabling CIG-based decision support systems to provide more patient-specific advice through linkage to electronic health records [Latoszek-Berendsen10]. A 2013 review [Peleg13] gives a good overview of the methods developed for CIG and these will be highlighted in this section. Additionally, more recent work will also be highlighted, especially for CIGs in the case of multimorbidity, which was identified as an emerging theme by Peleg. This particular area has been explored in the following works: [Zamborlini14, Zamborlini16, PT15].

CIG has been researched for over 20 years and numerous research areas have been explored based on the CIG lifecycle - from the analysis and design of CIG; deployment and usage; to maintenance and sharing of CIG [Peleg13]. A large body of work exists for the development of CIGs. However, as highlighted by [PKH08], few systems have progressed beyond the prototype stage, a similar finding by the review by Fraccaro [Fraccaro15]. Other CIG topics not covered by Peleg’s review are CIG modeling using case-based reasoning and rule-based formalisms and language, such as the Arden syntax, which are covered by works such as [Peleg03, ONN13]. These were not included in the review as rule-based systems cannot explicitly model alternative pathways or sequence of tasks represented in complex, multistep clinical guidelines [Peleg03]. The review by Peleg [Peleg13] fits into eight themes that cover the CIG lifecycle.

3.4.2.1 Analysis and Design

The CIG lifecycle begins with the analysis of clinical practice guidelines and the design of CIGs. As CIGs are usually based on previously published narrative CPGs, there is a period of knowledge acquisition and specification for improved CIG design. CIGs are defined using CIG modeling languages, following CIG acquisition and specification methodologies.

CIG modeling languages can be categorized into document models; decision trees and probabilistic models; or task-network models. Examples of a document model is the Guideline Element Model (GEM) [Shiffman00] is an XML-based knowledge model for guideline documents. It contains 110 elements (covering areas of guideline identity, developer, purpose, intended audience, development method, target population, knowledge components, testing and review plan) and is a standard of the American Society for Testing and Materials (ASTM). Another approach for representing a CIG’s algorithm is to use decision trees, which can be viewed as a probabilistic model with expected utility or outcome and an optimal strategy, as in [Colombet05, SBC05, SNO00]. Task-network models (TNMs) represent CPGs formally and hierarchically decompose clinical guideline algorithms (care processes) into networks of component tasks that unfold over time. TNMs allow a CIG execution engine to execute the represented knowledge against patient data. TNM formalisms include GLIF [Boxwala04], Asbru [SMJ98], GLARE [Anselma06], GASTON [deClercq04], PROforma [SF03], among others.

Knowledge acquisition and specification methods and tools have been developed to support the CIG design process. Cognitive methods represent the translation of CPGs into formal CIGs as problem-solving task and relies on the collaboration of clinical experts and knowledge engineers [Patel01]. Most methods use existing CPGs as the starting point for developing CIGs. Markup tools, e.g. Stepper [SR03], DELT/A [DELT]; authoring tools, e.g. Protégé [Protégé] and AsbruView [KM01]; and editors, e.g. BRIDGE-Wiz [Shiffman12] are available to support this process.

CIG integration into EHRs and organisational workflow. Clinical decision support systems should be integrated into organizational workflow and with information systems, electronic health records (EHRs) in particular [Bates03]. To improve the effectiveness of CIGs, they should be considered for integration with EHRs and organizational workflow. Approaches to knowledge-data mapping have been proposed to reduce the burden and errors when CIGs provide patient-specific advice. For example, Knowledge-data ontology mapper (KDOM) [PKD08] provides semantic interoperability between CIG knowledge and EHR data. Its standard patient data model is based on HL7-RIM-based models, such as virtual Medical Record (vMR) [Johnson01]. Terminology services, such as MEIDA [GLS09], assist in matching CIG concepts to EHR data.

For integrating organizational workflow with CIG-based decision support systems, the two main approaches identified by Peleg [Peleg13] are CIG formalisms that support workflow, such as NewGuide [Cicarese05] and SAGE [Tu07]; and the use of hierarchical task networks to create patient-specific clinical pathways from Asbru CIGs [González-Ferrer13].

Since Peleg's review in 2013, there has been more recent works in the area of knowledge-data mapping. Archetype-based interoperability of CIGs and EHRs has been explored by Marcos et al. [Marcos11, Marcos13]. Meanwhile, the study by Gonzalez-Ferrer et al. [González-Ferrer16] has evaluated the use of HL7 vMR and openEHR archetypes as intermediate schemas for capturing clinical statements from CIGs that are mappable to EHRs containing patient data and patient-specific recommendations.

CIG validation and verification are important in the CIG life cycle as CPGs and their CIG implementations aim to decrease errors and increase quality and safety. CIG validation establishes that the CPG requirements are captured by the CIG specification. The inspection technique is where clinical experts inspect CIGs to locate errors in the clinical algorithm's logic, with the assistance of knowledge engineers [Shalom08, Peleg09]. As medical experts find this hard, testing is also used to test the CIG with simulated or real patient data to determine if the recommendation out of the CIG execution is in line with the CPG recommendations. IMM/Serve is an example where test cases have been automatically generated [MFS01]. CIG verification checks for inconsistencies and if CIG specification satisfies a set of properties. There are approaches for single and concurrent CIGs. For the latter, inconsistencies between concurrent CIGs are checked for comorbid patients. Model checking (e.g. SPIN model checker [Bottrighi10]) and theory proving (e.g. [Teije06]) are techniques used to check for temporal-logic properties, while conflict resolution has been used by Wilk et al. [Wilk13]. Peleg highlights that there are few papers addressing this issue.

3.4.1.1 Deployment and Usage

The following phase of the CIG life cycle is the delivery of CIG-based decision support using CIG execution engines. During the CIG execution, exceptions may arise, and these need to be handled to provide safe CIG-based decision support applications.

Execution engines are developed for different CIG formalisms. For example, GLEE [Wang04] is the GLIF3 guideline execution engine and it provides defined interfaces to EHRs and other clinical applications to facilitate integration with the clinical information systems, such as in [Peleg09] for the management of diabetic foot. GESDOR [Wang03] is a generic execution model for sharing CPGs and has been used to execute CIGs in GLIF3 and PROforma. As for the Spock execution engine [Young07], it can execute guidelines represented in Hybrid-Asbru intermediate framework and is integrated within the DeGeL framework. Finally, the GASTON toolset [deClercq01a, deClercq01b] has an execution engine for the GASTON formalism.

Supporting CIG tools include the Digital Electronic Guideline Library (DeGeL) [Shahar04] which allows for the gradual conversion of guidelines from text to a formal representation in a selected target guideline ontology. Its feasibility has been demonstrated for Asbru and GEM. Another tool is Vaidurya [MS09], a clinical guideline search engine, which facilitates concept-based and context-sensitive searches in a library with a large number of guidelines.

Exception handling in CIGs. Work in the area of management of exceptions that arise from CIG execution has been lead largely by Grando and colleagues. They developed a goal-oriented framework [GPG10] for specifying clinical guidelines and handling medical errors. It uses a state-based model to link plans, goals, monitored effects and exceptions by extending PROforma with Petri Net semantics

for scheduling constraints [Grando11]. An extension to this work led to defining the goal-based patterns of collaborative work, with the patterns providing generic and reusable solutions to detect exceptions. A further extension considered an argumentation-based decision-support systems for a more expressive specification of actors, roles and actor constraints, with the added notions of patients and healthcare organisations [GGB12].

3.4.1.2 CIG maintenance

After the CIGs starts being used, the maintenance phase also begins to keep the CIG updated with new versions of the CPGs.

Compliance analysis looks at the clinicians' compliance with CIGs. Measuring compliance occurs by studying the log files of CIG execution engines with data from EHRs, while taking into account that medical records are often incomplete. Methods to measure compliance include comparing actual clinical actions with CIG-recommended actions [KGZ10]; measuring the compliance based on the intentions of the guideline to allow for deviations, such as in the Quality Indicator Language (QUIL) [ASM01]. Another type of compliance analysis methods is process mining, where process logs are analysed, e.g. [Aalst2011]. The visualization of CIG compliance results enables the exploration of how contextual information impacts performed treatment steps, such as CareVis [AM06].

Versioning of CIGs occur due to the evolution over time or local adaptations. Retrospective querying also need to be supported. Efficient access to large collections of multi-version clinical guidelines has been studied by Grandi et al. [GMM12], while the LASSIE tool was developed to support guideline evolution [KM09].

3.4.1.3 CIG sharing

The sharing of CIGs is essential for the benefit of the community and to leverage the efforts in formalizing CPGs as CIGs. The GLIF formalism was developed with sharing in mind. The GELLO object-oriented guideline expression language and the vMR information model were developed for sharable purposes and are now HL7 standards. A multi-layered framework for sharing knowledge was also developed for sharing knowledge [Boxwala11]. Additionally, there are some initiatives to promote reuse, such as accelerating the development of licensing, standards and addressing the medico-legal concerns [Kawamoto13]. Libraries of CIG and executable components in different CIG formalisms are being set up, e.g DeGeL, openclinical.org.

3.4.1.4 CIG and Multimorbidity

In Peleg's review [Peleg13], some emerging themes were identified, with the main ones relating to having concurrent CIGs in the case of multimorbidity. Several research projects have been identified as conducting research in this area. Some recent work since Peleg's review will also be briefly described in this section.

Detecting interactions and conciliation. With multimorbidity comes the need to combine knowledge from several guidelines [Zamborlini16, Zamborlini14] propose an extension to their earlier work of a conceptual modelling approach – Transition-based Medical Recommendations (TMR) to increase the reasoning capabilities of CIGs. The extension, called TMR4I, allows the automatic detection of interactions among recommendations that require the attention of experts. They also looked at using Semantic Web technologies to exploit existing medical knowledge available as Linked Open Data.

While Zamborlini et al. focused on the automatic detection of interactions, Piovesan et al. [PT15] explored a mixed-initiative approach to reconcile guidelines or part of guidelines and propose a framework to propose to clinicians suggestions and management options to do this.

3.4.1.5 Relevant projects

MobiGuide

The European FP7 MobiGuide project: Guiding Patients Anytime Anywhere (2011-2015) [MobiGuide] developed an intelligent decision-support system for patients with chronic illnesses. The MobiGuide decision-support tool uses biosignals from the sensors worn by the patient, together with

the patient's historical clinical data, analyses these to alert the patient about actions that should be taken. The recommendations are based on evidence-based, state-of-the-art clinical guidelines. The project focused on the following clinical conditions: atrial fibrillation, gestational diabetes and gestational hypertension.

Relevant areas addressed by MobiGuide are: patient-centric CIG-based decision support systems, and the development of ubiquitous CIG-based guidance systems.

K4CARE

The European FP6 K4CARE project: Knowledge Based Homecare eServices for an Ageing Europe (2006-2009) [K4CARE] developed a platform to manage the information needed to guarantee an ICT Home Care service. As part of this project, the relevant area was the development of an ontology for formally represent healthcare concepts related to chronically ill patients with comorbid conditions [Riaño12].

3.5 Other Regional Approaches

The current section presents recent Swedish approaches of reconciliation for multiple treatment plans and new patient pathways.

3.5.1 Web based national decision support (RGS)

Rådgivningsstödet (RGS) is a national web based decision support used by nurses in primary and secondary care and at the national telephone patient support (1177.se) for quality assured medical advices to patients, including for appointment planning [RGS]. RGS is produced by Inera, cooperatively owned by the Swedish county councils organisations (Swedish Association of Local Authorities and Regions). Each text is quality assured at least every second year by a quality reference group in order to verify correctness and being up to date. In surveys among users, RGS is considered helpful, though for poly symptomatic patients and/or in patients with multiple diseases not so well functioning.

3.5.2 Swedish information services for drug treatment (SIL)

SIL (Svenska Informationstjänster för Läkemedel) is the national platform for drug and prescription information used by all EHR systems [SIL]. SIL is produced and maintained by Inera and quality assured in a similar way as described in section 3.5.1. Amongst other things it also provides the "national list – avoid in elderly" based on the national quality indicators from the National Board of Health and Welfare (Socialstyrelsen). From 2005 to 2014, the prescription of drugs listed on the national list has been reduced with 41% in patients 75 years and older. SIL also provides information from the drug interaction database "Sfinx" from Stockholm county council.

3.5.3 Geriatric support

"Geriatric support" ("Geriatriskt stöd") is a collaboration between RJH and all 8 municipalities, to provide support to caregivers in individual complicated cases. The core group consists in a double specialist in family medicine and geriatrics, a specialist nurse in geriatrics, a nutritionist, a pharmacist. They collaborate with hospital specialists, family physicians, social workers, community specialist nurses, etc.

3.5.4 The Swedish SALAR national competence group for primary care

RJH is participating in a new national competence group for primary care initiated by SALAR (Swedish Association of Local Authorities and Regions) targeting chronic diseases and multi-morbidity in primary care.

3.5.5 Better life for most sick elderly

The national project “Better life for most sick elderly” (“Bättre liv för sjuka äldre”, 2011 – 2014) aimed at a more integrated care for primary, secondary and municipality care. RJH and all eight municipalities in the county participated. A lasting more common, standardized and evidence based way of working resulted from the project [BetterLife].

3.5.6 National advisory board for diabetes

Swedish national advisory board for diabetes - Mikael Lilja of RJH participates in the development of the national guidelines for diabetes and in diabetes in pregnancy (2015).

3.5.7 HPMM: High Performance Medicines Management

High Performance Medicines Management (HPMM) is developed by the national corporation of Swedish pharmacy (Apoteket AB). RJH has acted as a pilot site to test HPMM in clinical environment.

3.5.8 Strengthened hospital discharge of patients

An automatic locally constructed algorithm is used in RJH at patient discharge from hospital (“förstärkt utskrivning”). Based on the patient’s age, diagnosis and number of diagnosis and medication patients are stratified for the risk of re-referral. For patients at extra high risk for a new hospitalisation extra contacts with the municipality care are taken for collaboration regarding the treatment plan. Extra telephone contacts are also taken with the patient. “Förstärkt utskrivning” has locally, in an unpublished study, been compared to a similar module in ACG, demonstrating at least non-inferiority for “förstärkt utskrivning”.

3.6 Related standards

While Clinical Decision Support (CDS) systems can be highly effective at improving care quality and ensuring patient safety, early CDS systems generally used proprietary knowledge representations that were tuned to the local system’s database engine and to the EHR’s workflow, making it difficult to port across environments. This section will investigate the standardisation efforts on various aspects of CDS to promote CDS reuse. Some of these approaches have been mentioned in Section 3.4.2 previously while looking more specifically at computer-interpretable guidelines.

3.6.1 Standards on CDS Knowledge Representation

The work of developing and maintaining a comprehensive set of CDS rules can be very expensive, when a medical center may deploy as many as 2000 CDS rules [JH10]. A standard way to replicate the decision logic would help disseminate new clinical knowledge to other medical organisations. Health informatics researchers have put substantial effort into creating standard formats to encode and share clinical knowledge. CDS scripting language such as Arden Syntax was created as early as 1990s to encode if-then-else rules so the rules could run on different EHR systems [ARDEN]. Arden Syntax has been maintained by HL7 thereafter [HL7-ARDEN]. Arden Syntax logic modules, often called Medical Logic Modules (MLM), consist of Categories, each containing several slots to capture the rule logic. The *evoke* slot determines the triggering event that initially causes the rule to be evaluated. The *logic* slot contains the actual clinical logic, while the *action* slot defines the message that the rule sends to the clinician when triggered. Although an Arden rule contains machine executable if-then-else code that could be made to run against any system, the syntax only contains a textual description of the database action that is necessary for the rule to be able to access EHR data. The text is not executable code, since there was no standard data model or database language to base it on. This means the Arden rules have to be hand-coded to the local database system.

Due to this inherent limitation of Arden approach, HL7 began efforts to create new standards that were based on the HL7 Version 3 Reference Information Model (RIM). One HL7 V3-based attempt was the GELLO Expression Language [GELLO]. GELLO is an object-oriented expression language that was designed to access and compute clinical data. The GELLO Expression Language was started in 2001 and introduced in 2002; in 2005, GELLO was adopted as an international standard by HL7 and

ANSI for a decision support language. It is compatible with the HL7 version 3.0 RIM. GELLO Release 2 was completed and approved by ANSI in 2010. GELLO uses an abstract "virtual medical record" (vMR) so that the same GELLO code can run on multiple systems accessing data stored in different formats. The vMR is a simplified view of the HL7 RIM and is discussed in more detail in section 3.6.2. The GELLO language can be used to build up queries to extract and manipulate data from medical records, and construct decision criteria by building up expressions to reason about particular data features/values. These criteria can be used in decision-support knowledge bases such as those designed to provide alerts and reminders, guidelines, or other decision rules. GELLO was used with Guideline Interchange Format (GLIF), as it is the most expressive expression language in the context of GLIF [WS08].

US ONC launched Health eDecisions (HeD) as a major Standards & Interoperability (S&I) project in 2013 [HeD]. The goal of the HeD initiative is to identify, define and harmonize standards that facilitate the emergence of systems and services whereby shareable CDS interventions can be implemented via:

- standards to structure medical knowledge in a shareable and executable format for use in CDS, and,
- standards that define how a system can interact with and utilize an electronic interface that provides helpful, actionable clinical guidance.

The HeD group's work focused on two main use cases. The first use-case, CDS Artifact Sharing, aimed to address and refine standards for encoding CDS logic which could be imported into vendor products. The second use-case, CDS Guidance as a Service, focused on invoking remote CDS services, and is discussed in more detail in section 3.6.3. In support of the first use case, HeD developed the CDS Knowledge Artifact schema to structure medical knowledge in a shareable and executable format for use in CDS [HL7-CDSKAS]. A CDS Knowledge Artifact may be constituted of three different types of CDS content: Event Condition Action (ECA) rules, Order Sets, and Documentation Templates. An ECA rule is an artifact with the general syntax "on event, if condition is true, then do action." The event triggers the invocation of the rule. The condition is a logical test that, if satisfied or evaluates true, causes an action. The action part consists of a set of operations to execute. These actions may in turn cause further events to occur, which may in turn cause other ECA rules to fire. An order set is a pre-defined and approved group of orders related to a particular clinical condition (e.g., hypertension treatment and monitoring) or stage of care (e.g., hospital admission to Coronary Care Unit). An order set is used as a checklist for the clinician when managing a patient with a specific condition. It is a structured collection of orders (or actions in the HeD schema) relevant to that condition and presented to the clinician in a computerized provider order entry system (CPOE). A documentation template is a structured form for recording information on a patient into a set of pre-defined data slots. These templates are used to guide structured data entry within an EHR or other clinical information system. Some types of clinical documents that can be represented via the documentation template artifacts are encounter summaries, procedure notes, patient-reported outcomes, and flowsheets. A documentation template is a structured collection of what is known variously as documentation concepts, form elements, or observation items. Each documentation concept also can be thought of as a question to the user entering the data. Elements within the documentation concept guide and constrain the user's responses, for example, a list from which to choose an answer, whether an answer is a number, a date, or some other type, and the cardinality of the answer. The latest version of the CDS Knowledge Artifact Specification, Release 1 DSTU 3 (R1.3), replaced the expression logic representation components with the Expression Logical Model (ELM) representation as specified by the Clinical Quality Language Specification (CQL). CQL defines a representation for the expression of clinical knowledge that can be used within both the Clinical Decision Support and Clinical Quality Measurement (CQM) domains [CQL].

Another approach to standardizing CDS knowledge has been to focus on standards for encoding the specification of the clinical knowledge itself, as a precursor to standardizing an "executable" form of the knowledge. For example, GEM is a standard for using XML to encode human-readable guidelines. Guidelines that follow the GEM encoding are theoretically more readily translatable to computerized form. The CDS Consortium took a similar layered encoding approach to CDS rule specifications

[BRM11]. The CDS Consortium defined a 4-layer model, where the top layers focused on human readable specification and the lower layers focused on executable forms of the value sets and rule logic.

3.6.2 Standards on CDS Clinical Data Model

As noted above, a major limitation of the Arden Syntax approach is the lack of a standard way to define access to the clinical data in the EHR. The term vMR has historically been used in the CDS community to refer to a simplified representation of the clinical record that is suitable and safe for a CDS knowledge engineer to directly manipulate in order to derive patient-specific assessments and recommendations. Historically, the challenge has been that different organizations used different vMRs. As a consequence, CDS resources (e.g., decision rules) written against one vMR could not be directly re-used by a different organization. HL7 vMR for CDS is the HL7 effort to define a standard vMR that can be used across CDS implementations and is simple and intuitive for both typical CDS artifact authors and implementers to understand, use, and implement [VMR]. The vMR is intended to serve several related roles: (i) the underlying data model for use in inference engines; (ii) a potential payload format for representing the inputs and outputs from such inference engines; and (iii) the core components of CDS knowledge artifacts such as order sets and documentation templates. The HL7 vMR for CDS standard, or simply vMR, includes:

- a specification of the vMR logical model,
- a specification of a constrained version of the HL7 version 3 Release 2 data types for use in the vMR,
- structural specifications for CDS engines' inputs and outputs, which are composed primarily of vMR data,
- a structural specification for identifying input and output data requirements for specific CDS use cases,
- guidance on how to represent common patterns of clinical information using the vMR.

Because most CDS knowledge engineers in most organizations have little or no previous knowledge of HL7 v3 concepts and conventions such as null flavors, mood codes, and negation indicators, the vMR uses a simplified version of the HL7 v3 release 2 data types from the 2012 Normative Edition, through constraining away a number of optional elements and attributes, in particular the optional null flavor attribute, from the full model, and data types that are not referenced in the vMR. The vMR also uses a simplified representation of clinical content that may be mappable to HL7 version 3 semantics, in particular the CCDA Release 1.1. A primary aspect of simplification is reducing the deep level of nesting that exists in many HL7 v3 models. In addition to the classes that represent clinical concepts, the vMR also includes classes to model CDS input/output, which may be used as the primary input/output data payload for a CDS guidance service compliant with the HL7 Decision Support Service standard, and classes to model CDS input/output specification, which specifies the specific CDS input/output data required for a specific CDS use case. A set of (about 87) vMR templates are further defined to constrain the base vMR model to facilitate semantic interoperability for specific interoperability settings [VMR-TEMPLATES]. The vMR has XML [VMR-XML] and GELLO [VMR-GELLO] implementations.

Because decision support provides guidance for clinical best practices, and clinical quality measures (CQM) assess whether clinical best practices have been followed, it is assumed that the same common reference model can be used for both types of applications. In the US Realm, under Meaningful Use, the common reference model for quality measures is the Quality Data Model (QDM) [QDM]. The proposed unified model is known as the Quality Information and Clinical Knowledge (QUICK) logical model, drawing upon both QDM and vMR [QICORE]. The QUICK model is an initiative of the Clinical Quality Information (CQI) and CDS HL7 Work Groups. QUICK was originally developed independent of FHIR. However, recognizing the broader community focus on FHIR, the decision was made by the CDS and CQI working groups to align QUICK with FHIR, and use the FHIR resources to define the QUICK model. This alignment not only creates a common model for quality and interoperability, but will also make it easier in the future to leverage other FHIR-related efforts, such as CDA on FHIR. The FHIR QICore profiles provide a physical implementation of QUICK, making data for quality

improvement and decision support applications accessible via the FHIR interface. QICore has been harmonized with certain other FHIR-based initiatives, in particular, the Data Access Framework (DAF). DAF is a U.S. Realm Implementation Guide that maps Meaningful Use data elements to FHIR resources, and is discussed in detail in section 5.4.2. The data elements in DAF are also in QICore, and the value sets required by DAF are preferred (but not required) in QICore. As a result, conforming to DAF automatically satisfies a significant subset of the conformance requirements of QICore. QICore conformance involves supporting certain additional data elements not required by DAF, because they are needed for quality measures. On the other hand, QICore is less restrictive than DAF, allowing QICore to be used outside the US Realm. More information on DAF is provided in Section 5.4.5.

3.6.3 Standards on CDS Service

As was outlined in section 3.6.1, it is challenging to define standards with widespread adoption for encoding CDS knowledge. An alternative is to standardize decision support service (DSS). Service-oriented CDS addresses the problem of requiring all EHRs to be able to embed complicated CDS knowledge. In service-oriented CDS, the patient's data is abstracted out of the EHR and sent to a remote CDS service for evaluation. A DSS can be conceptually understood as the guardian of one or more modules of medical knowledge, wherein each DSS knowledge module is capable of utilizing coded patient data to arrive at machine-interpretable conclusions regarding the patient under evaluation. The scope of a typical DSS knowledge module is the assessment of a single patient in a specified topic area. The topic area may be narrow (e.g., the need for a glycated haemoglobin test for a patient with diabetes) or broad (e.g., the existence of contraindications to any medications prescribed or about to be prescribed for a patient). When requesting a patient evaluation, a DSS client specifies the knowledge modules to use for the evaluation, and the client submits the patient data required by the knowledge modules. In return, the DSS returns inferences regarding the patient in a format that has been pre-defined for that knowledge module.

The first release of a normative specification for HL7 decision support service (DSS) was published in 2011 [DSSR1], through the Healthcare Services Specification Project (HSSP), a joint effort between HL7 and OMG. HL7 DSS Release 1 includes a platform-independent model (PIM) for the DSS as well as a platform-specific model (PSM) for SOAP XML Web services. The specification defines three service interfaces that a compliant service implementation should support:

- Metadata Discovery Interface lists and describes the supported service operations and semantic requirements that knowledge modules of the DSS instance fulfil e.g. keywords, steward organization, language support, and allowed or required information models.
- Query Interface enables the discovery and characterization of knowledge modules, such as identification of knowledge modules meeting client needs, information on the data required for evaluating a patient using the specified DSS knowledge modules, specification of the meaning and format of the patient evaluation results that will be returned by the specified DSS knowledge modules.
- Evaluation Interface evaluates a patient using the specified knowledge modules. The evaluation can be designated to time in the past or the future, or conducted iteratively.

As discussed in section 3.6.1, the ONC HeD initiative aimed to address two use cases. The second use case, CDS guidance service, focused on the consumption of CDS interventions through a web service. In support of the use case, HeD updated HL7 DSS R1, which added a new profile to support RESTful Web services for the Evaluation interface as an alternative to the original SOAP interface [DSSR2]. HeD also published an implementation guide for delivering CDS guidance as a Web service. The IG used the HL7 DSS standard as the interface for requesting and receiving a CDS evaluation result, and used the HL7 vMR XML Specification Release 1 for the CDS input and output content payloads.

A number of implementations of the HL7 DSS standard exist, most notably the OpenCDS project [OPENCDS]. OpenCDS is a multi-institutional, collaborative effort to develop open-source, standards-based clinical decision support (CDS) tools and resources that can be widely adopted to enable CDS at scale. OpenCDS is licensed under the Apache 2 license. OpenCDS provides a reference implementation of HL7 DSS and vMR standards. OpenCDS is built on JBoss Drools [DROOLS]. Drools is an open-source rule engine supported by JBoss. It includes authoring and knowledge management tools at two

levels: web-based knowledge creation, testing, versioning and packaging using a built-in Drools tool named "Guvnor" in Drools 5 or "KIE" in Drools 6; low-level technical rule creation and testing using the open-source Eclipse Integrated Development Environment (IDE) for Drools and Java. JBoss Drools and the Guvnor/KIE knowledge management tools are central components of OpenCDS. From release 2.1.2, OpenCDS supports FHIR as an alternative to use of the vMR. Currently, OpenCDS supports vMR 1.0 and FHIR DSTU 2.0 as the input models via DSS SOAP interface, and FHIR DSTU 2.1 via REST interface, and supports vMR 1.0 and FHIR DSTU 2.1 as output data models. HL7 vMR or FHIR can also be used as the logical model for inferencing.

4 PATIENT EMPOWERMENT PLATFORM

4.1 Introduction

Having multi-morbidity is already an important burden for the patients. The associated challenges of poly-pharmacy and fragmented care create additional problems; these increase the likelihood of a non-adherence behaviour. Patients and their informal care givers including family are therefore central to integrated care, to ensure that their needs and preferences are respected in care decision making.

Evidence from a study carried out by health care professionals from Harvard Medical School and Royal College of Physicians of Ireland shows that shared decision making improves patients' understanding, sense of empowerment, decision quality and reduces major surgery by 20% in favour of conservative treatment, suggesting a potential for cost reduction in the health care system [TH13]. A statin choice randomized trial conducted by Mayo Clinic found that patients who received the decision aid were 22.4 times more likely to know their estimated cardiovascular risk than those in the usual care group, had greater decisional comfort, and better self-reported adherence [WMGG07].

According to systematic reviews published in English language journals between January 1998 and December 2013, there are evidences on the effect of concrete actions and initiatives that confirm the beneficial role of self-management in areas such as increased knowledge and / or experience, efficient use of services, cost reduction and improved health outcomes (considered as welfare, mental health and physical) [SSM14].

Since the last decade, Patient Empowerment has been an important trend of research in European Union. In H2020 (current eighth framework programme funding research, technological development, and innovation by the European Commission), two other projects share like C3-Cloud the research pillar on patient empowerment. Started in 2015, the PICASO project aims to provide a European service platform that is intended to become a Europe-wide Continuum of Care service platform that will improve cooperation and exchange of knowledge between professional caregivers in health, rehabilitation and social care domains. The platform will actively include patients and their relatives in the integrated care settings thus supporting patient empowerment and self-care. As C3-Cloud, PICASO intends to reinforce medical knowledge and create new care models for management and treatment of patients with multi-morbidity conditions [PICASO]. The project EmERGE, started in 2016, will explore the context of patient empowerment by the development of a platform to enable self-management of HIV in patients with stable disease [EmERGE].

4.2 Medixine Suite™

The SME Medixine, partner of the C3-Cloud project, is one of the world leaders in e-services for healthcare and connects patients and care providers. Medixine is the developer of the products, which provide patient engagement tools that are used in Europe, Asia and the US by over 200,000 patients. The product Medixine Suite™ is based on a powerful and versatile core that can be extended with a set of product modules. This enables customers to choose the right combination of modules for achieving their goals in a cost-effective way. Medixine Suite™ provides comprehensive monitoring and collaboration tools for all parties involved in the care process: patient's engagement, care professional and administration.

Patient Portal, Telehealth Monitoring, Remote Education and Coaching:

- Personal Health Record (PHR)
- Secure communication between patients and care providers
- Effective prevention and population screening
- Engage patients and families to participate in their own care

The Medixine Suite Patient shows the following functionalities:

- General: Manage Patient Settings And Access; Health Programs; Smart Tasks; Reminders and notifications
- Communicate with patients: Safe Messaging; Video Appointments; Realtime Chat (roadmap)
- Collect information from patients: Forms & Questionnaires; Connected Devices; Personal Health Record.
- Provide guidance to the patients: Health Info Access; Automated Health Coaching; or use any of the Communication tools

While the Medixine Suite Professional shows the next functionalities:

- General: Enroll patients into the Care teams; Manage patient settings and access; Manage organization settings.
- Communicate with your patients: Safe Messaging; Video Appointments; Realtime Chat (roadmap)
- Collect information from patients: Case management and triage tools; Forms & Questionnaires; Personal Health Record.
- Provide guidance to patients: Use any of the communication tools to provide personalized guidance; Recommend and help patients use the o other guidance tools

Medixine Suite™ contains extensive general features to manage settings and general functionality like Portla programs, Smart tasks and Reminders and Notifications. Medixine Suite™ uses the available communication tools to exchange messages and talk with patients about their health. To collect information from patients, the product uses data collection, tracking and forms and questionnaires functionality. All collected information is stored in the personal health record of the patient. Finally the relevant and non-personalized health guidance and information are provided to patients by means of available guidance and communication tools.

The product has both Web and mobile interfaces. All Medixine Suite™ functionality can accessed both via the provided applications and their user interfaces and via the modern integration service interfaces of Medixine Suite™. It allows the easy integration of the functionality to the user applications and systems.

4.3 Personal Health Folder: The Basque Country implementation

The Patient Empowerment Platform of Basque Country, named as Personal Health Folder (PHF), serves as an information, education and communication channel. Through it, the patients have access to a lot of useful information and can be an active part of their health can care through the medical system.

4.3.1 Remote monitoring of their medical data

With PHF, patients can consult and download their hospital discharge reports, surgical, analytical, radiology and pathology, as well as from (on request) primary care. They are able to see their drug history with prescriptions and active treatment sheets, vaccination history and exposure to radiation

from medical tests. They can also consult their appointments with general practitioner, nurse, midwife or hospital specialists.

4.3.2 Access to health information

More generally, within PHF, patients can access information about diseases or common health problems and links of their interest. They can complete questionnaires on healthy habits (like diet, physical activity and snuff) and obtain personalized recommendations.

4.3.3 Empowered patient

Patients can record additional information and incorporate it into their medical record in “my journal”. The doctor can see these records in the consultation. It is also possible for patients to incorporate their external reports to Osakidetza (the Basque Country Health Public Service) in PHF by “Uploading reports”.

PHF also improves communication with patients: they are able to send questions - messages to their primary care physician - through the “Patient Doubts”, upon acceptance. The doctor can also send information via messages to the patient.

Finally, the patients can register themselves in self-monitoring programs to control health parameters such as blood pressure, weight, tobacco usage, and alcohol intake. These must be validated by their healthcare professional.

4.3.4 Administrative services

Several other administrative services available within Personal Health Folder are available for the patient, including:

- change to the reference General Practitioner,
- update personal contact details,
- view the history of appointments,
- check next appointments.

4.3.5 Security

The access to "My Health Folder" is secured by mechanisms that guarantee the identity and confidentiality of patient information. Patients may access it using a card reader and a smart card with built-in digital signature, or by using a username, password and coordinates matrix.

4.3.6 Health professional benefits

Besides the benefits that patients may find, the Personal Health Folder also provides utilities for Health professionals, like:

- avoid delivering reports or active treatment sheets in face to face consultations, avoid issuing health reports,
- direct the patient to the information about their health problem and then discuss any questions they may have,
- recommend the completion of questionnaires on healthy habits and get recommendations,
- communicate with the patient in non-face to face methods.

4.4 Existing approaches

This section presents relevant research projects in the area of patient empowerment.

4.4.1 MobiGuide

In MobiGuide project (previously described in section 3.4.1.5), the patient wears sensors that can monitor biosignals (e.g. heart rate, blood pressure); these signals are transmitted to their smartphone

and from there to a powerful "backend" computer. The MobiGuide decision-support tool, which also has access to the patient's historical clinical data, such as their hospital records, analyses the data and alerts the patient about actions that should be taken. It asks the patient questions, in case additional information is needed. The system also makes recommendations regarding lifestyle changes or contacting care providers. All recommendations regarding therapy are transmitted to the patients' care providers. The recommendations are based on evidence-based, state-of-the-art clinical guidelines. During the project the experts intend to focus on the following clinical conditions: atrial fibrillation, gestational diabetes and gestational hypertension.

4.4.2 Innovative Care for Chronic Conditions Framework

The Innovative Care for Chronic Conditions Framework (ICCCF), by WHO, provides a comprehensive framework for updating health care to meet the needs of chronic conditions by summarizing the basic elements for improvement in health systems at the policy level, health care organisation and community level, and the patient interaction level. As its ultimate goal, the ICCCF envisions informed, activated communities and patients - thus empowered patients - interacting with a prepared, proactive, motivated practice team, resulting in high-quality, satisfying encounters and improved outcomes [ICCCF].

4.4.3 Chronic Disease Self-Management Program

Many chronic diseases, like diabetes and obesity, are essentially self-managed diseases and coping with them requires patients to successfully perform optimal self-management. The Chronic Disease Self-Management Program [CDSMP] developed by the School of Medicine at Stanford University is an evidence-based program organised as workshops for facilitating self-management by people with different chronic health problems. The program has been successfully adapted in several countries including Austria, Denmark, England and Germany. A review of the program concludes there is moderate to strong evidence that the program improves the patients self-rated health, health distress, pain, fatigue, disability, cognitive symptom management, physical activity and self-efficacy [DNBoH]. Patients who take the program also spend fewer days in the hospital, and there is a trend towards fewer out-patient visits and hospitalizations.

4.4.4 Active Patient: Educational Program

In the Basque Country, the **Active Patient Program** helps chronic patients or caregivers acquire knowledge and skills related to the disease and its management. The goal is to provide information to a better understand of disease and train skills in self-care and disease management. Currently there are two programmes focused to "diabetic patients" and to "an active self-care". The educational programme is based on the Stanford Methodology, which provides workshops in self-management of the disease. Emphasis is placed on tools for enhancing proactive self-care as improvements in diet, physical activity patterns, disease information, emotional managements, communication skills and medication adherence. They are also trained to set their own goals and solve problems related to their condition, and to participate actively in their health. Specifically related to the self-management support, the Active Patient Program aims that activated patients and healthcare professionals educate and empower patients to take control of their health. The healthcare professionals introduce themselves as leaders of the program and not as healthcare professionals.

4.5 Related standards

This section describes important standards related to patient empowerment platforms.

4.5.1 HL7 CCOW

The HL7 CCOW (Clinical Context Object Workgroup) Standard is vendor independent and allows clinical applications to share information at the point of care [HL7-CCOW]. Using a technique called "context management", CCOW provides the clinician with a unified view on the information held in separate and disparate healthcare applications referring to the same patient, encounter or user. This

means that when a clinician signs on to one application within the group of disparate applications tied together by the CCOW environment, that same sign-on is simultaneously executed on all other applications within the group. Similarly, when the clinician selects a patient, the same patient is selected in all the applications. CCOW then builds a combined view of the patient on one screen.

CCOW works for both client-server and web-based applications. The CCOW Technical Committee became a part of HL7 two years ago after starting out as an independent healthcare industry consortium. In that short time, the committee has developed and ratified four versions of the CCOW Standard. This unprecedented pace has been, in part, due to the modular component-based nature of the architecture upon which the standard is based, enabling new specifications to be developed in a complementary and add-on manner.

CCOW's Context Management Architecture (CMA) was founded on the principle that common context can be established across applications by identifying things—such as a patient—or concepts—such as a clinical encounter—in a manner that different applications can nevertheless recognize.

The core architecture is comprised of three main types of components: applications; a context manager that coordinates and synchronizes applications; and mapping agents that can represent the various synonymous real-world identifiers used to identify clinical patients, users, etc. The architecture defines the roles and responsibilities for each of these components and precisely prescribes the interfaces that enable them to communicate. The architecture does not define or dictate the implementation of any of the components.

The user sets the context using any CCOW-compliant application, for example, to select a patient of interest. The application then tells the context manager that it wants to set the patient context and provides the context manager with an identifier that indicates the context subject, which, in this case, might be the medical record number for the patient of interest.

The context manager then tells the other applications that the context has been changed, and each application obtains the patient's identifier from the context manager. Each application then adjusts its internal state and data display accordingly. This all happens in real-time.

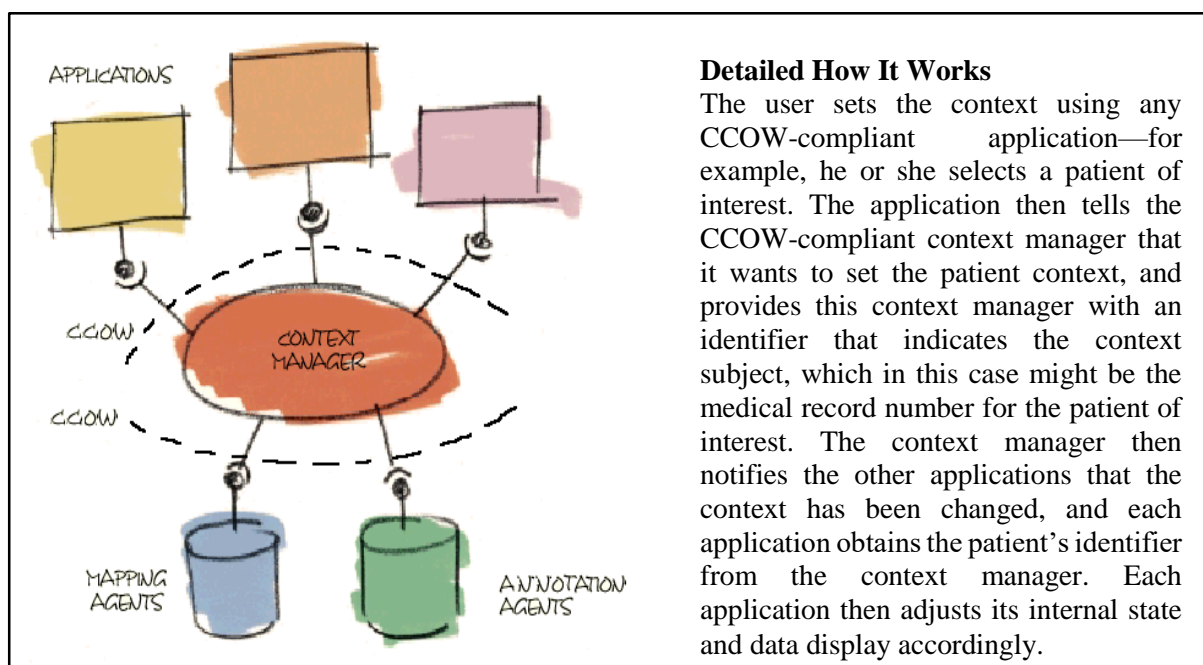


Figure 14 Clinical Context Object Workgroup overview [CCOW]

4.5.2 Smart-On-FHIR

SMART-on-FHIR is an open application programming interface that allows developers to create apps (and clinicians to select apps) that work with their EHR system, regardless of vendor.

- The SMART project key focus is to develop a SMART platform architecture to achieve two major goals: develop a user interface to allow substitutability for medical apps based on shared basic components and create a set of services to enable efficient data capture, storage, retrieval and analytics. The overarching mission of SMART is to "create an ecosystem of substitutable apps that can run on any EHR system," according to its website. Substitutability is defined as the capability to seamlessly replace one app with another of similar functionality without requiring any re-engineering or technical expertise.
- FHIR, Fast Healthcare Interoperability Resources, is a standards framework created by HL7, an organization that develops standards related to the exchange and sharing of electronic health data. FHIR solutions are built from modular components in such a way that any EHR system can read extensions in app coding for seamless implementations (HL7 FHIR is described in more detail in Section 5.4).

Blending the two together, SMART-on-FHIR is the SMART project's latest platform offering whose vision is to provide the resources for developers to build medical apps using "developer-friendly APIs" that integrate into any EHR system at the point of care allowing for "plug and play" usability [SMART-on-FHIR].

5 TECHNICAL AND SEMANTIC INTEROPERABILITY ARCHITECTURE

5.1 Introduction

To achieve long-term, continuous coordination of care, treatment sites need to exchange the most recent context of the patient through medical summaries, discharge notes, care summaries to establish seamless transitions of care and share individual treatment plans to be reconciled as an integrated care plan. The C3-Cloud Coordinated Care and Cure Delivery Platform needs to communicate with these healthcare information systems to facilitate such information exchange, which introduces a technical interoperability challenge. The Personalised Care Plan Development Platform also needs to access the electronic healthcare records of the patient to be able to facilitate creation of an integrated care plan based on the health conditions of the patient.

The C3-Cloud Technical Interoperability Platform will provide unified access to all electronic health records of the patient distributed in various providers to those involved in the care of the patient, to realise informed and shared decision-making, by establishing an interoperable architecture between C3-Cloud application components and health information systems in various care settings. Moreover, IT-systems need to be able to do more than simply exchange information. They need to be able to "interpret" its content and resolve semantic mismatches among different healthcare information systems. Solving the semantic integration challenge is at the core of the C3-Cloud Semantic Interoperability platform.

5.2 The challenge of interoperability

In order to support the Clinical Decision Support Modules of the C3-Cloud concept, significant ICT challenges need to be overcome in the areas of interoperability, common standards for data integration, data presentation, recording, scalability, and security. Medical data are complex and spread in various healthcare information systems. From a technical perspective, the C3-Cloud interoperability approach will achieve access to patient and care provider data by seamlessly integrating with the EHR, summary care record systems (SCR), personal health record systems (PHR) and home/community care information systems, including medical sensors providing real-time patient data, thus addressing the technical barriers of "silos" in care, especially disease specific healthcare information systems. The challenge of interoperability is considered from two different viewpoints: 1) technical interoperability is the access, exchange of data between information systems, 2) semantic interoperability (SIOp) is central to healthcare interoperability and guarantees that the meaning of data is shared to allow the (re-)use and (re-)interpret of the data that is exchanged.

To support interoperability between systems and meaningful sharing of data, health information standards must cover both the syntax (structure) and semantics (meaning) of the data exchanged. Interoperability standards are not software or hardware, but are the blueprints that technology developers can use to develop health information systems that will be inherently compatible with other systems adhering to these same standards.

Since the last decade of the past century considerable efforts have been invested into the development of standards for health information representation and communication, with an increasing focus on semantic interoperability. Standardised vocabularies and information models are facilitators of SIOp, opposed to local coding systems or natural language. Insufficient SIOp bears the risk of suboptimal decision-making. One difficulty is that despite efforts from Standards Development Organizations (SDOs) (Health Level Seven International (HL7), Digital Imaging and Communications in Medicine (DICOM) or CEN Technical Committee 251 (CEN TC251)) and regardless of the international initiative of “Integrating the Healthcare Enterprise” (IHE), most clinical data in Electronic Healthcare Records (EHR) applications are still not natively interoperable. Several European projects have been founded in FP7 and H2020 that address, in specific contexts, the challenges of interoperability (see section 5.2). The main architecture in these projects requires client systems to interact remotely with server-based resources across organizational and geographical boundaries, and can be broadly classified as a distributed system. The state-of-the-art in distributed system design employs service-oriented architectures (SOA).

SOA is not a set of standards or technological framework, but an architectural design paradigm that enables and promotes modularity, extensibility, reuse and interoperability. The SOA paradigm is centred on defining a set of loosely coupled services with well-defined interfaces. This enables client applications that can call upon and orchestrate many different services to accomplish a task. The relative independence of services and the standardized interface enables different implementations of services to be exposed and accessed, while hiding the heterogeneity of embedded and legacy systems (EHR/SCR/PHR). The modularity and independence of services enable the system to be smoothly extended by exposing additional services that clients can orchestrate.

It is interesting to note that lately, there has been an intense focus from the genetics community directed to the issue of developing and maintaining shareable, multipurpose, high-quality computable algorithms operating on different data sources thanks to standardized access to data [Weng10]. Recognizing the growing need of data integration and its relation to sustainability and scalability issues, the FAIR Data Initiative has been launched in January 2014 [FAIR]. This new movement, coming from the genetics community, provides guidelines to adopt standards in order to develop FAIR data repositories and networks where valuable scientific data is ‘FAIR’ in the sense of being Findable, Accessible, Interoperable and Reusable [Wilkinson16]. An important step in the FAIR Data approach is to publish existing and new datasets in a semantically interoperable format that can be understood by other humans (not the producers of the data) and computer systems in specific settings. By semantically annotating data items to be integrated with metadata, computer systems can be used to (semi-)automatically combine different data sources, resulting in richer knowledge discovery activities.

This initiative aims at facilitating the necessary breaking down of information systems but the challenge of exploiting data in legacy systems still remains as well as issues of exploiting new kinds of data for which standards do not yet exist (Internet of Things, Social Media such as discussion boards, Twitter, etc.). If healthcare studies now focus these new sources of data [PD11, LPD13], the lack of base reference and the unstructured and moving nature of the common language do this field a remaining challenge for automatic comprehension [SFHA14].

Nowadays, Semantic Interoperability platforms are key components when data need to be exchanged within operational or decisional processes within a domain. However, in the healthcare domain, operational solutions for SIOp have still small audiences, due to the inability of health applications to conform to interoperability standards. Several reasons have been in particular highlighted in the context of the European ASSESS-CT project [ASSESS-CT]. Some of them are relevant in the context of the C3-Cloud pilots, such as: *(i) applications around care plans operate today in silos for specific set of operations; (ii) the different sites don't use the same standards and good practices when they use some; (iii) there is a lack of awareness among communities about the health information and knowledge*

representation interoperability standards that exist in the areas of clinical research and clinical care, and still a limited availability of mapping tools that can support the semantic harmonisation of heterogeneous health and life sciences data; and (v) the sites have their own framework of policies and standard operating rules, appoints an ethics and governance board, and spends time developing materials and gaining approvals from data providers, patient representatives and other stakeholders.

5.3 Existing approaches of Technical and Semantic Interoperability

With the aim to orchestrate the care across multiple care givers and treatment sites, the C3-Cloud Interoperability Middleware inevitably requires interoperability to exchange medications, conditions, interventions, episodic treatment plans, preferences, monitoring data etc. As said earlier, the role of the **Semantic Interoperability Platform** is to support Clinical Decision Support Modules to correctly classify and map the medications, conditions, observations and results represented in different content models and coded with different terminology systems among patient data and care plans exchanged by multiple care givers. One of the first tasks in the C3-Cloud project is to identify the **best-fit standards and interoperability profiles**, which will support and advance patient-centric interoperable care coordination across multiple care providers for informed decision making.

C3-Cloud envisages a pragmatic approach, leveraging existing solutions (relevant services and components) as much as possible. We will particularly build upon the following projects, which closely involve several of the C3-Cloud partners.

5.3.1 TRANSFoRm

TRANSFoRm (Translational Research and Patient Safety in Europe), an EU FP7 project (2010-2015), developed rigorous, generic methods for the integration of Primary Care clinical and research activities [TRANSFoRm], to support patient safety and clinical research via:

- Rich capture of clinical data, including symptoms and signs rather than just a single diagnosis. A generic, dynamic interface, integrated with electronic health records (EHR), facilitates both diagnostic decision support and identification of patients eligible for research, thus enhancing patient safety.
- Distributed interoperability of EHR data and other data sources that maintain provenance, confidentiality and security, which enables large-scale phenotype-genotype association studies and follow up of trials.
- Software tools and services to enable use of controlled vocabulary and standardized data elements in clinical research.

Providing interoperability between different clinical systems, across national boundaries, and integration of clinical systems and research systems were the focus of TRANSFoRm. The project designed and developed a unified interoperability framework based on semantic mediation approach to enable federated access to primary care EHRs and aggregated research repositories. The cornerstone for the mediation approach was standardised clinical data elements described in computable formalisms [SLCK], which established a unified mechanism for query formulation and data capture in a heterogeneous environment and facilitated automated local execution at different data sources. openEHR Archetype Description Language (ADL) was chosen as the formal specification language to define clinical data elements within the project. An ontology Clinical Data Integration Model (CDIM) was designed to enable translation between TRANSFoRm archetypes and local data source models (DSMs) [CDIM]. DSMs captured the structural models of individual data source, such as the SQL database schema or XML file schema, in a uniform representation. CDIM, DSMs and CDIM to DSM mappings were loaded and stored in LexEVS (a terminology server that provides a common terminology model and open access to a wide range of terminologies, terminology value sets, and cross-terminology mappings needed by NCI and its partners, which provided the necessary functionality to search ontology concepts and navigate ontology relations. Through the bindings between TRANSFoRm archetype and CDIM, a semantic mediator was able to automatically reason CDIM and DSMs, map the archetype into local data source schema and generate executable data extraction queries dynamically.

In the context of the interoperability framework, an integrated vocabulary service was developed to enable easy access to a large number of healthcare code systems distributed in diverse formats and facilitate integration with TRANSFoRm system [TRANSFoRm VS]. With a focus on European primary care systems, the service extracted and loaded a subset of UMLS Metathesaurus, which contained the most important code systems for European primary care such as SNOMED CT, ICPC, ICD10, Clinical Terms v3, LOINC, DICOM, HL7, including their European language variants, as well as genetic ontologies such as Gene Ontology and OMIM. A number of national code systems e.g. UK Read Codes v2 and British National Formulary (BNF) were also integrated. Built on LexEVS, the service provided a web-based terminology browser and web services API to integrate with other TRANSFoRm software e.g. query formulation workbench and electronic data capture (EDC) tools.

Based on the interoperability framework, TRANSFoRm designed and developed the distributed query and data extraction infrastructure, which could be configured to support a number of types of applications, including broad classes of observational studies and point-of-care applications such as Randomised Clinical Trials (RCTs) and decision support. As a central component of the TRANSFoRm software platform, this infrastructure facilitated patient identification and reuse of routine healthcare data for research studies. The infrastructure distributed patient queries, such as eligibility criteria or data extraction definitions as part of a retrospective study or a randomized trial, to individual data source for local interpretation and execution. The TRANSFoRm platform interacted with disparate patient registries and EHR systems via the Data Node Connector, which communicated with local systems through web service APIs as agreed between TRANSFoRm and local data source to facilitate integration. Patient queries, formulated in the form of logical/temporal constraints upon archetypes, were translated into executable local data source queries by Semantic Mediator, which was deployed together with Data Node Connector and used heuristic algorithms to reason the mappings between CDIM and DSMs for the data model translation. Data Node Connector coordinated the query execution and collected results. Depending on the requirement of the research study, Data Node Connector either sent the extracted data files to a Trusted Third Party (TTP) in the case of a retrospective study, or populated case report forms for research data collection in the case of a clinical trial. A suite of services and tools were built on top of the distributed query and data extraction infrastructure to facilitate end-user access and support different types of research workflow.

Three representative clinical use cases were carefully chosen to drive, evaluate and validate the TRANSFoRm software and services, including an epidemiological study on genotype-phenotype associations, an RCT, and diagnostic decision support. Evaluation studies were conducted at pilot sites in four European countries: UK, Netherlands, Poland and Belgium, involving both research repositories and EHRs.

5.3.2 SALUS

The SALUS project [SALUS] (Scalable, Standard based Interoperability Framework for Sustainable Proactive Post Market Safety Studies), is an R&D project co-financed by the European Commission's 7th Framework Programme (FP7). SALUS has explored new ways of accessing and analyzing data found in electronic health records to provide an infrastructure that will enable execution of safety studies for mining and analyzing real-time patient data. The long term goal is to ensure safety through early detection of rare adverse events; to provide the pharmaceutical industry faster medication innovation by decreasing time to market for new, safe and effective drugs, and to reduce the load of overwhelmed medical practitioners at the same time.

SALUS Project's main objective is to provide a comprehensive IT solution supported with ready-to-use tools in order to enable the secondary use of the already available Electronic Health Record (EHR) data in patient care domain, for clinical research purposes. SALUS particularly aims to strengthen the spontaneous reporting process by automated adverse drug event (ADE) detection on disparate EHR systems; enable standards based ADE reporting by automatically extracting the available information from the EHRs; realize the execution of post-market analysis and effectiveness queries for different subpopulations selected from multiple, distributed EHRs as target cohorts; contribute to the signal detection processes; and facilitate wide scale outcome and effectiveness research to be able to observe selected cohorts of patients over an extended period of time screening multiple, distributed, heterogeneous EHR systems to identify long term safety issues of a product.

SALUS project started in February 2012 and ended by April 2015. Using the SALUS system, it is now possible to:

- detect Adverse Drug Events on patient summaries using predefined detection rules,
- prefill Individual Case Safety Reports (ICSRs) with available patient data,
- submit ICH E2B (standard for electronic transmission of ICSR) based case safety reports to regulatory bodies,
- perform effectiveness studies on available EHR data by submitting various queries for different purposes such as case series characterization and temporal association screening,
- perform post market drug surveillance on selected cohorts coming from different EHR sources and make analytical calculations.

To achieve this, SALUS Project has developed comprehensive semantic and technical interoperability framework to seamlessly access heterogeneous EHRs. A standard-based interoperability framework has been developed including: a) Functional interoperability profiles enabling exchange of EHRs, b) semantic interoperability solutions enabling meaningful interpretation of the exchanged EHRs, c) security and Privacy mechanisms ensuring EHRs are shared in an ethical and safe way.

As a part of SALUS Semantic interoperability suite, a Semantic Metadata Registry (Semantic MDR) is provided [Sinaci2013] [SALUS-D4.2.1], which enables machine processable definitions of Common Data Elements (CDEs) defined by different entities to be searched, to be re-used and to be linked with each other. As a result, it facilitates the query of the mappings among different CDEs in different domains to address semantic interoperability challenges. The federated semantically enabled metadata registries (MDR) conforms to ISO 11179 standard where CDEs maintained in different MDRs can be uniquely identified, queried and linked with each other through Linked Data principles. Semantic MDR implements the IHE Data Element Exchange (DEX) profile [DEX], as a standard means to communicate with the metadata registry to query and retrieve data element definitions.

SALUS MDR is an open source project and the source code can be found at GitHub Repository [GITHUB-MDR].

In C3-Cloud Task 6.2, we will build a Semantic Interoperability Platform to handle structural mappings among different information models. In this process we aim to utilize the SALUS Semantic MDR as an ISO/IEC 11179 compliant metadata registry that will act as the semantic dictionary of the common building blocks of the content models required by C3-Cloud (i.e. medical summary and care plan models).

5.3.3 EHR4CR

Innovative Medicines Initiative (IMI) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) have funded the EHR4CR (Electronic Health Records for Clinical Research) project (2011-2015). EHR4CR is one of the largest public-private partnerships aiming at providing adaptable, reusable and scalable solutions (tools and services) for reusing data from Electronic Health Record systems for Clinical Research. The EHR4CR project aims to improve the efficiency and reduce the cost of conducting clinical trials, through better leveraging routinely collected clinical data in electronic healthcare records (EHRs) and using it at key points in trial design and execution life-cycle. The EHR4CR platform is an open IT platform that unlocks the information stored in Electronic Health Records for improving clinical research while fully respecting patient privacy and ensuring a high level of security [EHR4CR]. The platform enables efficient communication between sponsors and investigators, speeding up clinical trial protocol design and patient recruitment. Hospitals connecting to this platform will increase their participation to clinical trials and as such facilitate patient access to new and better treatments.

The EHR4CR platform automates the reuse of EHR data stored in existing EHR systems or Clinical Data Warehouses (CDWs). During the lifetime of the project, three use cases were implemented and accessible through end-user platform services:

- (PFS) Protocol Feasibility : Leverage clinical data to design viable trial protocols and estimate recruitment => Need of distributed queries over heterogeneous EHRs or CDWs

- (PRS) Patient Recruitment : Detect patients eligible for trials and better utilize recruitment potential => Need of distributed queries over heterogeneous EHRs or CDWs and workflow execution
- (CTE) Clinical Trial Execution & Serious Adverse Events Reporting : Optimize clinical trial execution by re-using clinical data to pre-populate eCRFs and adverse event reporting => Need workflow execution and pre-population of forms (thanks to distributed queries over heterogeneous EHRs or CDWs)

In this context the objectives of the **Semantic Interoperability Services** provided by the EHR4CR platform are to allow:

- Clinicians in hospitals, while using their own words, to simultaneously utilize the most appropriate reference codes for meaningful re-use of routinely collected clinical data in electronic healthcare records (EHRs) in the context of clinical research conducted at an international level.
- Investigators of the EHR4CR network to use a semantically-enabled platform to efficiently perform sophisticated web searches across European hospitals, to find clinically relevant results that can help improve clinical research.

The EHR4CR project developed a semantic interoperability platform providing a **consistent integrative semantic abstraction** on top of existing application representations that enables to mediate across heterogeneous healthcare information systems. The approach is based on the assumption that the co-existence between several standard semantic artefacts - namely information models (e.g. EN ISO 13606 information model and archetypes, openEHR, HL7 RIM, C-CDA and FHIR specifications, CDISC ODM, etc.) and terminologies/ontologies (e.g. LOINC, ATC, SNOMED CT, etc.) – as well as proprietary implementations for representing the content of health information in systems (EHR systems, CDWs, CTMS, EDC systems, etc.) will endure. Then, the semantic interoperability platform mediates different particular information models:

- Source information models of information systems used in hospital sites to collect clinical data during patient care (EHRs) or to process it for secondary use (CDWs).
- Target information models of information systems (Clinical Trial Management Systems (CTMS), Clinical Data Management Systems (CDMS), Electronic Data Capture (EDC) systems) used in clinical research sites to collect information of clinical trials including clinical data from participating hospital sites.

The EHR4CR platform has an open, standards based, service oriented architecture. The open architecture encourages development of alternative and new tools both at the platform level as for use locally at a hospital.

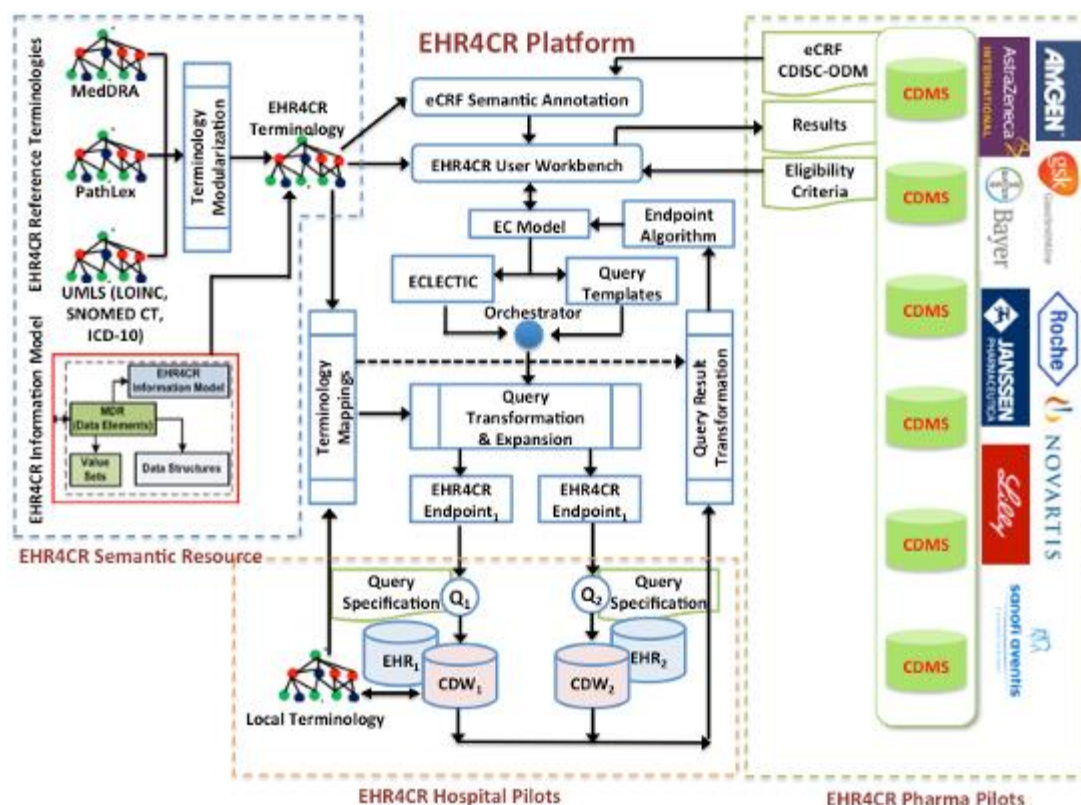


Figure 15 EHR4CR Semantic Interoperability platform: a set of EHR4CR Semantic Resources and Semantic Interoperability Services (SIS) are used during EHR4CR use case execution.

The EHR4CR project provides a mediation model – the EHR4CR Common Information Model (CIM) consisting in a set of multilingual semantic resources based on multiple standards. The EHR4CR templates are based on FHIR resources (Patient, Encounter, Condition, Observation, Procedure and MedicationStatement). FHIR-based resources were organized into categories based on HL7 CCD sections and UMLS semantic types: Demographics, Encounters, Advance directives, Problems, Family History, Social History, Alerts, Medications, Immunizations, Vital Signs, Results (lab, anatomic pathology), Procedures, Plan of Care, Lifestyle Choice, Ethical consideration. FHIR resources were enriched in order to fulfil the requirements of the project and represent the required semantic content. Some specific value sets were defined for some data elements of the FHIR templates.

EHR4CR templates are composed of data elements that are bound to a set of international reference terminologies selected by the project: ICD, SNOMED-CT, LOINC, ATC, ICD-O, Pubcan, TNM, PathLex. These terminologies are, when possible, imported into the collaborative editor from the official source of the terminology provider in order to bind the EHR4CR resources to up-to-date terminologies. The terminology binding is done through the definition of value sets corresponding to the data elements of each template. As much as possible, reference terminologies are enriched and/or merged in order to build multilingual terminologies and value sets (in English, French at least and when possible in the four languages of the EHR4CR partners: English, French, German and polish).

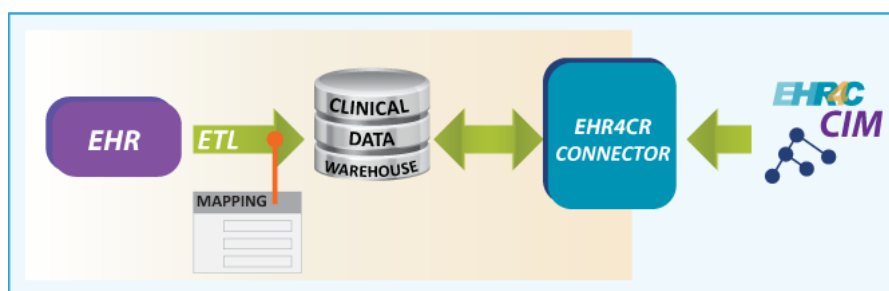
The semantic resources are stored into a semantic metadata repository (MDR). The international standard ISO/IEC 11179 is used to define metadata. This standard provides the definition of a "data element" registry, describing disembodied data elements. It is important to note that ISO/IEC 11179 covers just the definition of elements and does not dictate the persistence structures or retrieval strategies. In the healthcare domain, another ISO standard – ISO 21090 – plays a key role in the ISO/IEC 11179-based data element definitions since it provides the appropriate formal representation of the data type for Data Element Concept and of any type of the Value Domain data type. ISO 21090 especially provides a formal of the coded data types and addresses the binding with terminologies.

During the time of the project, additional tools have been developed for supporting:

- the management of the mediation model (CIM Editor)
- the mapping between hospital local sources and the mediation model that are used for clinical data transformation (standardization) during the ETL processes and/or query transformation. (TMS)
- the terminology mapping between electronic Clinical Research Forms (eCRFs in CDISC ODM format) and the mediation model supported by the SDM-ODM CDISC Editor extension.

The EHR4CR Common Information Model was developed and evolves through repeated cycles using a "Learning by Doing" approach. The first iteration of the CIM, based on a bottom up approach, started to cover the scope of 14 clinical trials selected to demonstrate the "Protocol Feasibility Services" (PFS) use case (EHR4CR CIM version 0.1), a second iteration covered the scope of 17 additional clinical trials selected to demonstrate the "Patient Recruitment Services" (PRS) use case (EHR4CR CIM version 0.2) and the third iteration covered the scope of 28 additional clinical trials selected to demonstrate the "Clinical Trial Execution" (CTE) implemented for (EHR4CR CIM version 0.3).

One important aspect is the connectivity of a new healthcare information system to the platform. Indeed, EHR data is not natively structured according to the EHR4CR CIM. The combination of an ETL (Extract, Transform and Load) step and the EHR4CR semantic integration layer takes care of the transformation between the local information models and the EHR4CR CIM.



Hospitals can become an EHR4CR endpoint by following this technical scenario:

- an initial data quality study is performed to verify that the site measures up to the minimum standard required for joining the platform,
- an EHR4CR clinical data warehouse (CDW) is instantiated (EHR can connect to i2b2) and a suitable ETL process is defined to populate it,
- the EHR4CR connector software is installed locally at the hospital as a virtual machine. It is subsequently hooked up to the CDW,
- an initial mapping between the local and EHR4CR information models is created that can be subsequently refined,
- the local installation is verified and prepared for registration in the EHR4CR platform.

The site is now part of the EHR4CR platform and can be activated as soon as the administrative and contractual processes are finalised.

5.4 Related Standards

Decades of efforts in healthcare ICT industry have developed three major standards frameworks for the exchange, integration, sharing, and retrieval of electronic health information between healthcare systems, namely HL7 Clinical Document Architecture (CDA), HL7 Fast Healthcare Interoperability Resources (FHIR), and openEHR. Various standards and profiles have been developed for specific clinical contexts and pathways within the three frameworks and through vendor collaboration such as Integrating the Healthcare Enterprise (IHE). This section will investigate the latest development in the standards frameworks.

5.4.1 HL7 Consolidated CDA

The HL7 CDA is a document markup standard that specifies the structure and semantics of "clinical documents" for the purpose of exchange [CDA]. A clinical document is a documentation of clinical observations and services. Encoded in XML, CDA documents are defined and complete information objects that can include text, images, sounds, and other multimedia content, and derive their machine processable meaning from the HL7 Reference Information Model (RIM) and use the HL7 Version 3 Data Types. The XML structure for a CDA document nests data in the following way:

- Header
- Body
 - Section(s)
 - Narrative Block
 - Entry(s)

The **Header** sets the context for the clinical document, which enables clinical document exchange across and within institutions, facilitates clinical document management and facilitates compilation of an individual patient's clinical documents into an electronic patient record. The **Body** contains the clinical report and can contain an unstructured "blob" or structured content organized in one or more **Sections**. Each **Section** contains one **Narrative Block** and zero to many coded **Entries**. Examples of sections include allergies, medications, problems, immunisations, vital signs etc. **Narrative Blocks** allow "human-readability" of a CDA document. Within a document section, the narrative block represents content to be rendered for viewing. **Entries** allow "machine-readability" (e.g. decision support applications). Within a document section, an entry represents structured content for further computer processing.

Following the publication of CDA R2, duplicative and conflicting implementation guides (IGs) had been published by different standards development organizations (SDOs) (e.g. HITSP, HL7, IHE, Health Story), which were approved/balloted at different times. As disparate SDOs (HL7, IHE, HITSP, etc.) developed CDA IGs, multiple approaches for documenting template requirements began to diverge threatening interoperability. The Office of the National Coordinator (ONC) within the US Department of Health and Human Services (HHS) hosted a collaboration among the standards community in order to address CDA documentation issues which were hampering understanding and consistent implementation. The project was carried out within the ONC's Standards and Interoperability (S&I) Framework as the CDA Consolidation Project, with one of goals being providing a set of harmonized CDA templates for the US Realm. Through the joint efforts of HL7, IHE, the Health Story Project, and ONC, the project examined and analyzed CDA Templates across the existing documentation, identified and addressed errors, issues of ambiguity and conflict, and consolidated prior documentation to a new single IG and ballot (approve) through HL7. Consolidated CDA (C-CDA) DSTU Release 1.1 was published in 2012 [C-CDA 1.1]. C-CDA DSTU Release 2.1 was published in 2015. C-CDA R1.1 is being used by The US Centers for Medicare & Medicaid Services (CMS) and ONC in the context of the 2014 Edition Certified Electronic Health Record Technology (CEHRT) requirements in the US [C-CDA MU2].

C-CDA R1.1 defines the US Realm Header, 9 document templates, 60 section templates and 82 entry templates. Table 2 lists the C-CDA 1.1 document templates.

Table 2 C-CDA 1.1 Document Templates

Document Template	Description
Consultation Note	A Consultation Note must be generated as a result of a physician or non-physician practitioner's (NPP) request for an opinion or advice from another physician or NPP. Consultations must involve face-to-face time with the patient or fall under guidelines for telemedicine visits. A Consultation Note must be provided to the referring physician or NPP and must include the

	reason for the referral, history of present illness, physical examination, and decision-making component (Assessment and Plan).
Continuity of Care Document (CCD)	The CCD is a core data set of the most relevant administrative, demographic, and clinical information facts about a patient's healthcare, covering one or more healthcare encounters. It provides a means for one healthcare practitioner, system, or setting to aggregate all of the pertinent data about a patient and forward it to another practitioner, system, or setting to support the continuity of care. The primary use case for the CCD is to provide a snapshot in time containing the pertinent clinical, demographic, and administrative data for a specific patient.
Diagnostic Imaging Report (DIR)	A DIR is a document that contains a consulting specialist's interpretation of image data. It conveys the interpretation to the referring (ordering) physician and becomes part of the patient's medical record. It is for use in Radiology, Endoscopy, Cardiology, and other imaging specialties.
Discharge Summary	<p>The Discharge Summary is a document that is a synopsis of a patient's admission to a hospital; it provides pertinent information for the continuation of care following discharge. The Joint Commission requires the following information to be included in the Discharge Summary:</p> <ul style="list-style-type: none"> • The reason for hospitalization • The procedures performed • The care, treatment, and services provided • The patient's condition and disposition at discharge • Information provided to the patient and family • Provisions for follow-up care
History and Physical (H&P) Note	A H&P Note is a medical report that documents the current and past conditions of the patient. It contains essential information that helps determine an individual's health status. The first portion of the report is a current collection of organized information unique to an individual, typically supplied by the patient or their caregiver, about the current medical problem or the reason for the patient encounter. This information is followed by a description of any past or ongoing medical issues, including current medications and allergies. Information is also obtained about the patient's lifestyle, habits, and diseases among family members. The next portion of the report contains information obtained by physically examining the patient and gathering diagnostic information in the form of laboratory tests, imaging, or other diagnostic procedures. The report ends with the clinician's assessment of the patient's situation and the intended plan to address those issues. A History and Physical Examination is required upon hospital admission as well as before operative procedures. An initial evaluation in an ambulatory setting is often documented in the form of an H&P Note.
Operative Note	The Operative Note is a frequently used type of procedure note with specific requirements set forth by regulatory agencies. The Operative Note or Report is created immediately following a surgical or other high-risk procedure and records the pre- and post-surgical diagnosis, pertinent events of the procedure, as well as the condition of the patient following the procedure. The report should be sufficiently detailed to support the diagnoses, justify the treatment, document the course of the procedure, and provide continuity of care.
Procedure Note	Procedure Note is a broad term that encompasses many specific types of non-operative procedures including interventional cardiology, interventional radiology, gastrointestinal endoscopy, osteopathic manipulation, and many other specialty fields. Procedure Notes are documents that are differentiated from Operative Notes in that the procedures documented do not involve incision or excision as the primary

	act. The Procedure Note is created immediately following a non-operative procedure and records the indications for the procedure and, when applicable, post-procedure diagnosis, pertinent events of the procedure, and the patient's tolerance of the procedure. The document should be sufficiently detailed to justify the procedure, describe the course of the procedure, and provide continuity of care.
Progress Note	A Progress Note documents a patient's clinical status during a hospitalization or outpatient visit; thus, it is associated with an encounter. Taber's medical dictionary defines a Progress Note as "An ongoing record of a patient's illness and treatment. Physicians, nurses, consultants, and therapists record their notes concerning the progress or lack of progress made by the patient between the time of the previous note and the most recent note." Mosby's medical dictionary defines a Progress Note as "Notes made by a nurse, physician, social worker, physical therapist, and other health care professionals that describe the patient's condition and the treatment given or planned." A Progress Note is not a re-evaluation note. A Progress Note is not intended to be a Progress Report for Medicare. Medicare B Section 1833(e) defines the requirements of a Medicare Progress Report.
Unstructured Document (UD)	An unstructured document is a document used when the patient record is captured in an unstructured format that is encapsulated within an image file or as unstructured text in an electronic file such as a word processing or Portable Document Format (PDF) document. There is a need to raise the level of interoperability for these documents to provide full access to the longitudinal patient record across a continuum of care. Until this gap is addressed, image and multi-media files will continue to be a portion of the patient record that remains difficult to access and share with all participants in a patient's care. The Unstructured Document type addresses this gap by providing consistent guidance on the use of CDA for such documents. An UD document type can (1) include unstructured content, such as a graphic, directly in a text element with a mediaType attribute, or (2) reference a single document file, such as a word-processing document, using a text/reference element.

For greater expressivity and decrease ambiguity, the latest C-CDA implementation guide R2.1 was developed and produced by the HL7 Structured Documents Workgroup in 2015. It updates the C-CDA R2 (2014) guide to support "on-the-wire" compatibility with R1.1 systems. The C-CDA R2 guide was developed and produced through the joint efforts of HL7, two Sub-Work Groups of ONC S&I Framework — Longitudinal Care Plan (LCP) and Long-Term Post-Acute Care (LTPAC) Transition — and through the SMART C-CDA Collaborative hosted by ONC and Harvard Medical School. The ONC Longitudinal Care Coordination Standards and Interoperability (LCC S&I) Work Group and community providers identified a set of priority data elements for shared care and transfer of care for a patient moving from one setting to another. These data elements identified gaps in the existing CDA document types. R2.1 includes three new document types (Referral Note, Transfer Summary, and Care Plan) and one existing document type (Consultation Note) to address the gaps. Additionally, R2.1 includes 70 section templates (including 3 deprecated) and 111 entry templates (including 5 deprecated). Table 3 lists the 3 new C-CDA 2.1 document templates.

Table 3 C-CDA 2.1 New Document Templates

Document Template	Description
Care Plan	A Care Plan is a consensus-driven dynamic plan that represents a patient's and Care Team Members' prioritized concerns, goals, and planned interventions. It serves as a blueprint shared by all Care Team Members

	<p>(including the patient, their caregivers and providers), to guide the patient's care. A Care Plan integrates multiple interventions proposed by multiple providers and disciplines for multiple conditions. A Care Plan represents one or more Plan(s) of Care and serves to reconcile and resolve conflicts between the various Plans of Care developed for a specific patient by different providers. While both a plan of care and a care plan include the patient's life goals and require Care Team Members (including patients) to prioritize goals and interventions, the reconciliation process becomes more complex as the number of plans of care increases. The Care Plan also serves to enable longitudinal coordination of care. The CDA Care Plan represents an instance of this dynamic Care Plan at a point in time. The CDA document itself is NOT dynamic. Key differentiators between a Care Plan CDA and CCD (another "snapshot in time" document):</p> <ul style="list-style-type: none"> • Requires relationships between various acts: <ul style="list-style-type: none"> ○ Health Concerns ○ Problems ○ Interventions ○ Goals ○ Outcomes • Provides the ability to identify patient and provider priorities with each act • Provides a header participant to indicate occurrences of Care Plan review
Referral Note	<p>A Referral Note communicates pertinent information from a provider who is requesting services of another provider of clinical or non-clinical services. The information in this document includes the reason for the referral and additional information that would augment decision making and care delivery. Examples of referral situations are when a patient is referred from a family physician to a cardiologist for cardiac evaluation, or when patient is sent by a cardiologist to an emergency department for angina, or when a patient is referred by a nurse practitioner to an audiologist for hearing screening, or when a patient is referred by a hospitalist to social services.</p>
Transfer Summary	<p>The Transfer Summary document is exchanged by healthcare providers in instances when a patient moves between health care settings and care teams temporarily or permanently (e.g., long term care facility to hospital, hospital to skilled nursing facility or home health agency, or from one Primary Care Physician to a new Primary Care Physician). The Transfer Summary provides comprehensive information regarding the patient's history, current status, and care plan. The CCD is a subset of the Transfer Summary and contains just the most clinically important patient information. It is a snapshot in time and may be generated for a single visit or a set of visits. The CCD can be used as an alternative to the Transfer Summary when minimal information needs to be conveyed, or for reporting updates to clinical registries and centralized data repositories.</p>

5.4.2 HL7 FHIR

FHIR is a next generation standards framework created by HL7 [FHIR]. FHIR combines the best features of HL7 v2, HL7 v3 and CDA product lines while leveraging the latest web standards and applying a tight focus on implementability. Multiple FHIR servers are publicly available for testing. Open source implementation libraries are available for different programming languages, including Java, .NET, Delphi, JavaScript and Swift. FHIR is designed to be evolutionary from existing standards such as HL7 Version 2, V3 and CDA, so standards can co-exist and leverage each other. FHIR supports multiple information exchange paradigms: RESTful, service, messaging and documents. The

specification is free for use with no restrictions. The current version of FHIR is Draft Standard for Trial Use (DSTU) 2. The new version Standard for Trial Use (STU) 3 is under active development. Its pre-release is available at [FHIR STU3]. The specification is targeted for 2018 to reach Normative level.

The basic building block in FHIR is Resource. All exchangeable content is defined as a resource. Resources are defined and represented in a common way, built from data types that define common reusable patterns of elements. Resources share a common set of metadata and has a human-readable wire format for ease of use by developers. In addition, each resource carries a human-readable text representation using html as a fallback display option for clinical safety. This is particularly important for complex clinical information where many systems take a simple textual/document based approach. Resources are assembled into working systems that solve real world clinical and administrative problems in a wide variety of contexts, such as mobile phone apps, cloud communications, EHR-based data sharing, server communication in large institutional healthcare providers, etc.

The current version of FHIR specification (DSTU2) defines about 93 resources, which are classified into 6 sections:

1. Clinical: The content of a clinical record. Clinical resources include
 - General resources such as **AllergyIntolerance**, **Condition**, and **Procedure** that appear throughout the patient record. Other general resources include
 - **FamilyMemberHistory**
 - **ClinicalImpression**
 - **RiskAssessment**
 - **DetectedIssue**
 - Care provision resources that support planning of care provision, including
 - **CarePlan**
 - **Goal**
 - **ReferralRequest**
 - **ProcedureRequest**
 - **NutritionOrder**
 - **VisionPrescription**.
 - Medication management resources that support the medication and immunization processes, including
 - **Medication**
 - **MedicationDispense**
 - **MedicationOrder**
 - **MedicationStatement**
 - **Immunization**
 - **ImmunizationRecommendation**.
 - Diagnostics resources concerned with observing the patient, and the diagnostic service process built around this, including
 - **Observation**
 - **DiagnosticReport**
 - **DiagnosticOrder**
 - **Specimen**
 - **BodySite**
 - **ImagingObjectSelection**
 - **ImagingStudy**
2. Identification: These resources provide support for identifying the various entities involved in healthcare: people, organizations, substances, devices, etc. Identification resources include **Patient**, **Organization**, **Location**, **Device**, and more.
3. Workflow: The resources manage the healthcare process, such as **Encounter**, **EpisodeofCare**, etc for encounters; **Appointment**, **Schedule**, etc for scheduling; **Order**, **SupplyRequest**, **SupplyDelivery**, etc for order management.
4. Financial: Resources that support the billing and payment parts of FHIR.
5. Conformance: Resources use to manage specification, development and testing of FHIR solutions. For example, A **Conformance** is a statement of a set of system capabilities for use as system discovery, or conformance expectations.

6. Infrastructure: These resources provide generally useful functionality, and/or are referenced directly from the base FHIR framework e.g. RESTful API, messaging, documents. Infrastructure resources include for example [Questionnaire](#), [QuestionnaireResponse](#), [Provenance](#), [AuditEvent](#), [Composition](#), [DocumentReference](#), [Media](#), [MessageHeader](#), [OperationOutcome](#), and so on.

Extensibility and interoperability are key design considerations of FHIR. The base FHIR specification is a "platform specification" - it creates a common platform or foundation on which a variety of different solutions are implemented. Base resources can be used as is, but can also be adapted to particular contexts of use. Typically, these adaptations specify:

- rules about which resource elements are or are not used, and what additional elements are added that are not part of the base specification,
- rules about which API features are used, and how,
- rules about which terminologies are used in particular elements,
- descriptions of how the Resource elements and API features map to local requirements and/or implementations.

Implementation Guide (IG) is a coherent and bounded set of adaptations that are published as a single unit. Validation occurs within the context of the Implementation Guide. A group of related adaptations that are published as a group within an Implementation Guide is a Package. Typically, Implementation Guides both restrict and extend APIs, resources and terminologies. FHIR provides a set of resources that can be used to represent and share the decisions that have been made, and allows implementers to build useful services from them. These resources are known as the conformance resources. The conformance resources describe two different uses for profiles on resources: Resource Profiles and System Profiles. Resource Profiles describe the general features that are supported by the system for each kind of resource. Typically, this is the superset of all the different use-cases implemented by the system. This is a resource-level perspective of a system's functionality. System Profiles describe the information handled/produced by the system on a per use case basis. Typically, these profiles are a series of variations on the same set of resources - different use cases leading to handling the resources that represent them differently. A number of IGs are developed and published as part of a FHIR release to address some particular use cases that are common or important, including US Data Access Framework (DAF) IG, C-CDA on FHIR IG, etc. Data Access Framework is discussed in detail in section 5.4.4.

C-CDA on FHIR IG is being developed as part of FHIR STU 3, currently available as a pre-release [C-CDA-FHIR]. The scope of this IG is to represent Consolidated CDA Templates for Clinical Notes (C-CDA) 2.1 templates using FHIR profiles. The first stage of the project defines all the C-CDA document-level profiles and their contained sections, including profiles of C-CDA US Realm Header, Care Plan, CCD, Consultation Note, Diagnostic Imaging Report, Discharge Summary, History and Physical Note, Procedure Note, Progress Note, Referral Note, Operative Note, and Transfer Summary. The C-CDA on FHIR CCD profile also defines several entry-level profiles by referencing relevant U.S. DAF FHIR profiles, such as DAF AllergyIntolerance, Condition, DiagnosticOrder, DiagnosticReport, MedicationStatement, Results, Vital Signs, Organization, Patient, Practitioner, Procedure, and Related Person Profiles.

5.4.3 openEHR

5.4.3.1 Presentation

OpenEHR is a comprehensive open standard specifications for building semantically interoperable and future-proof EHR systems. Over the last decade it has been successfully applied both as a self-standing health IT system and as a tool which provide interoperability in multi-system environments and tool for computer aided clinical decision support. OpenEHR describes the management and storage, retrieval and exchange of health data inside and between EHR systems. OpenEHR in a non-profit and open source organization and specification documents are freely accessible together with openEHR

tools [openEHRtools]. OpenEHR servers are available for testing. OpenEHR supports multiple information exchange paradigms such as RESTful and SOAP.

The openEHR approach is originally based on the results of the European Union's GEHR-Project in the early 1990s. Following GEHR several projects extended and refined its results (e.g. the Australian GEHR projects and the EU Synapses and SynEx projects). All these projects influenced the openEHR architecture [openEHRarchi] and the pioneering of a two level modelling approach for EHRs. That is, separation of the technical design and the clinical concerns of EHR systems. The first level takes care of the technical concerns and deals with the information structure [openEHRrefmod] (aka reference model) and data types with a small set of information model classes, upon which the core of EHR systems can be built – thus ensuring data interoperability. The second level of model handles the concerns of the clinical domain, which are about how to represent and communicate the semantics of the clinical content in forms of archetypes and templates – thus ensuring semantic interoperability.

Archetypes are the keystone of the openEHR architecture. They define the maximum data set of a clinical concept, they are used to express re-usable structured data-item definitions in the form of constraints on a reference model. Archetypes are defined based on topic, independent of use context. Archetypes support the binding of data nodes, names and values to concepts from external terminologies. They are also multi-lingual, and support all languages that can be expressed in Unicode. The archetypes' data have the same meaning in every EHR and everywhere in the EHR. Thus there are safely interpreted, and enable interoperability on the level of knowledge. Templates are used to create definitions of content such as a particular document or message, required for specific use cases, such as specific screen forms, message types or reports. Typical examples include 'acute care discharge summary', 'GP referral' and radiology report', by aggregation of different archetypes. Archetypes can be use as is, or can be modify for the specific needs (extending, removing and constraining elements). Once a template is defined, it is then compiled and expressed in a machine-understandable language such XML.

The openEHR Foundation provides the archetype model specification [openEHRarchmod] and also tools [openEHRtools] for their authoring and editing, which can be used without technical knowledge. They also manage the openEHR Clinical Knowledge Manager (CKM) [openEHRCKM], an open international repository, which currently contain about 1000 archetypes (such as: Care plan, Goals, Medication list).

The formal language for expressing archetypes is the Archetype Definition Language (ADL) [openEHRADL]. The syntax can be parsed, and describes an archetype in four sections:

1. Identification: Each archetype has a unique identifying name. The 'concept' statement connects the archetype to the described concept.
2. Description: This section contains metadata such as the purpose, use, or author of the archetype.
3. Definition: The allowed object structures and constrains are defined by instantiate classes of the reference model and determine their hierarchical arrangement, value ranges, and occurrence.
4. Ontology: The semantic of the archetype is added in this section. Thereto the items are lodged with textual descriptions and optionally term bindings.

Two versions are available: ADL 1.4, and ADL 2, The 1.4 release of ADL and its "object model" counterpart Archetype Object Model (AOM) are the basis for the CEN and ISO "Archetype Definition Language" standard (ISO standard 13606-2, [ISO136006-2]).

Semantic interoperability and sustainability are key concept in openEHR. The Archetype Query Language (AQL) [openEHRAQL] is a declarative query language developed specifically for expressing queries used for searching and retrieving the clinical data found in archetype-based EHRs. It is applied to the openEHR EHR Reference Model (RM) and the openEHR clinical archetypes, but the syntax is independent of applications, programming languages, system environment, and storage models. The minimum requirement for data to be querying with AQL (including with archetype structures and terminology) is for the data to be marked at a fine granularity with the appropriate archetype codes and terminology codes. This may be native openEHR-structured data, or legacy system data to which the

relevant data markers (mainly archetype paths and terminology codes) have been added. Unlike other query languages, such as SQL or XQuery, AQL expresses the queries at the archetype level, i.e. semantic level, other than at the data instance level. This is the key in achieving sharing queries across system boundaries or enterprise boundaries.

5.4.3.2 Guideline Definition Language (GDL)

The GDL is designed to represent clinical knowledge for computerized decision support, by expressing clinical logic as production rules and algorithms. Discrete GDL rules, each containing if-then statements, can be combined together as building blocks to support single decision making process and more complex decision making processes. The GDL rules can be used to drive at-point-of-care decision support applications as well as retrospective populational analytics. It is also possible to chain the execution of several CDS rules in order to support complex decision making processes. And to reuse the CDS rules in different decision support applications in different clinical context.

The GDL designed to be natural language-independent and reference terminology-independent by leveraging the designs of openEHR Reference Model and Archetype Model. It achieves this by using openEHR archetypes both as input and output of GDL guidelines.

An authoring tool for GDL is available as open-source software for the openEHR community. The GDL editor is a multiplatform desktop application and will allow users to create, edit and run GDL files. The editor is capable of generating forms based on the archetype elements defined in the GDL. These forms can be used to take input from the user and trigger the rules. More information about this tool can be found in the GDL Editor Manual [GDLEditorManual] and can be downloaded at [openEHRDS].

CAMBIO Inc., a partner on the C3-Cloud project, authors the openEHR Guideline Definition Language (GDL) and maintains the open source implementation of GDL.

5.4.3.3 OpenEHR implementation

- OpenEHR as part of national standards and commercial solutions:

OpenEHR archetypes are being used, currently, by the National e-Health Transition Authority of Australia, the UK NHS Health and Social Care Information Center (HSCIC), the Norwegian National IKT organization, Sweden and the Slovenian Ministry on Health. In Brazil openEHR was selected as the basis for the standardize EHR systems.

The full list of current and contracted future deployment of openEHR solutions by countries is available [openEHRlist].

OpenEHR is also utilized in commercial solutions throughout the world. A comprehensive list of openEHR-based IT solutions can be found at the site of openEHR Industry Partners [openEHRindus].

- EU-funded projects:

MobiGuide (described in section 4.3.1), similarly to TRANSFoRM, (which mentioned in section 5.2.1) also used openEHR as the key platform for interoperability [MobiGuidePaper]. While in the case of TRANSFoRM openEHR Archetype Description Language (ADL) was chosen as the formal specification language to define clinical data elements within the project, in this case of MobiGuide openEHR provided the link between hospital EHRs and clinical decision support systems. For this purpose PHR was developed by combining openEHR archetypes and the HL7 Virtual Medical Record standard, supported by a service oriented framework for data exchange. It also demonstrated that the HL7 and the ISO/CEN 13606 by using an openEHR-based approach can be successfully while used together.

CHIRON - a European Research Project co-financed by the ARTEMIS Joint Undertaking project including 27 partners - intended to combine state-of-the art technologies and innovative solutions into an integrated framework designed for an effective and person-centric health management along the complete care cycle of patients with atrial fibrillation [CHIRON]. Data captured from the ECG electrodes has been directly translated into OpenEHR archetypes and openEHR templates were used as GUI toward the clinicians.

5.4.4 US ONC Data Access Framework

The US ONC Standards and Interoperability (S&I) Data Access Framework (DAF) Initiative develops US Realm implementation guidelines on the standards and profiles that can be used to enable access to clinical documents and discrete data for individual patients, multiple patients or aggregations of patients for patient care and for research within an organization and across organizations [DAF]. DAF Phase 1 and Phase 2 focused on identifying standard APIs for accessing data within an organization (also called as Local DAF) and from trusted external organizations (also called as Targeted DAF) for treatment and payment purposes. DAF Phase 3 on the other hand will focus on enabling researchers to access data from multiple organizations in the context of Learning Health System (LHS). The capabilities created as part of DAF Phase 3 are intended to be leveraged to build national data infrastructure for a Learning Health System. DAF Phase 3 for Research intends to adopt HL7 FHIR to standardize query, data extraction APIs, mapping/formatting and results reporting. The data access mechanisms defined by DAF Phase 1 & 2 include Document Metadata based Queries and Data Element based Queries.

Document Metadata based DAF Queries access data using the metadata associated with clinical documents. The metadata associated with clinical documents is typically captured as part of clinical workflows. Examples of metadata include:

- type of the clinical documents (for e.g., Visit Summaries, Discharge Summaries, Operative Notes, History and Physical notes) used to record various clinical encounters,
- patient identifier information such as patient id or medical record number,
- metadata such as time of creation, modification time, practice type, and other ebRS/ebRIM based metadata as documented in IHE ITI TF-3: 4.2.3,
- there are no limitations on the types of the documents that can be accessed using Document Metadata. Some example document types include C-CDA, Referral Notes, Lab Reports, etc.

Data Element based DAF Queries access data using information that is part of the patient's clinical record. Information that is typically present within a patient's record includes:

- Patient Demographics information such as race, ethnicity, gender, age.
- Lab Results information
- Medications, Immunizations, Problems etc.

Granularity of data being returned in query results can be individual patient level data or aggregate population level data. Patient level data can be complete clinical documents such as C-CDA or it could be in the form of HL7 FHIR resources such as Problems, Medications. Standards such as C-CDA, HL7 FHIR resources, QRDA Category I and HL7 v2.5.1 message formats are used to encode individual patient level data. Population level data are summary information about the population that meets the query criteria. Population information could be number of patients that meet a criterion, percentage of patients that meet criteria, or de-identified patient list report. Standards such as QRDA Category III Report, conceptual QRDA Category II Report, and HL7 FHIR resources are used to encode population level data.

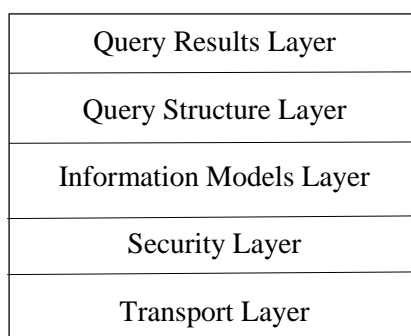


Figure 16 DAF Query Stack

DAF identifies five building blocks for technical implementation called DAF Query Stack (see Figure 16). Transport Layer defines the standards and specifications used to transport queries and query results. An example standard would be HTTP. Transport Layer also identifies the standards used to package the queries and query results along with the necessary metadata. These standards typically bridge the generic transport standards like HTTP to specific domains like healthcare. An example standard would be SOAP 1.2 which is used to bridge HTTP and the healthcare specific queries. Security Layer is used to specify standards for various security aspects including authentication, access control and authorization, message integrity, confidentiality, auditing, disclosure requirements, consent, security metadata for Query and Query Results to enable any of the above security functions. Information Models Layer is used to specify the information models and the corresponding data definitions that are used to define the queries and the query results. Query Structure Layer is used to specify the standards, vocabularies and value sets that will be used to construct queries. Query Results Layer is used to specify the standards, vocabularies and value sets that will be used to construct query results.

DAF used a modular approach to define the query stack. The standards defined by each layer of the query stack need to be independent of the other layers. For example, if the query structure uses eBRIM/ebXML based standards and query results uses C-CDA document standards, changes to standards in either layer should have minimal to no-effect on each other and similarly should have minimal effect on the transport and security standards selected. This modular capability of the query stack will allow for evolution of DAF use cases in a flexible manner, whereby a new DAF use case can prescribe new standards for query structures while reusing the standards for security, transport and query results.

In Phase 1 and 2 for patient care, DAF adopted IHE standards for Document Metadata based Queries and HL7 FHIR for Data Element based Queries.

5.4.4.1 DAF Document Metadata Based Access Implementation Guide

IHE PCC published The Data Access Framework (DAF) Document Metadata Based Access Implementation Guide in September 2015 [IHE DAF]. This US National Extension provides requirements and guidance on accessing clinical documents created during clinical workflows. The guide accomplishes this using RESTful resources based on HL7 FHIR and the more traditional SOAP based IHE Profiles. The IG specifies two Query Stacks for Document Metadata based access to data: the SOAP Query Stack and the RESTful Query Stack. The SOAP Query Stack uses:

- HTTP as the transport protocol
- SOAP 1.2 as the packaging/envelope specification
- TLS for message integrity and confidentiality
- XUA (SAML) for access control
- ATNA for audit logging
- BPPC/DS4P for consent
- XCA for Patient Level Query Structure
- MPQ for Population Level Query Structure
- C-CDA for Query Results
- XCPD for discovery of patient identifiers based on patient demographics
- PIX/PDQv3 for patient demographic information model

The RESTful Query Stack uses:

- HTTP as the transport protocol
- HTTP Message Structure as the packaging/envelope specification
- TLS for message integrity and confidentiality
- IUA and FHIR Tags for access control

- ATNA and FHIR Security Event for audit logging
- FHIR Consent Resource/DS4P for consent
- MHDv2 for Patient Level Query Structure
- C-CDA for Patient Level Query Results
- PDQm for discovery of patient identifiers based on patient demographics
- PIX/PDQv3 for patient demographic information model

5.4.4.2 DAF FHIR Implementation Guide

DAF uses existing IHE profiles XCA, XCPD and MHDv2 to standardize access to documents such as a CCD, History and Physical Notes etc. while HL7 FHIR is leveraged to access granular information such as problem lists, medications and patient demographics. DAF FHIR IG 1.0 was published as part of FHIR DSTU2 in September 2015 [FHIR DAF]. This US realm implementation guide provides guidance on the use of FHIR profiles to access discrete data elements identified in the ONC 2014 Edition Standards and Certification Criteria (S&CC) related to Meaningful Use Stage 2 (MU2) [ONC MU2]. The DAF Query Stack on FHIR uses FHIR RESTful API based on HTTP protocol along with FHIR data types, FHIR search and both xml and JSON FHIR Resource Formats. DAF profiles were created for each ONC 2014 edition S&CC conceptual data element. Table 4 provides a top-level mapping of the ONC 2014 edition S&CC conceptual data elements to the corresponding DAF Resource profile along with the identification of the base FHIR resource.

Table 4 Meaningful Use Data Element Mapping

Meaningful Use conceptual data element	DAF profile	FHIR Resource
Medication allergies	DAF-AllergyIntolerance	AllergyIntolerance
Laboratory Order(s)	DAF-DiagnosticOrder	DiagnosticOrder
Laboratory Test(s)	DAF-DiagnosticReport	DiagnosticReport
Encounter Diagnoses	DAF-Encounter	Encounter
Family Health History	DAF-FamilyMemberHistory	FamilyMemberHistory
Immunizations	DAF-Immunization	Immunization
Laboratory Result Value(s)	DAF-Results	Observation
Medications	DAF profiles for medications: DAF-Medication DAF-MedicationStatement DAF-MedicationAdministration DAF-MedicationDispense DAF-MedicationOrder	Medication MedicationStatement MedicationAdministration MedicationDispense MedicationOrder
Patient name Sex Date of Birth Race Ethnicity Preferred Language	DAF-Patient	Patient
Problems	DAF-Condition (Problem)	Condition
Procedures	DAF-Procedure	Procedure
Smoking status	DAF-SmokingStatus	Observation

Meaningful Use conceptual data element	DAF profile	FHIR Resource
Vital Signs (Height, weight, BP, BMI)	DAF-VitalSigns	Observation
MedicationAllergies list Problem list Medication List Immunizations Encounters Laboratory Result Values Procedure List	DAF List: DAF-AllergyList DAF-ProblemList DAF-MedicationList DAF-ImmunizationList DAF-EncounterList DAF-ResultsList DAF-ProcedureList	List
	DAF Supporting Profiles: DAF-Organization DAF-Location DAF-Practitioner DAF-Substance DAF-RelatedPerson DAF-Specimen	Organization Location Practitioner Substance RelatedPerson Specimen

6 SECURITY AND PRIVACY

6.1 Introduction

C3-Cloud components will need to enable access and processing of patient specific clinical data for facilitating personalized clinical care plan development, execution and monitoring by a team of multidisciplinary professionals, when needed across care sites. Hence ensuring security and privacy of the clinical data being accessed and processed by these tools is essential. In response to this need, C3-Cloud project will provide the necessary authentication, authorization and audit services. While doing so, we will build on widely accepted international standards. In the following sections a survey of existing security and privacy standards are presented.

6.2 Related standards

The current section describes important standards related to the security and privacy in the context of management of clinical data and electronic health systems.

6.2.1 OASIS security and privacy standards

This section is devoted to OASIS security and privacy standards, which can be used in the C3-Cloud project. These standards are:

- to exchange user attributes (authorized identity, role, purpose):
 - Security Assertion Markup Language (SAML)
 - Cross-Enterprise Security and Privacy Authorization (XSPA) Profile of SAML
- to define Access Control Policies, and Access Control Request/Responses:
 - eXtensible Access Control Markup Language (XACML)
 - Cross-Enterprise Security and Privacy Authorization (XSPA) Profile of XACML
- to pass Access Control Request/Responses through a standard protocol:
 - SAML XACML Profile

6.2.1.1 OASIS Security Assertion Markup Language (SAML)

The Security Assertion Markup Language (SAML) defines the syntax and processing semantics of assertions made about a subject by a system entity. SAML version 2.0 was approved as an OASIS Standard in March 2005 [SAML]. SAML is an XML-based framework for communicating user authentication, entitlement, and attribute information. It allows business entities to make assertions regarding the identity, attributes, and entitlements of a subject (an entity that is often a human user) to other entities, such as a partner company or another enterprise application. The main drivers behind the adoption of the SAML standard are single sign-on, federated identity and being applicable in Web services and other industry standards.

SAML consists of building-block components that together allow a number of use cases to be supported. The core SAML specification defines the structure and content of both *assertions* and *protocol* messages used to transfer authentication, attribute, and entitlement information. SAML assertions carry statements about a principal that an asserting party claims to be true. The valid structure and contents of an assertion are defined by the SAML assertion XML schema. SAML protocol messages are used to make the SAML-defined requests and return appropriate responses. Similarly, the structure and contents of these messages are defined by the SAML-defined protocol XML schema.

The means by which lower-level communication or messaging protocols (such as HTTP or SOAP) are used to transport SAML protocol messages between participants is defined by the SAML *bindings*. Finally, SAML *profiles* are defined to satisfy a particular business use case, for example the Web Browser single sign-on (SSO) profile. Profiles typically define constraints on the contents of SAML assertions, protocols, and bindings in order to solve the business use case in an interoperable fashion. The relationship between these basic SAML concepts is provided in the following figure.

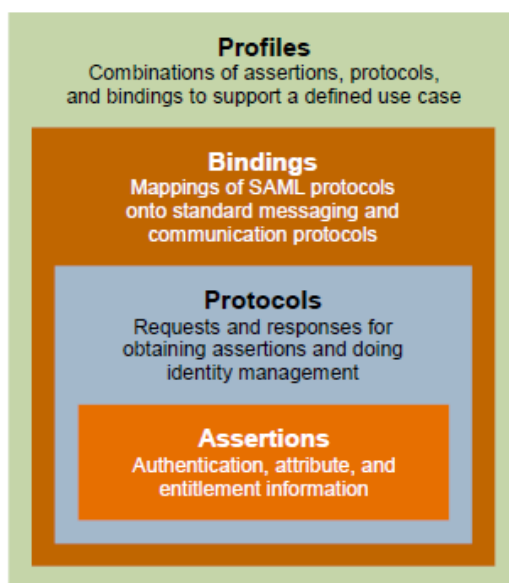


Figure 17 Basic SAML concepts [SAML-TO]

Now, some further details and examples regarding these basic SAML concepts will be provided. SAML defines three kinds of statements that can be carried within an *assertion*:

- **Authentication statements:** These are created by the party that successfully authenticated a user. At a minimum, they describe the particular means used to authenticate the user and the specific time at which the authentication took place.
- **Attribute statements:** These contain specific identifying attributes about the subject (for example, that user “John Doe” has “Gold” card status).
- **Authorization decision statements:** These define something that the subject is entitled to do (for example, whether “John Doe” is permitted to buy a specified item).

SAML defines a number of generalized request/response *protocols*, some of which are presented below:

- **Authentication Request Protocol:** Defines a means by which a principal can request assertions containing authentication statements and, optionally, attribute statements.
- **Single Logout Protocol:** Defines a mechanism to allow near-simultaneous logout of active sessions associated with a principal.
- **Assertion Query and Request Protocol:** Defines a set of queries by which SAML assertions may be obtained.

SAML *bindings* detail exactly how the various SAML protocol messages can be carried over underlying transport protocols. Some example bindings defined by SAML 2.0 are:

- **HTTP Redirect Binding:** Defines how SAML protocol messages can be transported using HTTP redirect messages (302 status code responses).
- **HTTP POST Binding:** Defines how SAML protocol messages can be transported within the base64-encoded content of an HTML form control.
- **SAML SOAP Binding:** Defines how SAML protocol messages are transported within SOAP 1.1 messages, with details about using SOAP over HTTP.

Finally, SAML *profiles* define how the SAML assertions, protocols, and bindings are combined and constrained to provide greater interoperability in particular usage scenarios. Some example profiles defined by SAML 2.0 are:

- **Web Browser SSO Profile:** Defines how SAML entities use the Authentication Request Protocol and SAML Response messages and assertions to achieve single sign-on with standard Web browsers. It defines how the messages are used in combination with the HTTP Redirect, HTTP POST, and HTTP Artifact bindings.
- **Single Logout Profile:** Defines how the SAML Single Logout Protocol can be used with SOAP, HTTP Redirect, HTTP POST, and HTTP Artifact bindings.
- **Assertion Query/Request Profile:** Defines how SAML entities can use the SAML Query and Request Protocol to obtain SAML assertions over a synchronous binding, such as SOAP.

6.2.1.2 OASIS eXtensible Access Control Markup Language (XACML)

eXtensible Access Control Markup Language (XACML) [XACML] is an XML-based language for access control that has been standardized in OASIS. XACML describes both an access control policy language and a request/response language. The policy language is used to express access control policies (**Who** can access **what**, under what **conditions**, and for what **purpose**). The request/response language expresses queries about whether a particular access should be allowed (requests) and describes answers to those queries (responses). The latest approved version of XACML is 2.0; work is in progress for version 3.0.

XACML defines some major roles as presented in the following basic data-flow diagram. It should be noted that some of the data-flows represented in the diagram may be facilitated by a repository, and XACML does not prescribe a particular communication protocol for any of the data flows.

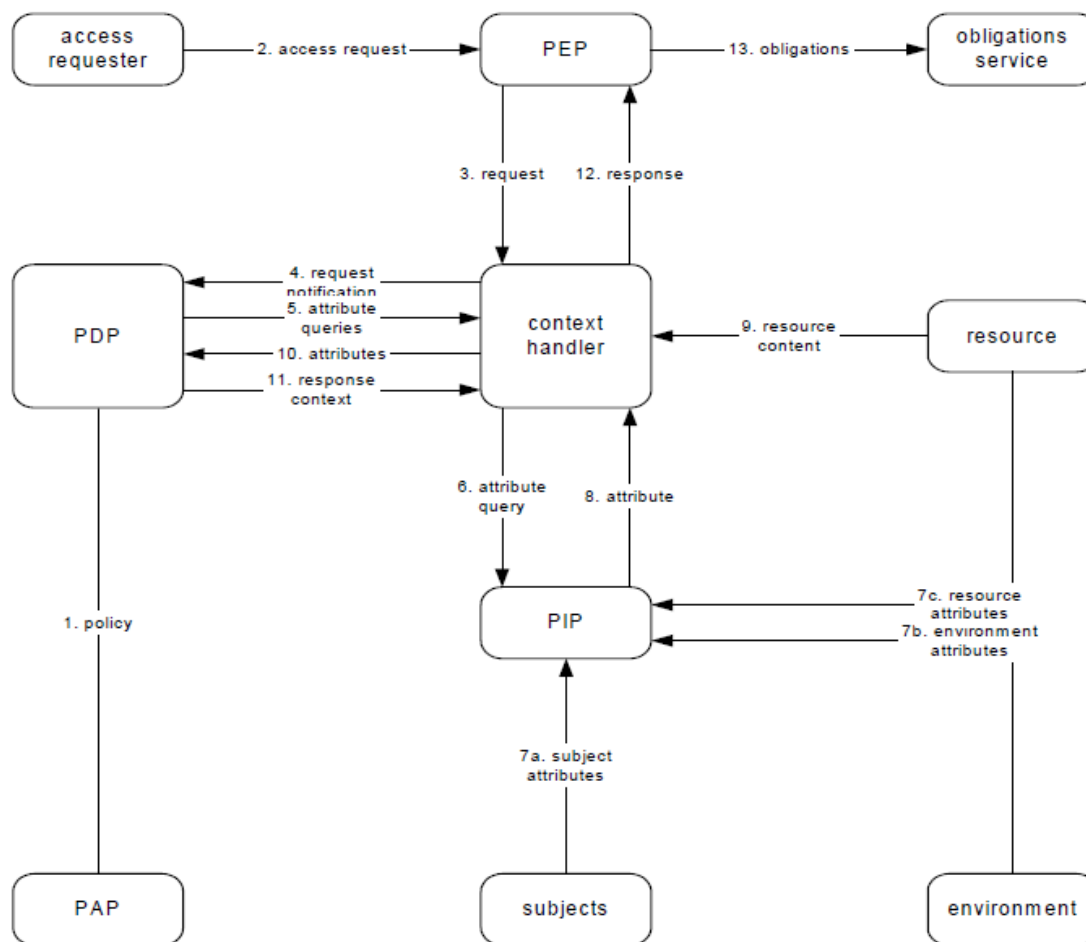
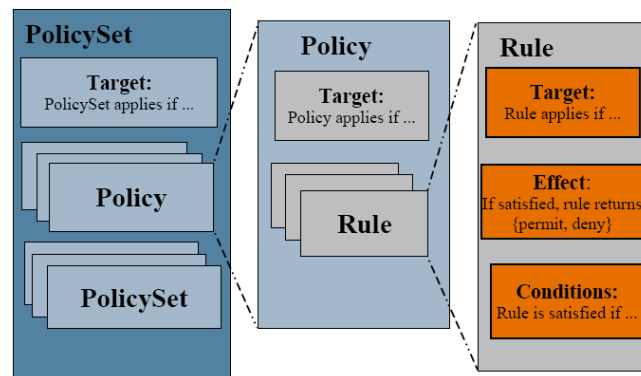


Figure 18 XACML Data-flow Diagram [XACM-Core]

Policy Enforcement Point (PEP) is responsible for protecting access to one or more resources. When a resource access is attempted, the PEP sends a description of the attempted access to a *Policy Decision Point (PDP)* in the form of an authorization decision request. PEP may obtain attributes from on-line Attribute Authorities (AA) or from Attribute Repositories into which AAs have stored attributes. The PDP evaluates this request against its available policies and attributes and produces an authorization decision that is returned to the PEP. The PEP is responsible for enforcing the decision. The Policy Administration Point (PAP) basically administers and maintains the policies. The Policy Information Point (PIP) facilitates the PDP in acquiring any additional security attributes of resources and subjects in order to determine whether an access request is to be granted or denied.

XACML Policy language model

XACML defines three top-level policy elements: `<Rule>`, `<Policy>` and `<PolicySet>`. The `<Rule>` element contains a Boolean expression that can be evaluated in isolation, but that is not intended to be accessed in isolation by a PDP. So, it is not intended to form the basis of an authorization decision by itself. It is intended to exist in isolation only within an XACML PAP, where it may form the basic unit of management, and be re-used in multiple policies. The `<Policy>` element contains a set of `<Rule>` elements and a specified procedure for combining the results of their evaluation. It is the basic unit of policy used by the PDP, and so it is intended to form the basis of an authorization decision. The `<PolicySet>` element contains a set of `<Policy>` or other `<PolicySet>` elements and a specified procedure for combining the results of their evaluation. It is the standard means for combining separate policies into a single combined policy.



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Figure 19 XACML Basic Policy Structure

The policy language model as a plain class diagram is presented in the next figure.

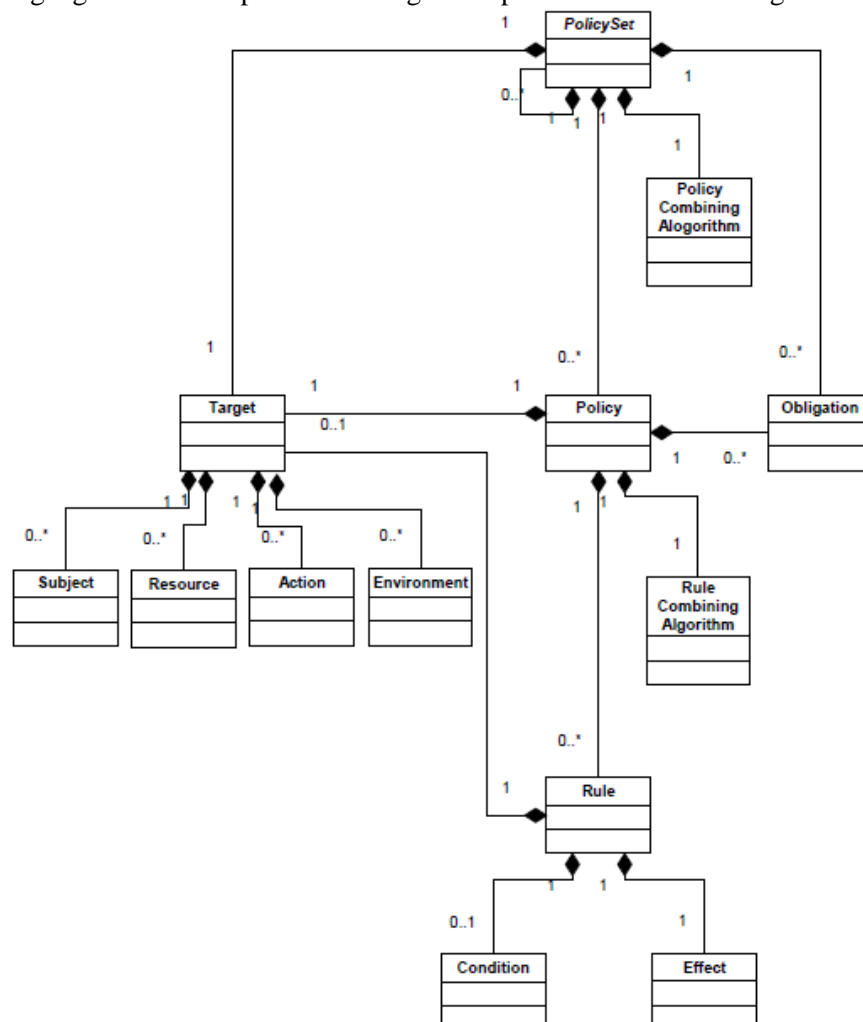


Figure 20 XACML Policy Language Model [XACML-Core]

Rule:

A **rule** is the most elementary unit of **policy**. It may exist in isolation only within one of the major actors of the XACML domain. In order to exchange rules between major actors, they must be

encapsulated in a policy. A rule can be evaluated on the basis of its contents. The main components of a rule are:

- a target,
- an *effect* and
- a condition.

The *target* defines the set of *resources*, *subjects*, *actions* and *environment* to which the rule is intended to apply. The *effect* of the rule indicates the rule-writer's intended consequence of a "True" evaluation for the rule. Two values are allowed: "Permit" and "Deny". *Condition* represents a Boolean expression that refines the applicability of the rule beyond the predicates implied by its target. Therefore, it may be absent.

Policy:

As it can be seen from the data-flow model, rules are not exchanged amongst system entities. Therefore, a PAP combines rules in a *policy*. A policy comprises four main components:

- a target;
- a rule-combining algorithm-identifier;
- a set of *rules*; and
- obligations.

Policy set:

Policy set has a very similar structure with the policy; instead of links with the rules, it has links to policies:

- a target;
- a policy-combining algorithm-identifier;
- a set of *policies*; and
- obligations.

XACML Request/Response Example

In this sub-section, an example XACML policy, and request and response examples related with this policy are presented. First, the sample policy is presented below:

```
<PolicySet xsi:schemaLocation="urn:oasis:names:tc:xacml:2.0:policy:schema:os
http://docs.oasis-open.org/xacml/access_control-xacml-2.0-policy-schema-os.xsd"
PolicySetId="A67E444C-5C74-7ABB-5CF6-86387ED40DBC"
PolicyCombiningAlgId="urn:oasis:names:tc:xacml:1.0:policy-combining-algorithm:deny-overrides"
xmlns="urn:oasis:names:tc:xacml:2.0:policy:schema:os"
xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <Description>Doctor Consent Document</Description>
  <Target/>
  <Policy PolicyId="12345678hnnvsad" RuleCombiningAlgId="urn:oasis:names:tc:xacml:1.0:rule-
combining-algorithm:permit-overrides">
    <Description>Doctors can update my hospital visits and operations</Description>
    <Target>
      <Subjects>
        <Subject>
          <SubjectMatch MatchId="urn:oasis:names:tc:xacml:1.0:function:string-equal">
            <AttributeValue
DataType="http://www.w3.org/2001/XMLSchema#string">ROLECODE:DOCTOR</AttributeValue>
            <SubjectAttributeDesignator
AttributeId="urn:oasis:names:tc:xacml:1.0:subject:subject-id"
DataType="http://www.w3.org/2001/XMLSchema#string"/>
          </SubjectMatch>
        </Subject>
      </Subjects>
      <Resources>
        <Resource>
          <ResourceMatch MatchId="urn:oasis:names:tc:xacml:1.0:function:string-equal">
```

```

        <AttributeValue
DataType="http://www.w3.org/2001/XMLSchema#string">RESOURCECODE:HOSPITALVISIT</AttributeValue>
        <ResourceAttributeDesignator
AttributeId="urn:oasis:names:tc:xacml:1.0:resource:resource-id"
DataType="http://www.w3.org/2001/XMLSchema#string"/>
        </ResourceMatch>
    </Resource>
    <Resource>
        <ResourceMatch MatchId="urn:oasis:names:tc:xacml:1.0:function:string-equal">
            <AttributeValue
DataType="http://www.w3.org/2001/XMLSchema#string">RESOURCECODE:OPERATION</AttributeValue>
            <ResourceAttributeDesignator
AttributeId="urn:oasis:names:tc:xacml:1.0:resource:resource-id"
DataType="http://www.w3.org/2001/XMLSchema#string"/>
            </ResourceMatch>
        </Resource>
    </Resources>
    <Actions>
        <Action>
            <ActionMatch MatchId="urn:oasis:names:tc:xacml:1.0:function:string-equal">
                <AttributeValue
DataType="http://www.w3.org/2001/XMLSchema#string">READ</AttributeValue>
                <ActionAttributeDesignator
AttributeId="urn:oasis:names:tc:xacml:1.0:action:action-id"
DataType="http://www.w3.org/2001/XMLSchema#string"/>
                </ActionMatch>
            </Action>
            <Action>
                <ActionMatch MatchId="urn:oasis:names:tc:xacml:1.0:function:string-equal">
                    <AttributeValue
DataType="http://www.w3.org/2001/XMLSchema#string">UPDATE</AttributeValue>
                    <ActionAttributeDesignator
AttributeId="urn:oasis:names:tc:xacml:1.0:action:action-id"
DataType="http://www.w3.org/2001/XMLSchema#string"/>
                    </ActionMatch>
                </Action>
            </Actions>
        </Target>
        <Rule RuleId="12345678hnvdsad:rule1" Effect="Permit"/>
    </Policy>
</PolicySet>

```

Figure 21 Sample XACML Policy

This example is related with a health care scenario, in which a consent document is defined as an XACML policy, and access decisions are taken according to this consent document. Below, first the structure of the XACML request, and then an example XACML request are provided.



Figure 22 XACML Request Structure

```

<?xml version="1.0" encoding="UTF-8"?>
<Request xmlns="urn:oasis:names:tc:xacm:2.0:context:schema:os"
xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
xsi:schemaLocation="urn:oasis:names:tc:xacml:2.0:context:schema:os http://docs.oasis-
open.org/xacml/access_control-xacml-2.0-context-schema-os.xsd">
    <Subject>

```

```

        <Attribute AttributeId="urn:oasis:names:tc:xacml:1.0:subject:subject-id"
DataType="http://www.w3.org/2001/XMLSchema#string">
        <AttributeValue>
        ROLECODE:DENTIST
    </AttributeValue>
    </Attribute>
</Subject>
<Resource>
    <Attribute AttributeId="urn:oasis:names:tc:xacml:1.0:resource:resource-id"
DataType="http://www.w3.org/2001/XMLSchema#string">
        <AttributeValue>
        RESOURCECODE:CONDITION
    </AttributeValue>
    </Attribute>
</Resource>
<Action>
    <Attribute AttributeId="urn:oasis:names:tc:xacml:1.0:action:action-id"
DataType="http://www.w3.org/2001/XMLSchema#string">
        <AttributeValue>
        UPDATE
    </AttributeValue>
    </Attribute>
</Action>
<Environment/>
</Request>

```

Figure 23 Sample XACML Request

In this sample XACML request, a subject with "ROLECODE:DENTIST" is trying to get permission for "UPDATE" action on resource with "RESOURCECODE:CONDITION". In other words, a dentist is willing to update health care conditions (i.e. diagnoses) of a patient. However, as it is clear in the corresponding policy document (i.e. the consent), only "ROLECODE:DOCTOR" is permitted to "READ" and "UPDATE" "RESOURCECODE:HOSPITALVISIT"s and "RESOURCECODE:OPERATION"s of a patient.

Below, related with this situation, first the XACML response structure, and then the sample XACML response that corresponds to our example policy and request are provided.



Figure 24 XACML Response Structure

```

<Response>
    <Result>
        <Decision>Deny</Decision>
        <Status>
            <StatusCode Value="urn:oasis:names:tc:xacml:1.0:status:ok" />
        </Status>
    </Result>
</Response>

```

Figure 25 Sample XACML Response

As expected, the response is negative; i.e. "Deny". Other values for the decision attribute can be Permit, Not Applicable and Indeterminate.

6.2.1.3 XACML Security Assertion Markup Language (SAML) Profile

XACML itself defines the content of some of the messages necessary to implement this model, but deliberately confines its scope to the language elements used directly by the PDP and does not define protocols or transport mechanisms. Full implementation of the usage model depends on use of other standards to specify assertions, protocols, and transport mechanisms. XACML also does not specify how to implement a Policy Enforcement Point, Policy Administration Point, Attribute Authority, Context Handler, or repository, but XACML can serve as a standard format for exchanging information with these entities when combined with other standards.

One standard suitable for providing the assertion and protocol mechanisms needed by XACML is the OASIS Security Assertion Markup Language (SAML), Version 2.0. Hence, XACML SAML Profile [XAML-SAMLProfile] defines how to use SAML 2.0 to protect, transport, and request XACML schema instances and other information needed by an XACML implementation. There are also other XACML profiles such as Core and hierarchical role based access control (RBAC) profile and Privacy policy profile of XACML v2.0; however these are not presented in this document.

There are 6 types of queries and statements used in the SAML 2.0 profile of XACML v2.0:

- AttributeQuery – A standard SAML Request used for requesting one or more attributes from an Attribute Authority.
- AttributeStatement – A standard SAML Statement that contains one or more attributes. This statement may be used in a SAML Response from an Attribute Authority, or it may be used in a SAML Assertion as a format for storing attributes in an Attribute Repository.
- XACMLPolicyQuery – A SAML Request extension, defined in this profile. It is used for requesting one or more policies from a Policy Administration Point.
- XACMLPolicyStatement – A SAML Statement extension, defined in this profile. It may be used in a SAML Response from a Policy Administration Point, or it may be used in a SAML Assertion as a format for storing policies in a Policy Repository.
- XACMLAuthzDecisionQuery – A SAML Request extension, defined in this profile. It is used by a PEP to request an authorization decision from an XACML PDP.
- XACMLAuthzDecisionStatement – A SAML Statement extension, defined in this profile. It may be used in a SAML Response from an XACML PDP. It might also be used in a SAML Assertion that is used as a credential, but this is not part of the currently defined XACML use model.

The following diagram illustrates the XACML use model and the messages that are used to communicate between the various components. Not all components are necessary to be used in every implementation.

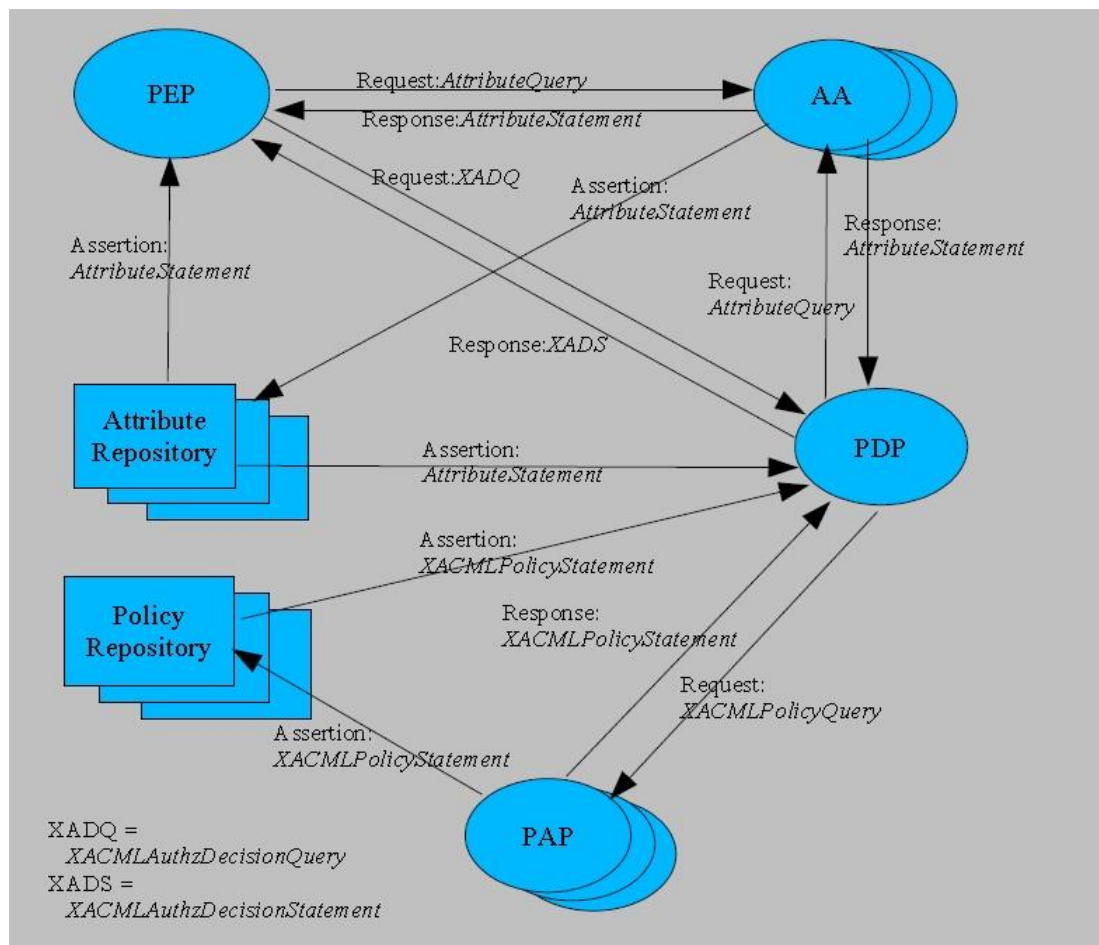


Figure 26 Use of XACML and SAML together [XACML-SAMLProfile]

6.2.1.4 OASIS Cross-Enterprise Security and Privacy Authorization (XSPA) Profile of SAML

The XSPA profile of SAML describes the minimum vocabulary necessary to provide access control over resources and functionality within and between healthcare information technology (IT) systems [XSPA-SAML].

The following figure displays an overview of interactions between parties in the exchange of healthcare information. The XSPA profile of SAML supports sending all requests through an Access Control Service (ACS). The Access Control Service on the Service User side receives the Service User request and responds with a SAML assertion containing user authorizations and attributes. To perform its function, the ACS collects all the attributes (e.g. organization-id, structural role, functional role, purpose of use, requested resource, and actions) necessary to create the Service User requested assertion. The Service Provider ACS is responsible for the parsing of assertions, evaluating the assertions against the security and privacy policy, and making and enforcing a decision on behalf of the Service Provider. The XSPA profile of SAML actually defines the semantics of the Service Request, Identity Assertion and Authorization Attributes that are seen in the figure below.

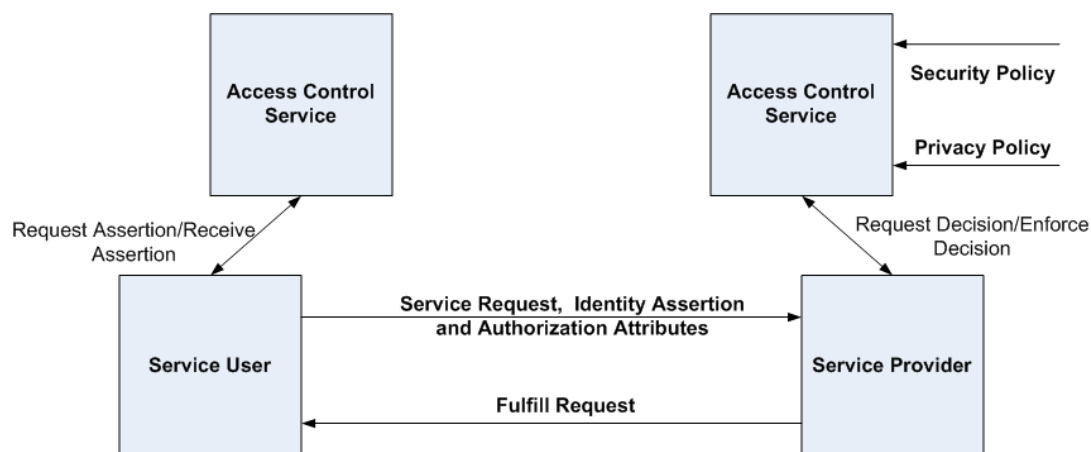


Figure 27 Interaction between parties in healthcare information exchange [XSPA-SAML]

The attributes that are defined by the XSPA profile of SAML are as follows:

1. Name
2. National Provider Identifier (NPI) – (optional)
3. Organization
4. Organization-ID
5. Structural Role

The allowed values are defined in “Healthcare Personnel that Warrant Differing Levels of Access Control” of ASTM 1986-98 (2005) Standard Guide for Information Access Privileges to Health Information
6. Functional Role
7. Permission (optional)
8. Action

The following HL7 RBAC Permission Catalog Actions are allowed: Append, Create, Delete, Read, Update, Execute
9. Execute (optional)
10. Object

HL7 RBAC Permission Catalog is specified as the object vocabulary
11. Purpose of Use (POU)

A value set defined; the allowed values are: TREATMENT, PAYMENT, OPERATIONS, EMERGENCY, SYSADMIN, RESEARCH, MARKETING, REQUEST, PUBLICHEALTH
12. Resource

HL7 RBAC Permission Catalog is specified as the resource vocabulary

6.2.1.5 OASIS Cross-Enterprise Security and Privacy Authorization (XSPA) Profile of XACML

The Cross-Enterprise Security and Privacy Authorization (XSPA) profile of XACML [XSPA-XACML] describes several mechanisms to authenticate, administer, and enforce authorization policies controlling access to protected information residing within or across enterprise boundaries. The policies being administered and enforced relate to security, privacy, and consent directives. This profile may be used in coordination with additional standards including Web Services Trust Language (WS-Trust) and Security Assertion Markup Language (SAML).

This profile specifies the use of XACML 2.0 to promote interoperability within the healthcare community by providing common semantics and vocabularies for interoperable policy request/response, policy lifecycle, and policy enforcement.

Similarly with XSPA profile of SAML, the following figure provides an overview of interactions between parties in the exchange of healthcare information.

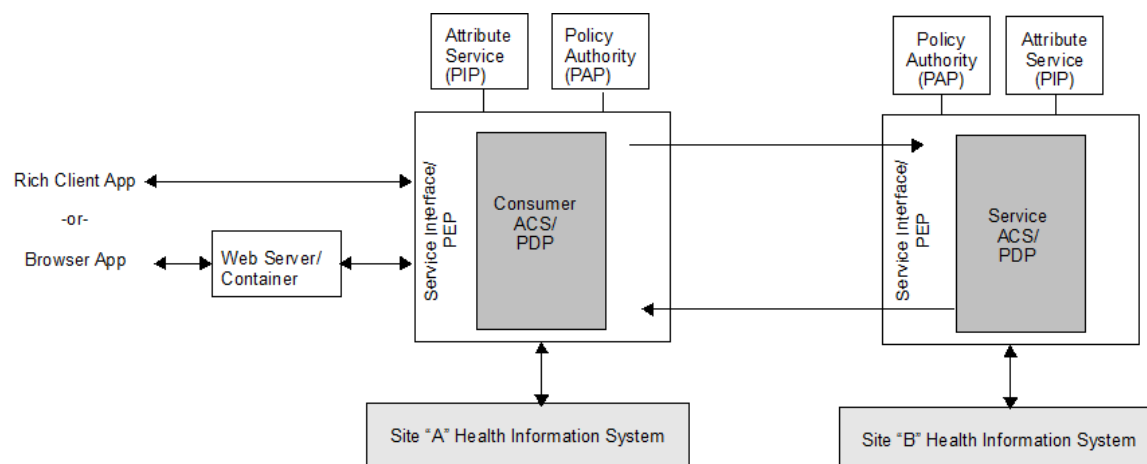


Figure 28 Interaction between parties in healthcare information exchange [XSPA-XACML]

With the help of XSPA profile for XACML, all XACML request and response attributes are identified by a Uniform Resource Name (URN) from its vocabulary. This enables seamless mapping of data values between the client interface and policy services. The normative attributes that are defined by this profile are provided in the table below:

Table 5 Normative attributes defined by XSPA profile of XACML

Attribute ID*	Identifier	Type	Valid Values
subject:subject-id	urn:oasis:names:tc:xacml:1.0:subject:subject-id	String	Is the name of the user as required by Health Insurance Portability and Accountability Act (HIPAA) Privacy Disclosure Accounting. The name will be typed as a string and in plain text.
subject:organization	urn:oasis:names:tc:xspa:1.0:subject:organization	String	Organization the requesting user belongs to as required by Health Insurance Portability and Accountability Act (HIPAA) Privacy Disclosure Accounting. The name will be typed as a string and in plain text.
subject:organization-id	urn:oasis:names:tc:xspa:1.0:subject:organization-id	anyURI	Unique identifier of the consuming organization and/or facility

Attribute ID*	Identifier	Type	Valid Values
subject:hl7:permission	urn:oasis:names:tc:xspa:1.0:subject:hl7:permission	String	Refer to [HL7-PERM] and its OID representation.
subject:role	urn:oasis:names:tc:xacml:2.0:subject:role	String	Structural Role refer to [ASTM E1986-98 (2005)] and its OID representation.
subject:purposeofuse	urn:oasis:names:tc:xspa:1.0:subject:purposeofuse	String	TREATMENT, PAYMENT, OPERATIONS, EMERGENCY, MARKETING, RESEARCH, REQUEST, PUBLICHEALTH
resource:resource-id	urn:oasis:names:tc:xacml:1.0:resource:resource-id	String	Unique identifier of the resource defined by and controlled by the servicing organization. In healthcare this is the patient unique identifier.
resource:hl7:type	urn:oasis:names:tc:xspa:1.0:resource:hl7:type	String	For minimum interoperability set of objects and supporting actions refer to [HL7-PERM] and their OID representations.
resource:org:permission	urn:oasis:names:tc:xspa:1.0:resource:org:hl7:permissions	String	Refer to [HL7-PERM] and its OID representation. This attribute holds permissions required by the servicing organization to grant access to a specific resource.
resource:org:role	urn:oasis:names:tc:xspa:1.0:resource:org:role	String	Structural Role refer to [ASTM E1986-98 (2005)] and its OID representation. This attribute holds roles required by the servicing organization to grant access to a specific resource.

Attribute ID*	Identifier	Type	Valid Values
resource:patient:confidentiality-code	urn:oasis:names:tc:xspa:1.0:resource:patient:hl7:confidentiality-code	String	Refer to [HL7-CONSENT] The default value for this attribute is N (normal operations.)
resource:hl7:dissenting-subject-id	urn:oasis:names:tc:xspa:1.0:resource:patient:dissenting-subject-id	String	US domain specific is National Provider issued by HHS/CMS and mandated by HIPAA.
resource:hl7:dissenting-role	urn:oasis:names:tc:xspa:1.0:resource:patient:dissenting-role	String	Structural Role refer to [ASTM E1986-98 (2005)] and its OID representation.
environment:locality	urn:oasis:names:tc:xspa:1.0:environment:locality	String	Unique identifier of the servicing organization.

6.2.2 IHE security and privacy profiles

In this section, the relevant integration profiles that are developed by Integrating the Healthcare Enterprise (IHE) for healthcare information security and privacy are presented. These integration profiles are:

- Enterprise User Authentication (EUA) Integration Profile
- Cross-Enterprise User Assertion (XUA) Integration Profile
- Audit Trail and Node Authentication (ATNA) Integration Profile
- Basic Patient Privacy Consents (BPPC) Integration Profile

6.2.2.1 IHE Enterprise User Authentication (EUA) Integration Profile

IHE Enterprise User Authentication Profile (EUA) defines a means to establish one name per user that can then be used on all of the devices and software that participate in this integration profile, within an enterprise [EUA]. EUA facilitates centralized user authentication management and provides users with the convenience and speed of a single sign-on. This profile leverages Kerberos (RFC 1510) and the HL7 CCOW standard, specifically the user subject. In brief, CCOW or Clinical Context Object Workgroup is an HL7 standard protocol designed to enable disparate applications to synchronize in real-time, and at the user-interface level. CCOW is the primary standard protocol in healthcare to facilitate "Context Management", which is the process of using particular "subjects" of interest (e.g., user, patient, clinical encounter, charge item, etc.) to 'virtually' link disparate applications so that the end-user sees them operate in a unified, cohesive way.

User authentication is a necessary step for most application and data access operations and it is a workflow improvement for the users. The IHE EUA Profile adds value to the CCOW specification for the user subject by specifying the user subject and CCOW user subject suffix. EUA profile does not address security features such as audit trails, access control, authorization management and PKI.

The most important property of EUA is that, the environment is assumed to be a single enterprise, governed by a single security policy and having a common network domain. On the other hand, health care information exchange necessitates cross-enterprise transactions in many use cases; hence the Cross-Enterprise User Assertion Profile (XUA) is proposed by the IHE as explained in the next section.

6.2.2.2 IHE Cross-Enterprise User Assertion (XUA) Integration Profile

In order to provide accountability in cross-enterprise transactions, there is a need to identify the requesting user in a way that enables the receiver to make access decisions and proper audit entries. The Cross-Enterprise User Assertion Profile (XUA) [XUA] provides a means to communicate claims about an authenticated principal (user, application, system...) in transactions that cross enterprise boundaries. The previous IHE profiles for an authenticated user identity (IHE Enterprise User Authentication Profile (EUA)) are not intended to function in cross-enterprise transactions. In a cross-enterprise environment, it is more likely that the transactions appear between two enterprises that maintain their own independent user directories. Hence, these type of transactions need the focus of Identity Federation standards.

The XUA Profile leverages Web-Services Security, SAML 2.0 Token Profile and the various profiles from W3C, and OASIS to support identity federation. XUA Profile is focused on Web service transactions, and specifies that when a Cross-Enterprise User Assertion is needed, these Web service transactions will additionally use the Web Services Security header with a SAML 2.0 Token containing the identity Assertion.

A very clear need on all use-cases is the recording of the user identity in security audit logs. The XUA profile does not define these auditable events; these are driven by other IHE transactions such as the Retrieve Document Set transaction. The method of authenticating the principal (user) and the method that the X-Service User Actor (e.g., XDS.b Document Consumer) uses to get the Identity Assertion are outside the scope of this profile.

There are principal (user) attributes that can be needed in the use-cases: Doctor, Patient, Guardian, Emergency-Access. The Identity Assertion can contain attributes about the principal (user). However, yet XUA does not identify what standards to use to represent these attributes and their values, so this is left to specific implementations that have defined a local vocabulary or vocabulary translation.

The actors and transactions involved in XUA Integration Profile are shown in the following figure. Actually, XUA defines only two actors: X-Service User and X-Service Provider, and one transaction: Provide X-User Assertion (ITI-40). The actors and transactions in dashed lines are the ancillary ones, whose specifications are not defined by this profile.

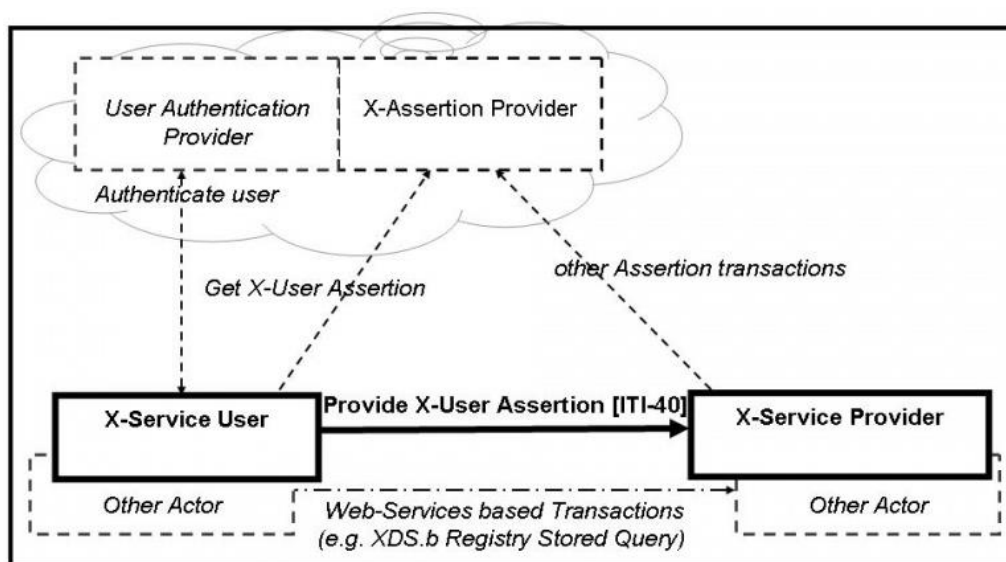


Figure 29 Cross-Enterprise User Assertion Actor Diagram [XUA]

6.2.2.3 XUA - Attribute Extension (XUA++)

XUA integration profile fills in a very important requirement by defining the actors and the main transaction for providing cross-enterprise user assertions. However, the problem with XUA is that, it has a very limited mandatory specification of attributes in ITI-40. In fact, it does not require any specific

attributes beyond the user identity that is used for audit logging. For this reason, Cross-Enterprise User Assertion – Attribute Extension (XUA++) extends the XUA profile with Options that will enable access controls on the service side [XUA++].

Basically, XUA++ facilitates the use of OASIS Cross-Enterprise Security and Privacy Authorization (XSPA) defined attributes and allowed vocabularies within XUA (for more details on XSPA, see the section on OASIS security and privacy mechanisms). The use cases of XUA++ come from current experience in the National Health Information Network (NHIN) in the USA, epSOS project in the EU, and other Health Information Exchanges globally.

Yet, XUA++ is not an approved IHE integration profile but it is a really important interoperability effort for those who are interested in implementing XUA.

6.2.2.4 IHE Audit Trail and Node Authentication (ATNA) Integration Profile

The Audit Trail and Node Authentication (ATNA) Integration Profile establishes security measures which, together with the security policy and procedures, provide patient information confidentiality, data integrity and user accountability [ATNA]. This environment is considered the Security Domain and can scale from a department, to enterprise or cross-border Affinity Domain. The ATNA model considers that within the secure domain the following is true:

- All machines are host authenticated. This authentication identifies the machine as being one that is known to the security system of the organization, with known security characteristics.
- The host identification is used to determine what (if any) access should be granted to automated processes on that host, and/or persons under the direction of that host's access controls.
- The secure node is responsible for providing reasonable access controls.
- The secure node is also responsible for providing security audit logging to track security events.

Basically, ATNA Integration Profile defines the Secure Node actor, which is to be grouped with any IHE Actor according to the user requirements, and 2 transactions: Authenticate Node (ITI-19) and Record Audit Event (ITI-20). It also benefits from the Maintain Time (ITI-1) transaction for consistent time handling. The relationship among these actors and transactions is presented in the following figure.

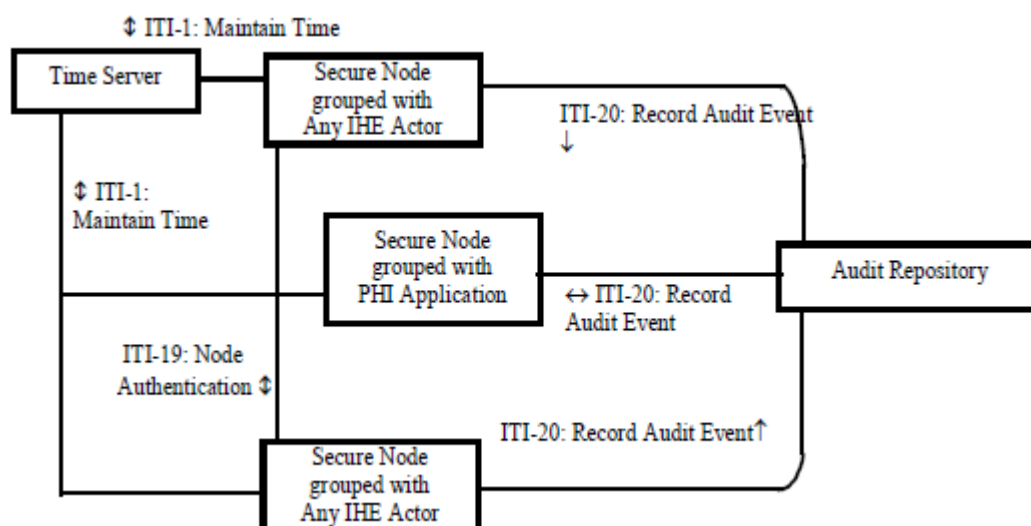


Figure 30 ATNA Actors and Transactions [ATNA]

The Secure Node Actor shall include:

- The Authenticate Node (ITI-19) transaction for all network connections that may expose private information.

- All local user activity (login, logout, etc.) protected to ensure only authorized users.
- The Record Audit Event (ITI-20) transaction.

In the following figure, the flow of an example scenario that shows access of an authorized node (Image Display Actor grouped with ATNA Secure Node Actor) to personal health information (i.e. images in this case) is provided. The steps that take place are as follows:

- Time synchronization occurs independently. These transactions may take place at any time. Correct time is needed to generate Audit Records with a correct timestamp.
- A user logs on to Image Display/Secure Node actor. The user enters valid credentials and is authorized to access the node.
- The node generates audit records.
- The user wants to query/retrieve and view some images. Before image transactions can take place, an authentication process between the Image Display/Secure Node actor and the Image Manager/Image Archive/Secure Node actor takes place.
- Following node authentication, the node initiates the query/retrieve transactions.
- The node generates audit records.

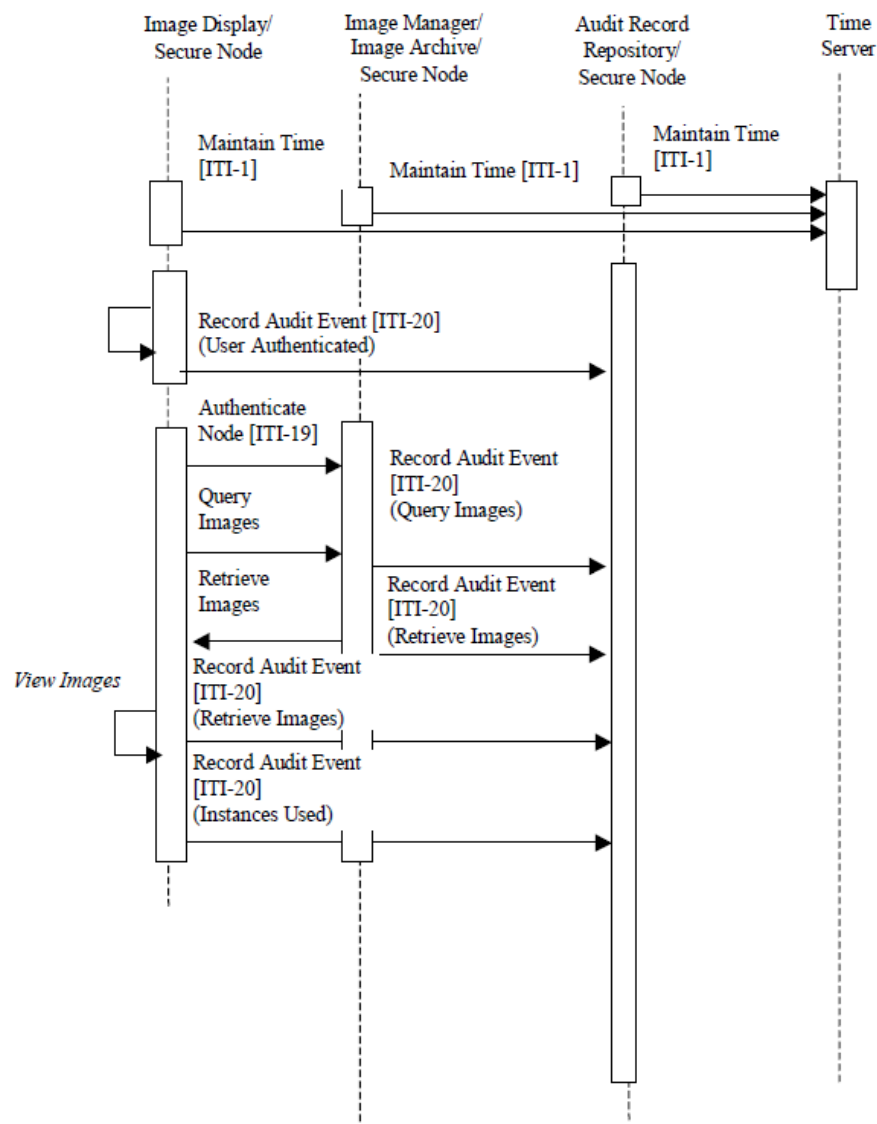


Figure 31 Authorized Node Process Flow [ATNA]

Similarly, the following figure shows an example unauthorized node process flow. First time an unauthorized node tries to access the Lab Automation Manager/Secure Node actor, it fails since no authentication takes place; i.e. the unauthorized node does not provide a certificate. In the second transaction of this scenario, this time it fails since the Lab Automation Manager/Secure Node does not trust the certificate presented. It should be noted that in each case, an audit record is generated and sent to the Audit Record Repository/Secure Node Actor.

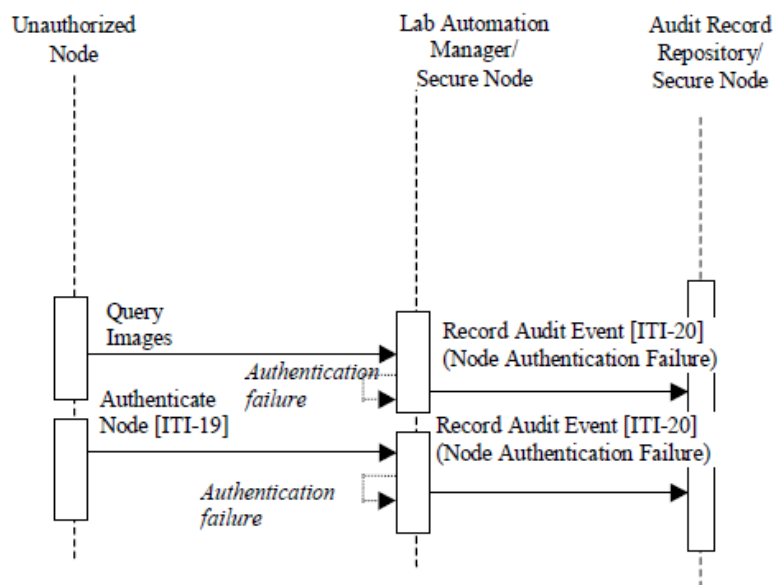


Figure 32 Unauthorized Node Process Flow [ATNA]

Finally, an example unauthorized user process flow is presented in the following figure. In this example, an unauthorized user tries to authenticate himself with the ECG Display/Secure Node actor, but this fails since the user name and password provided by the user are not valid. An audit record is generated and sent to the Audit Record Repository/Secure Node Actor for this failure.

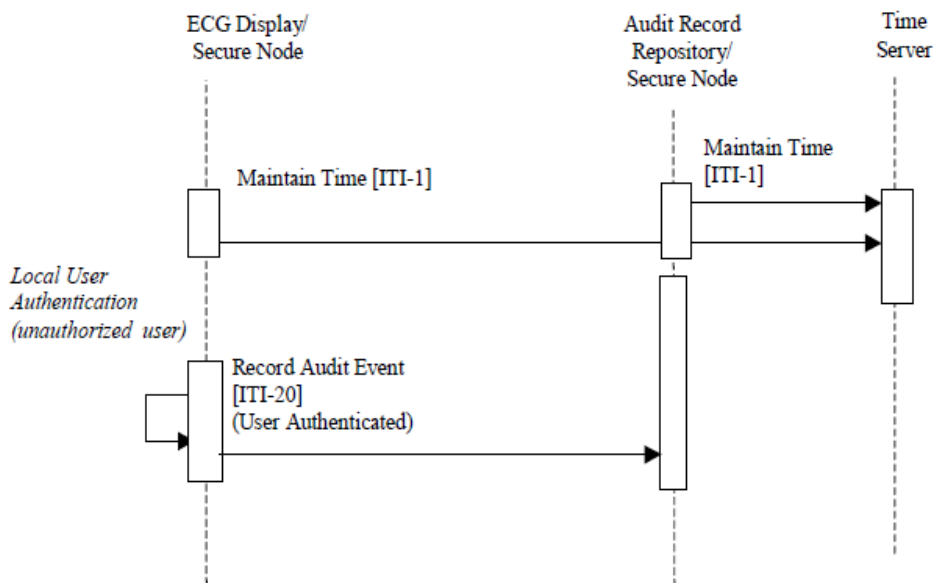


Figure 33 Unauthorized User Process Flow [ATNA]

Below, some further details and specifications of the Authenticate Node (ITI-19) and Record Audit Event (ITI-20) transactions are presented.

Authenticate Node (ITI-19)

- When Authenticating the Remote Secure Node, the Local Secure Node:
- Shall be able to perform certificate validation based on signature by a trusted certificate authority (CA) and
- Shall be able to perform direct certificate validation to a set of trusted certificates
- The certificates used for mutual authentication shall be X509 certificates based on RSA key with key length in the range of 1024-4096, where the key length chosen is based on local site policy.
- Maximum expiration time acceptable for certificates should be defined in the applicable security policy. The IHE Technical Framework recommends a maximum expiration time of 2 years.
- The method used to determine whether a node is authorized to perform transactions is not specified. This may be use of a set of trusted certificates, based on some attribute value contained in the certificates, access control lists, or some other method. Using a certificate chain back to an external trusted certificate authority to determine authorizations is strongly discouraged.
- When configured for use on a physically secured network, the normal connection mechanisms may be used in connections carrying protected information.
- When configured for use not on a physically secured network, implementations shall use the Transport Layer Security (TLS) 1.0 (RFC 2246) protocol, and the following cyphersuite shall be supported: TLS_RSA_WITH_AES_128_CBC_SHA.

Record Audit Event (ITI-20)

- ATNA profile defines two transport mechanisms for the audit messages:
- Transmission of Syslog Messages over TLS (RFC5425) with The Syslog Protocol (RFC5424)
- Transport utilizing the Transmission of Syslog Messages over UDP (RFC5426) with The Syslog Protocol (RFC5424)
- The Audit Record Repository shall support both transport mechanisms for the receipt of messages. Given that Audit Record Repository must accept both transports, the Secure Node Actors may choose to utilize either of the transport mechanisms, unless they also comply with another Profile that further restricts the use.
- The IHE Audit Trail format is an XML schema based on the standards developed and issued by the IETF, HL7, and DICOM organizations to meet the medical auditing needs as specified by ASTM.
- The Audit Record Repository shall accept the Audit Record message. The usage of the result by the Audit Record Repository is beyond the scope of the IHE ATNA profile.

Below, an example audit trail message from the epSOS project complying with the ATNA profile is presented.

```
<AuditMessage>
  <EventIdentification EventActionCode="E"
    EventDateTime="2012-02-21T17:15:31.077+02:00" EventOutcomeIndicator="8">
    <EventID code="epsos-11" codeSystemName="epSOS Transaction"
      displayName="epsosIdentityService::FindIdentityByTraits"/>
    </EventIdentification>
    <ActiveParticipant AlternativeUserID="Dr. Muller" UserID="ihelocal"
      UserIsRequestor="true">
      <RoleIDCode code="medical doctor"/>
    </ActiveParticipant>
```



```

<ActiveParticipant NetworkAccessPointID="95.9.71.171"
  UserID="T=Dr., SURNAME=HULUR, GIVENNAME=Unal, CN=epsos.saglik.gov.tr, OU=Bilgi Islem
  Daire Baskanligi, O=T.C. Saglik Bakanligi, C=TR" UserIsRequestor="true">
  <RoleIDCode code="MasterPatientIndex" codeSystem="epSOS" displayName="Master Patient
  Index"/>
</ActiveParticipant>
<ActiveParticipant NetworkAccessPointID="95.9.71.171"
  UserID="T=Dr., SURNAME=HULUR, GIVENNAME=Unal, CN=epsos.saglik.gov.tr, OU=Bilgi Islem
  Daire Baskanligi, O=T.C. Saglik Bakanligi, C=TR" UserIsRequestor="true">
  <RoleIDCode code="ServiceProvider" codeSystem="epSOS" displayName="epSOS Service
  Provider"/>
</ActiveParticipant>
<ActiveParticipant NetworkAccessPointID="131.254.209.23"
  UserID="Warning!: No Client certificate found!" UserIsRequestor="true">
  <RoleIDCode code="ServiceConsumer" codeSystem="epSOS" displayName="epSOS Service
  Consumer"/>
</ActiveParticipant>
<AuditSourceIdentification AuditSourceID="TR"/>
<ParticipantObjectIdentification ParticipantObjectID="4703"
  ParticipantObjectTypeCode="2" ParticipantObjectTypeCodeRole="3">
  <ParticipantObjectIDTypeCode code="9"/>
  <ParticipantObjectDetail type="errorMsg" value="[BASE64VALUE]"/>
</ParticipantObjectIdentification>
<ParticipantObjectIdentification
  ParticipantObjectID="37135141079^^^&2.16.17.710.813.1000.990.1&ISO"
  ParticipantObjectTypeCode="1" ParticipantObjectTypeCodeRole="1">
  <ParticipantObjectIDTypeCode code="2" codeSystemName="RFC-3881" displayName="Patient
  Number"/>
  <ParticipantObjectName>PatientSource</ParticipantObjectName>
</ParticipantObjectIdentification>
<ParticipantObjectIdentification
  ParticipantObjectID="urn:uuid:49ed2740-fc7c-498f-bdff-7cc8fba4b5f9"
  ParticipantObjectTypeCode="4">
  <ParticipantObjectIDTypeCode code="req" codeSystemName="epSOS Msg"
  displayName="Request Message"/>
  <ParticipantObjectDetail type="securityheader" value="[BASE64VALUE]"/>
</ParticipantObjectIdentification>
<ParticipantObjectIdentification ParticipantObjectID="" ParticipantObjectTypeCode="4">
  <ParticipantObjectIDTypeCode code="rsp" codeSystemName="epSOS Msg"
  displayName="Response Message"/>
  <ParticipantObjectDetail type="securityheader"
  value="PHNvYXB1bnY6SGVhZGVyIHhtbG5zOnNvYXB1bnY9Imh0dHA6Ly93d3cudzMub3JnLzIwMDMvMDUvc29hcC11
  bnZlbG9wZSIgZ4=""/>
</ParticipantObjectIdentification>
<ParticipantObjectIdentification
  ParticipantObjectID="37135141079^^^&2.16.17.710.813.1000.990.1&ISO"
  ParticipantObjectTypeCode="1" ParticipantObjectTypeCodeRole="1">
  <ParticipantObjectIDTypeCode code="2" codeSystemName="RFC-3881" displayName="Patient
  Number"/>
  <ParticipantObjectName>PatientTarget</ParticipantObjectName>
</ParticipantObjectIdentification>
</AuditMessage>

```

Figure 34 An example audit trail message from the epSOS project [EPSOS]

6.2.2.5 IHE Basic Patient Privacy Consents (BPPC) Integration Profile

Basic Patient Privacy Consents (BPPC) Integration Profile provides a mechanism to record the patient privacy consent(s) and a method for Content Consumers to use to enforce the privacy consent appropriate to the use [BPPC]. This profile complements Cross-Enterprise Document Sharing (XDS) Integration Profile by describing a mechanism whereby an XDS Affinity Domain can develop and implement multiple privacy policies, and describes how that mechanism can be integrated with the access control mechanisms supported by the XDS Actors (e.g. EHR systems). BPPC profile provide mechanisms to:

- Record the patient privacy consent(s),
- Enforce the privacy consent appropriate to the use.

There are two actors in the BPPC profile, the Content Creator and the Content Consumer. Content is created by a Content Creator and is to be consumed by a Content Consumer. The sharing or transmission of content or updates from one actor to the other is addressed by the use of appropriate IHE profiles described in the section on Content Bindings with XDS, XDM and XDR.

In the BPPC profile, the Affinity Domain (i.e. healthcare information network in XDS terms) organizers create a set of policies (i.e. patient consents). Each of these policies are given an object identifier (OID). Each OID can clearly identify one of the policies defined by the healthcare information network. The Affinity Domain organizers can define their own policies in as clear of language as is necessary for the patients, providers, and systems to understand.

The BPPC profile shows how to capture a patient's acknowledgment and/or signature of one or more of these previously generated policies. This is captured using a CDA document with optionally a scanned copy or optionally a digital signature. Preferably, the scanned copy is with the patient's wet signature on paper acknowledgment. Patients need to know what they are consenting to, and they can understand human text; not many can understand computer logic.

When a document is used, the document consumer actors are obligated to enforce the acceptable use. The document consumer actor is required to block access to documents that are not authorized. Any OIDs that are not understood by the document consumer actor must not be used to enable access.

The BPPC profile was developed for the first time in 2006, and the profile is called "basic" because there are still many gaps that need to be addressed. For example, the profile does not address directly computer processable and executable privacy consent document formats, such as the ones that can be defined with OASIS XACML 2.0. The patients have to choose among the previously defined set of policies, they cannot define their access control settings dynamically. Also, the profile does not present how access control is applied; this is left to implementers.

7 DISCUSSION AND CONCLUSION

7.1 Relevancy and limits of existing solutions for C3-Cloud project

7.1.1 Personalised care plan development and execution

In chapter 2 we have presented important efforts to standardize abstract, logical and implementation dependent models of care plan such as Contsys, IHE PPOC, and PtCP profiles, HL7 DAM, HL7 FHIR and ONC LCC Initiative. Among these, as a consortium **we aim to adopt the detailed descriptions provided by Contsys for care plan** also the associated clinical concepts closely linked with care plans such as care pathways and clinical guidelines. Currently at month 2, we are in the process of building a common dictionary for C3-Cloud project, and Contsys concept models are strong candidates to be utilized in this process.

HL7, IHE and ONC LCC have already been closely collaborating with each other, and most of the standards mentioned in this section have been evolved together sometimes building upon and replacing each other. As C3-Cloud project we aim to build upon the latest published version of these when there are alternatives available by different initiatives. For example, **we aim to adopt the Care Plan document templates available in CDA® Release 2: Consolidated CDA Templates for Clinical Notes** as a CDA representation of care plans, as this specification is a more recent joint work by ONC LCC and HL7 Structured Documents group which is an implementation of the latest HL7 DAM, which can be said to supersede the CDA templates provided by IHE PPOC and PtCP efforts. The other clinical document templates provided jointly by ONC LCC, and HL7 Structured Document group, such as Transfer Summary, Referral Note will also be valuable resources for us for the coordinated care and cure delivery processes we aim to support. As of now, **we aim to utilize the HL7 FHIR Care Plan model as the basis of our Personalized Care Plan Development Platform as the underlying model to be implemented for the Care Plan Repository** we aim to build, as it provides a simple Restful resource architecture very suitable for the CRUD functionalities we aim to support. Finally, HL7 CCS Service Functional Model is currently being utilized in the requirement analysis phase in identifying the functionalities to be covered by the Coordinated Care and Cure Delivery Platform by thoroughly discussing the proposed category of features with our end users.

7.1.2 Decision support modules for reconciliation of multiple treatment plans

Polypharmacy and clinical guidelines

Section 3.3 looked to the state of the art in polypharmacy management. From an IT-based clinical decision support perspective, there have been several tools developed to support polypharmacy management and decrease the complexity of prescriptions. Tools, such as PRIMA-EDS, STRIP Assistant and TRIM consider patient records and evidence-based sources, such as guidelines to provide recommendations to clinicians. The use of ontologies to model medication prescription has also been explored. Although these approaches require further evaluations for their clinical outcomes, they have shown promising results in supporting clinicians to semi-automatically identify potential areas of concern. Most of the approaches have used single EHR systems in specific health domains, such as primary care. In C3-Cloud, the research challenge is to address polypharmacy management as an integrated care function, across several healthcare providers.

Similarly, in Section 3.4, computer-interpretable guideline methods have been reviewed, as they are an essential part of a decision support system, for automatically or semi-automatically reconcile concurrent guidelines relevant to multimorbid patients. The sharing of computer-interpretable guidelines; the detection and conciliation of interactions; and the integration within EHR systems are emerging research themes that still need to be explored. In C3-Cloud, the focus on multimorbidity and the guideline decision support as part of care planning will help to address some of these unresolved areas.

HL7 standards

Section 3.6 investigated related HL7 standards on CDS knowledge representation, CDS data model and decision support service. It is observed that the standardization community is moving towards HL7 FHIR. Many existing standards are being redeveloped to align with FHIR, and new standards increasingly use FHIR as the design basis. C3-Cloud will observe closely the community trend and consider adopting FHIR as the main data model for CDS input, output and inferencing in the development of CDS modules. As discussed in section 3.6.1, there is no single standard with widespread uptake to encode portable CDS rules across EHR environments. A service-oriented approach is a more pragmatic option. Providing a reference implementation of HL7 DSS standard, OpenCDS supports both vMR and FHIR as the input/output and inferencing data model. JBoss Drools, the rule engine on which OpenCDS is built, is a well-established open source business rules management system (BRMS) with large community support and mature knowledge management tools, which can be leveraged to facilitate rules authoring and management. C3-Cloud will follow the HL7 DSS approach and align the development efforts with the OpenCDS community.

7.1.3 Patient empowerment platform

In chapter 4, we have presented some of the most relevant existing European Union funded projects in the patient empowerment research area, and two examples of patient empowerment tools provided by the consortium: the patient empowerment product Medixine Suite™ and the patient engagement tool available in one of our pilot sites, Basque Country, named Personal Health Folder (PHF).

One of the main goals of the C3-Cloud project is the active patient involvement and treatment adherence achieved through a Patient Empowerment Platform to assure that the patient needs are respected in decision making and taking into account preferences and psychosocial aspects. In the project the main research challenges related to Patient Empowerment will be focused on the following items: (i) Providing self-management support, (ii) Actively monitoring the goals, the expected outcomes and potential risks, (iii) Addressing multi-morbidity and poly-pharmacy and finally (iv) Addressing organizational and social aspects. C3-Cloud Patient Empowerment Platform aims the improvement of existing commercial products of consortium partners. C3-Cloud will implement enhanced patient empowerment mechanisms on top of CE Mark certified set of patient engagement tools, MEDIXINE Suite (phone and tablet) based, and also other system available in our pilot sites, as PHF (Basque Country). Along C3-Cloud project, the Patient Empowerment Platform will be enhanced with self-management, risk-monitoring and patient involvement in personalised care plan management tools.

7.1.4 Technical and semantic interoperability architecture

In chapter 5, we have presented the key aspects of the technical and semantic interoperability in a health system context. Related existing approaches in the domain were also presented, as well as the major related standards they implement.

In C3-Cloud, the same way to proceed and the same standards remain totally relevant. However, the notion of a well-defined context is primeval. To obtain an efficient technical interoperability between components, formats and structure of data of each involved actor need to be known, declared and mapped to the system. In the same way, the semantic interoperability needs to have access to the appropriate resources, according to the exploited context. The pre-existing methods and frameworks can be applied, but the semantics need to be adapted. These methods have been previously applied by the partners in the related projects: on a context of pharmacovigilance in SALUS and of clinical trial building in EHR4CR (see section 5.3.2 and 5.3.3). In the context of C3-Cloud - multimorbidity, polypharmacy and collaborative care plans -, semantic resources have to be chosen accordingly.

7.1.5 Security and privacy

In chapter 6, the most prominent security and privacy standards and interoperability profiles concerning the security and privacy of healthcare information exchange are presented. Almost all of these standards and integration profiles are industry level and being applied in the market and also in other research projects for many years. Hence, in the C3-Cloud project, what we need is not to reinvent the wheel, but make the best use from the existing solutions, customized according to our requirements. In this section, the relevancy of the existing solutions for C3-Cloud project are presented.

First of all, in C3-Cloud, it is necessary to establish a secure environment in which only authorized nodes are enabled to access healthcare information. It is also utmost importance to collect and preserve audit trail messages belonging to basic activities such as authentication, read access, update access, etc. In this respect, IHE Audit Trail and Node Authentication (ATNA) Integration Profile provides all the necessary actors and transactions. Although the final C3-Cloud requirements are not in place yet, it can be said that both Authenticate Node and Record Audit Event transactions will be implemented.

C3-Cloud dependency on federated identity management and role based access is not clear yet; node authentication achieved via implementing ATNA profile might be sufficient for ensuring the minimum required level of security in a system where the data is shared between authorized systems, and individual users try to authenticate themselves locally on these systems for access to data. In case cross-enterprise user authentication and authorization is needed according to the requirements to be finalized, then Cross-Enterprise User Assertion (XUA) Integration Profile is the best alternative to implement. Enterprise User Authentication (EUA) is not sufficient since it only deals with user authentication within an enterprise. In fact, not just the base XUA profile, but XUA++ would be preferred since it further refines XUA with integration of OASIS XSPA. SRDC, who is responsible for providing the open source toolsets for security and privacy, has experience in implementing all these standards; lately they are all implemented in the epSOS project.

As patient's medical data will be shared across care team members, patient consent mechanism will need to be in place. In that respect, OASIS XACML will be preferred for dealing with electronic patient consents. IHE Basic Patient Privacy Consents (BPPC) profile is not likely to be preferred for handling patient consents, due to its inefficiencies such as the obligation to choose among a predefined set of privacy policies.

7.2 Conclusion

The purpose of this deliverable was to provide a comprehensive survey of currently available standards, technologies and architectures in the field of advanced ICT systems and services for integrated care, that could support the design of the C3-Cloud architecture. At this stage of the project, the aim was mainly to gather and partners' experience and expertise from previous work and projects with the idea to share this information within the consortium. The survey has been enriched exploring additional and various sources of knowledge like academic literature or previous and current European Commission supported projects. We have proposed to organize this public deliverable around the

research pillars identified in C3-Cloud to achieve the set objectives of the project for delivering an ICT infrastructure enabling a collaborative care and cure cloud to enable continuous coordination of patient-centred care activities by a multidisciplinary care team and patients/informal care givers. Each chapter of the deliverable presents the key elements of the corresponding domain and describes related standards and existing approaches. The six chapters of the document cover the main blocks of the C3-Cloud architecture (see Figure 1). All partners were involved in the redaction of this deliverable. The partners from the pilot sites contributed more in the top levels blocks of the C3-Cloud architecture (Personalised care plan development and execution, patient empowerment as well as clinical decision support modules) while more technical partners were involved in the other blocks (Technical and semantic interoperability architecture and Security and privacy). The relevancy and limits of existing solutions for C3-Cloud for each chapter are discussed in the previous section (see section 7.1).

It is clear from this analysis that partners' experience, academic literature and existing standard will provide numerous key elements to the project and at every stage. Standards like HL7 FHIR Care Plan Model (see section 2.3.3), HL7 Consolidated CDA (see section 5.4.1) or OASIS security and privacy standards (see section 6.2.1), just to name a few, will be used as basis of our multiple design and implementations of C3-Cloud modules. On the same way, C3-Cloud will work and provide services on top of existing solutions from the consortium, like Medixine Suite (see section 4.2) or the Personal Health Folder (see section 4.3).

We believe that this piece of work will be a reference for the C3-Cloud partners who have different level of awareness, understanding and use of the health information and knowledge representation, interoperability standards and solutions that exist in the areas of clinical care plan, patient empowerment, decision support, technical and semantic interoperability, security and privacy. Throughout the development of the C3-Cloud architecture, this survey will be a key reference to the consortium, providing a strong basis of work and allowing implementations over reliable and proven solutions.

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