C3-Cloud

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

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EXECUTIVE SUMMARY

With over half of all older people having at least three chronic conditions, and a significant proportion with five or more, chronic conditions account for poor health and 70% of the healthcare expenditure in Europe. Poorly managed multimorbidity may increase the risk of disease complications and vulnerability due to acute deteriorations, for example hospitalizations, falls and death. However, the clinical management of patients with multimorbidity is much more complex and time-consuming than single diseases, due to the involvement of the number and type of care providers who need to align and coordinate care across teams and settings. As multimorbid patients experience gaps in their care provision, promoting good quality integrated care remains a key challenge that is being actively researched. There are several challenges in providing integrated care to elderly patients with multiple chronic conditions, including (1) Clinical practice guidelines are single disease centred and often fall short to organise care for patients with multimorbidity; (2) Multimorbidity often leads to polypharmacy due to multiple uncoordinated treatments; (3) Fragmented care and specialty silos arising from multiple health and social care providers not communicating and sharing information effectively; (4) Patients and their informal caregivers not having a voice in the management of their own care; (5) Existing organisational models and care pathways not being adequate for integrated care delivery; and (6) Lack of evidence base for multiple disease pathways.

In this context, the C3-Cloud project focuses on the increasing need to organise the care around the patient and not the disease, taking into account their multiple physical and psycho-social conditions and provides a digitally enabled way to deliver integrated care for patients with multimorbidity. In this final project report, we summarise the main activities and results that have contributed to C3-Cloud meeting its objectives.

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1. INTRODUCTION

1.1. Purpose of deliverable

The final report of the C3-Cloud project aims to provide an overview of the project objectives, activities, results and findings to an external audience. The report highlights the key areas that the C3-Cloud contributes to in the domain of integrated care systems for multimorbidity and polypharmacy management.

1.2. Structure of deliverable

Section 2 presents the context and objectives of the project. Then, in Sections 3 to 10, the main achievements of the project are highlighted with references to project deliverable documents, publications, and project milestones. These documents can be found on the project website: https://www.c3-cloud.eu. Finally, Section 11 provides details of the project partners, contacts and links where further project information can be found.

1.3. Abbreviations and acronyms

Abbreviation/ Acronym	Definition
C3DP	Coordinated Care and Cure Delivery Platform
CDS	Clinical Decision Support
EHR	Electronic Health Record
ETL	Extract-Transform-Load
FHIR	Fast Healthcare Interoperability Resources
HLC	C3-Cloud High Level Components
MDT	Multidisciplinary care team
PAR	Pilot application user requirement
PEP	Patient Empowerment Platform
SIS	Semantic Interoperability Suite
SPS	Security and Privacy Suite
TIS	Technical Interoperability Suite

2. SUMMARY OF CONTEXT AND PROJECT OBJECTIVES

2.1. Context

Older age is associated with an increase in the number of ongoing long-term medical conditions, known as *multimordibidy*. With over half of all older people having at least three chronic conditions, and a

significant proportion with five or more[1], chronic conditions account for poor health and 70% of the healthcare expenditure in Europe[2]. Poorly managed multimorbidity may increase the risk of disease complications and vulnerability due to acute deteriorations, for example hospitalizations, falls and death[3]. However, the clinical management of patients with multimorbidity is much more complex and time-consuming than single diseases, due to the involvement of the number and type of care providers who need to align and coordinate care across teams and settings. As multimorbid patients experience gaps in their care provision, promoting good quality **integrated care** remains a key challenge that is being actively researched.

Integrated care is "the management and delivery of health services so that citizens receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system"[4]. There are several challenges in providing integrated care to elderly patients with multiple chronic conditions:

- Clinical practice guidelines are single disease centred and often fall short to organise care for patients with multimorbidity.
- Multimorbidity often leads to polypharmacy due to multiple uncoordinated treatments.
- Fragmented care and specialty silos arising from multiple health and social care providers not communicating and sharing information effectively.
- Patients and their informal caregivers not having a voice in the management of their own care.
- Existing organisational models and care pathways not being adequate for integrated care delivery.
- Lack of evidence base for multiple disease pathways.

In this context, the C3-Cloud project focuses on the increasing need to organise the care around the patient and not the disease, taking into account their multiple physical and psycho-social conditions[5] and provides a digitally enabled way to deliver integrated care for patients with multimorbidity. Figure 1 depicts the personalised care plan creation and maintenance process in C3-Cloud, with the relevant patient data and decision modifiers.

[1] F. Luppi, F. Franco, B.B.L. Fabbri. Treatment of chronic obstructive pulmonary disease and its comorbidities. Proceedings of the American Thoracic society, vol. 5 (2008), p. 26

[2] Economist Intelligence Unit. Never Too Early. Tackling Chronic Disease to Extend Healthy Life Years, 2012. Available at: https://eiuperspectives.economist.com/healthcare/never-too-early

[3] Calderón-Larrañaga A, Vetrano DL, Ferrucci L, Mercer SW, Marengoni A, Onder G, Eriksdotter M, Fratiglioni L. Multimorbidity and functional impairment–bidirectional interplay, synergistic effects and common pathways. J Intern Med. 2019;285:255–271

[4] European Innovation Partnership on Active and Healthy Ageing, Action Plan on 'Replicating and tutoring integrated care for chronic diseases, including remote monitoring at regional levels'. http://ec.europa.eu/research/innovation-union/pdf/active-healthy-ageing/b3_action_plan.pdf

[5] Kadam U. Redesigning the general practice consultation to improve care for patients with multimorbidity, British Medical Journal. 2012 Sep 17;345:e6202

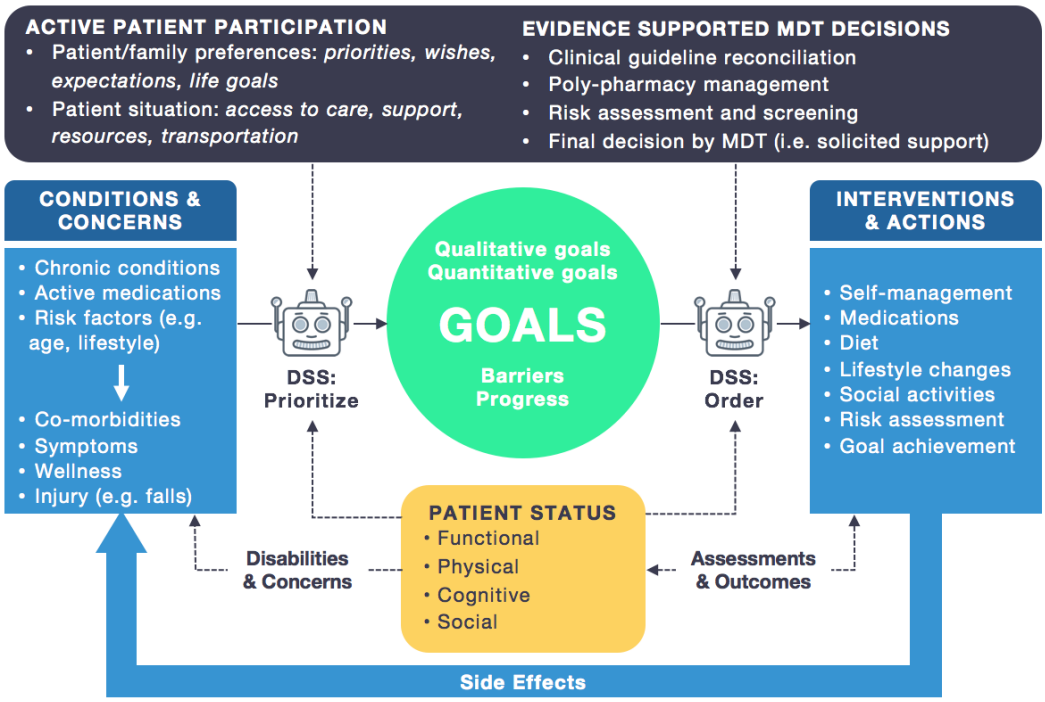

Figure 1: C3-Cloud personalised care plan management process

2.2. C3-Cloud objectives

C3-Cloud specific objectives are to:

- Enable the development of personalized care plans for multimorbid patients through systematic and semi-automatic reconciliation of digitally represented clinical guidelines for individual chronic conditions, by a group of collaborating health and social care givers, and the informed participation of the patients and their informal care givers.
- Provide an innovative online platform through which multidisciplinary care team (MDT) members can collaboratively manage the integrated personalized care plans.
- Provide several clinical decision support modules/services to support personalized care plan development and collaborative management of care plan execution.
- Ensure the active participation of patients and their informal care givers to the management of their multimorbid chronic conditions through a Patient Empowerment Platform to alleviate the non-adherence problem.
- Provide an Interoperability Middleware addressing technical, semantic and privacy/security interoperability challenges to seamlessly integrate with the existing health, social and community care information systems.
- Demonstrate the applicability of its integrated care approach and supporting set of innovative ICT components in varying clinical, technological and organizational settings by piloting in three European regions with different health and care systems and ICT landscapes.
- Examine and identify best practices in caring for patients with multiple conditions through the use of its platform.
- Develop, experiment and refine new adaptive models of integrated and person-centred care and organizational change management guidelines, in order to achieve the design and implementation of integrated care supported ICT in diverse settings.

3. DESIGN OF THE C3-CLOUD INTEGRATED CARE COORDINATION SYSTEM

3.1. Background

The building block of the C3-Cloud system is the overall design of the system based on the requirements of the stakeholders for an integrated care coordination platform. A good understanding of the healthcare systems and infrastructure where C3-Cloud will be used, is needed. At the same time, it is important to consider the latest research and technologies in the relevant areas within the project. Analysis of the requirements of the C3-Cloud system and its components, and the design of the overall architecture needs to ensure collaboration between the system end users and the technical teams.

3.2. Main results

One of the first tasks was to identify the clinical and personal needs of patients, their families and their care givers to improve the care of multi-morbid patients. This was performed at the three pilot sites in Spain, Sweden and the U.K. via the collaboration of local multi-disciplinary team members and patients with the use of patient scenarios. The group worked in close collaboration with the technical teams in the project to explore a series of encounters of a typical multimorbid patient needing care from different healthcare professionals, in the current pilot situation and in a C3-Cloud usage situation. From the scenarios, ***60 different pilot application user requirements (PARs) have been identified*** that have been mapped to different required high level components of the C3-Cloud system, notably: the Patient Empowerment Platform (PEP), the Coordinated Care and Cure Delivery Platform (C3DP), Technical Interoperability Suite (TIS), Semantic Interoperability Suite (SIS), Clinical Decision Support Modules (CDSM) and Security and Privacy Suite (SPS), and in some cases to already existing local care systems. The actual IT landscape at each pilot site has also been mapped and described, thus enabling the development of use cases and requirements for the pilot site application in the different regions.

A ***comprehensive survey of currently available standards, technologies and architectures in the field of advanced ICT systems and services for integrated care*** was conducted with the view to support the design of the C3-Cloud architecture. The survey gathered the project partners' experience and expertise, as well as broader sources of information, such as academic literature, knowledge and results of the previous European Commission supported projects. Existing solutions were also explored to better understand the benefits they bring and assess their limitations. In C3-Cloud, the aim is to address some of those limitations while working towards an integrated care solution for multimorbidity.

From the 60 pilot application user requirements, detailed technical requirements have been analysed for each of the high level C3-Cloud components and documented as a System Requirement Specification Document (SyRS) in accordance with the IEEE Std. 29148:2011 standard (Systems and Software engineering-Life cycle processes – Requirements engineering). ***72 different technical use cases*** have been identified to address these PARs. Further elaboration of these use cases enabled the extraction and documentation of formal requirement specification of the C3-Cloud components. A total of ***348 requirements have been identified*** which are categorized as Functional, Information, System Interface, User Interface, Usability, Performance, Reliability, Maintainability and Security requirements. Additionally, the requirements are linked to the user scenario descriptions through the Requirements Traceability Matrix, to ensure all features of the final solution addressed a particular clinical need (Figure 2).

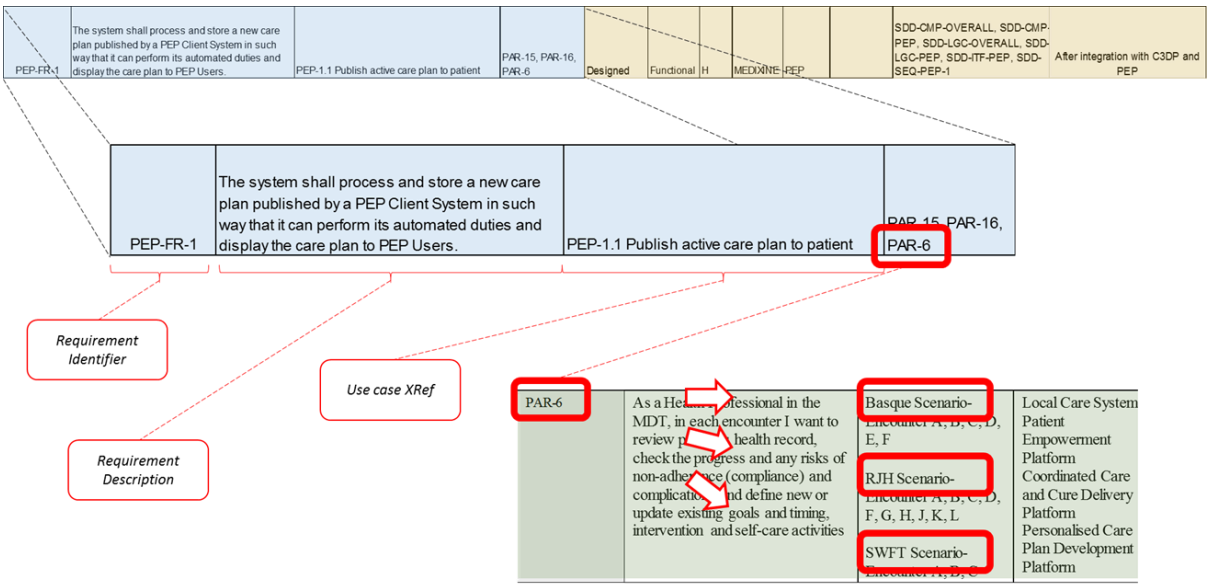

Figure 2: Traceability of C3-Cloud requirements to originating operational scenarios

From the system requirements and use cases, ***key communication interfaces among system components and their interaction workflow*** were developed in order to fulfil these requirements. The purpose of the design of C3-Cloud architecture at a conceptual level is to provide a technical reference for the implementation work for each C3-Cloud component. As an information intensive system, extensive information modelling has also taken place as part of the design activities and documented in accordance with the IEEE Standard 1016-2009 (IEEE Standard for Information Technology -- Systems Design -- Software Design Descriptions), organised into 5 design views:

- The *composition view* identifies communication interfaces between system components.
- The *logical view* analyses key business concepts and domain logic.
- *The information* view models key information items exchanged through the interfaces.
- Using the data models from the information view, the *interface view* defines operations for each interface identified in the composition view.
- The *interaction view* demonstrates how the operations in the interface view should be executed in order to fulfil each use case

The C3-Cloud architecture design is heavily based on the emerging FHIR standards[6] and FHIR-based open specifications, in particular the FHIR RESTful paradigm as the architecture foundation. FHIR resource models are used as the basis for the definitions of information items to be exchanged between C3-Cloud subsystems, and the creation of FHIR profiles.

The architecture of the C3-Cloud integrated system is shown in

Figure 3 with its key components: Coordinated Care and Cure Delivery Platform (C3DP), Patient Empowerment Platform (PEP), Clinical Decision Support Services (CDS), and Interoperability Middleware: Technical Interoperability Suite (TIS), Semantic Interoperability Suite (SIS) and Security and Privacy Suite (SPS).

[6] FHIR standards: https://www.hl7.org/fhir/summary.html

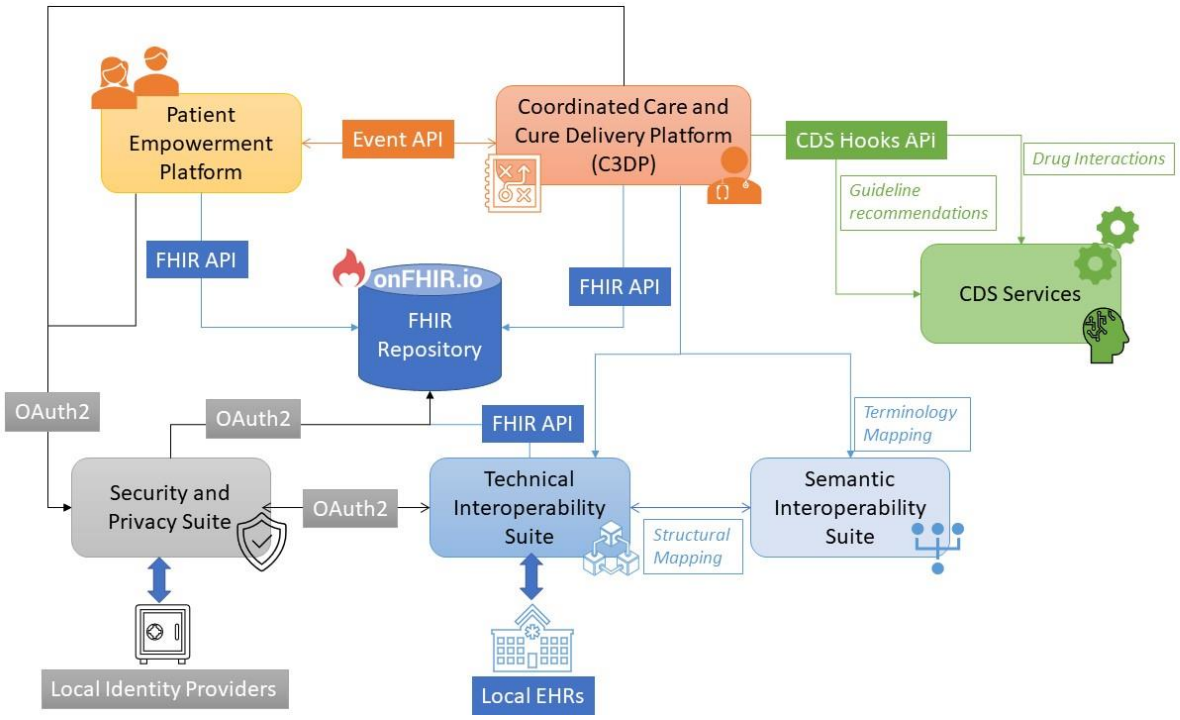

Figure 3: C3-Cloud integrated system architecture

3.3. Referenced deliverables and milestones

Deliverables listed below can be found on the C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D8.1	Use Cases and Requirement Specifications of the Pilot Application	8	RJH
D3.1	Survey of the State of the Art	3	INSERM
D3.2	Requirements Specification of the C3-Cloud Architecture	3	SRDC
D3.3	Conceptual Design of the C3-Cloud Architecture	3	WARWICK

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS1	C3-Cloud pilot application requirements and use cases, software requirements analysis	3, 8	SRDC
MS2	C3-Cloud conceptual architecture	3	WARWICK

3.4. Lessons learnt

- Having good traceability between use cases and technical requirements is important throughout the development of the system.

- Co-production among the different stakeholders, in particular between the technical teams and the clinical teams has been key to understand and capture the viewpoints and translate them into corresponding technical requirements. Especially at the beginning of the project, as the use of a common terminology was being developed within the project to overcome some gaps in our teams with diverse backgrounds and expertise areas.

3.5. Recommendations

- Standards for requirements documentation, for example the IEEE standard 29148, should be used whenever designing new software as this provides a framework to ensure all necessary aspects of the requirements and design are covered. A requirements traceability matrix should be employed so final functionality of the system can always be traced back to the original intention of the customer
- Co-production between staff developing a system and its intended user group should be used when designing a system to make sure the software being developed fits their needs. Technical jargon specific to one domain should be avoided when working with multidisciplinary groups so that all those involved can follow and contribute to discussions.

4. INTEROPERABILITY MIDDLEWARE FOR ENABLING PATIENT-CENTRIC CARE COORDINATION

4.1. Background

Aiming to orchestrate the care across multiple care givers and treatment sites, and automatically process patients' electronic health records (EHRs) to recommend personalized treatment goals and interventions, inevitably requires interoperability to exchange and seamlessly process medications, conditions, interventions, episodic treatment plans, preferences and patient reported data including sensor measurements. The C3-Cloud Interoperability Middleware has been built to address this challenge and seamlessly access patient data stored at existing local health IT systems at pilot sites.

We have chosen to build our interoperability layer based on clinical resources and RESTful interfaces of the HL7 Fast Healthcare Interoperability Resources (FHIR) STU3 standards framework. The C3-Cloud Integrated Care Platform, C3DP, accesses patient's most recent EHRs, via the C3-Cloud Interoperability Middleware through FHIR based interfaces implemented on top of the proprietary APIs provided by local EHR systems in our pilot sites.

The interoperability layer deals with interoperability challenges between the information systems in local care information systems and C3-Cloud platform, by semantically mediating different clinical information representations. The mediation is realized at two levels: structural mappings and semantic mappings. Structural mappings are involved in the translation between local pilot sites data in local format and FHIR resources data format used in C3-Cloud. Semantic mappings perform the translation between coding systems used in local sites and within C3-Cloud components. As part of the semantic mediation process, the Semantic Interoperability Middleware uses a terminology service for terminology mappings and a semantic metadata registry to process interoperability.

Besides, technical and semantic interoperability, we have also addressed the needs of implementing coherent security and privacy measures that are seamlessly integrated with and compatible with the local security and privacy policies and mechanisms of pilot sites.

4.2. Main results

The C3-Cloud Interoperability Middleware addresses technical, semantic and privacy/security interoperability challenges to seamlessly integrate with the existing health care, social care and

home/community care information systems to enable patient-centric care coordination in an informed manner with the involvement of all stakeholders. It has three components:

- The **Technical Interoperability Suite** (TIS) enables seamless data exchange between the local care systems and the C3-Cloud components. It provides a standard-based data exchange protocol, to enable information exchange between pilot sites and C3-Cloud components, such as C3DP (see below).
- The **Semantic Interoperability Suite** (SIS) addresses the challenge of heterogeneous clinical data representation formats. It handles both structural mappings among different information models and resolves semantic mismatches due to the use of different terminology systems and different compositional aggregations, as used to represent the same clinical concept.
- The **Security and Privacy Suite** (SPS) has been developed, based on open and modern specifications for authentication and authorization of care team members and for ensuring encrypted and auditable data exchange across C3-Cloud software components.

In the C3-Cloud architecture, the Interoperability Middleware is highlighted in Figure 4.

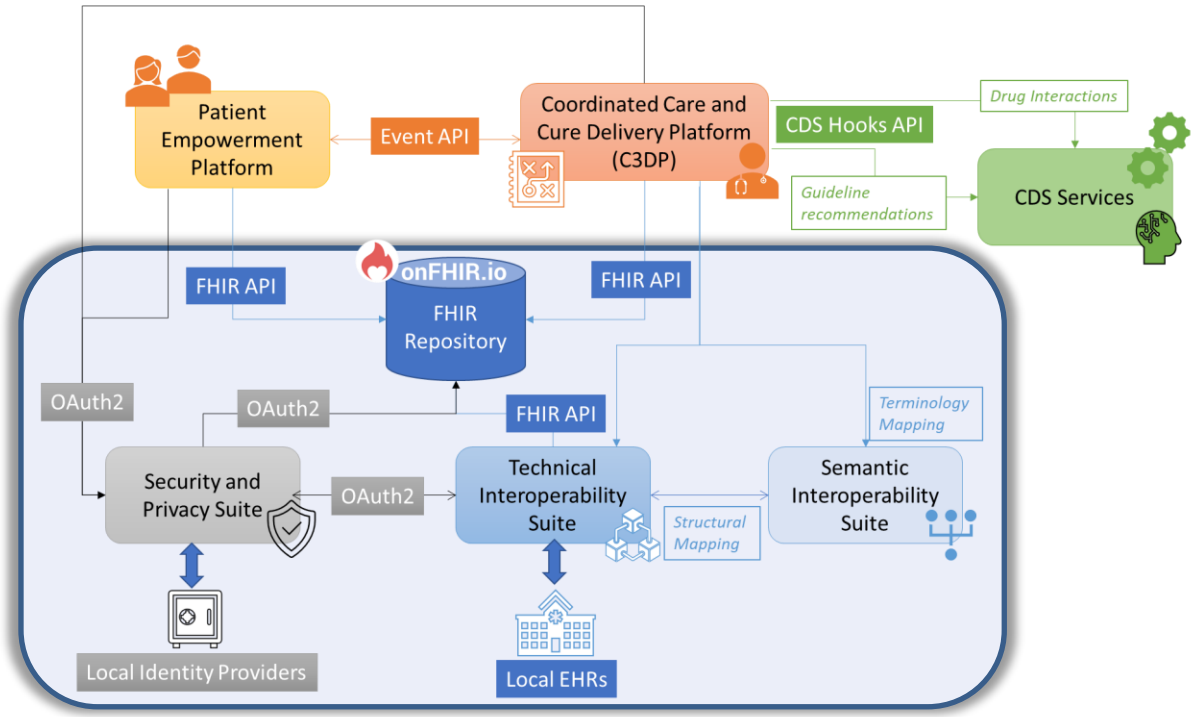

Figure 4: The Interoperability Middleware within the C3-Cloud architecture

4.2.1. Technical Interoperability Suite

The Technical Interoperability Suite (TIS) enables patient data synchronization from local health and social care systems to C3-Cloud but the framework, in tandem with the SIS structural mapper supports export to any similar FHIR based data repository. The TIS application follows an Extract-Transform-Load (ETL) approach, TIS extracts patient data from local EHRs by either querying their accessible endpoints or through upload of formatted extracts and parses the data into JSON, transforms the data into FHIR resources using the SIS Structural Mapping Service, and loads the FHIR data into the C3-Cloud FHIR repository using the HL7 FHIR communication standard for POSTing and PUTting data patient level data.

TIS is an extensible platform, built on Kotlin, Node.JS and MongoDB, that provides both a suite of ETL toolkits to support development of integration pipelines for a particular context of use, allowing configuration of connectors for integration with any web-based API, and a task execution engine that allows scheduling and management of the execution of ETL pipelines. A web-based control panel is

available that allows users to register patients, in cases where a study number needs to be assigned, such as the C3-Cloud study, schedule pre-configured integration tasks, either one off or recurring, and monitor the task execution using a descriptive audit log.

In addition to allowing a user to import data through the control panel, TIS also exposes a REST service that allows a data integration pipeline to be triggered by another software component (e.g., C3DP) in a synchronous manner, thus allowing end users of applications such as C3DP to trigger imports without having to access a second system.

Ultimately, the Technical Interoperability Suite is an API connector/integration engine, allowing a developer to build a connector to any API, query its available endpoints using configurable parameters and send that data to any other API endpoint, whether that be a FHIR repository, database or other application. This is achieved through the modular implementation approach adopted in C3-Cloud, as the structural mapper portion of SIS is a discrete component which can be swapped out for any other parser or formatter.

The TIS framework has been released on GitHub (https://github.com/C3-Cloud-eu/tis) as an open source solution under the Apache 2.0 license, allowing the wider development community to freely reuse and configure the tool for their own use.

4.2.2. Semantic Interoperability Suite

The architecture of the semantic Interoperability Suite (SIS) is articulated around two main sub-components: SIS Structural Mapper and SIS Semantic Mapper:

1) SIS **Structural Mapper** - The structural mapper of SIS is the internal SIS sub-component in charge of the generation of FHIR resources, which must be filled with data provided in pilot site local format by TIS. To achieve its purpose, the structural mapper consists of pilot site dedicated local format mappers. These mappers provide precise mappings to create correspondence to every relevant data exported by the pilot site to its correct interpretation and place in FHIR resource. FHIR resources mapped from pilot site data are defined in the C3-Cloud data dictionary
2) SIS **Semantic Mapper** - The semantic mapper of SIS is in charge of transforming, using the vocabulary used to describe data exported by pilot site into standard codes that will be used in the high-level components of C3-Cloud. A clinical concept mapping sheet is being maintained as the source of truth, which includes all the clinical concepts that are needed by the CDS services, in reference terminologies like SNOMED-CT and WHO ATC, and all the local codes that are used by the pilot sites for these concepts.

The main features of the resulting C3-Cloud SIS are the following:

- C3-Cloud SIS is implemented as a fully deployable exchange suite, running on independent Docker containers.
- It is based on HTTP communication standards, with embedded JSON content.
- It supports FHIR inputs and outputs, and previously mapped local format pilot site inputs.
- SIS is developed using Java 8 Maven.
- Regarding the terminology server, Python 3 is used to develop an application that reads the mappings from use case files and creates an HTTP service (Flask) that is able to achieve the tasks listed in the specifications.

The C3-Cloud Semantic Interoperability Suite can be easily deployed by running its related docker image as containers. The SIS implementation comes with 3 docker images: one for the SIS core server itself that handle TIS requests, one for the structural mapping storage and one for the terminological service. Only the first one is intended to directly interact with TIS and has to have designed IP according to this. Of course, all of the containers have to be accessible for SIS on the same virtual network.

The SIS Structural Mapper and client are available in GitHub: https://github.com/C3-Cloud-eu/c3cloud-semanticmapper and https://github.com/C3-Cloud-eu/c3cloud-semanticmapper-client.

4.2.3. FHIR common data model

The C3-Cloud FHIR Repository acts as the centralized data repository for existing clinical data of the patients and newly created care planning related data. It stores the data, which arrive from EHR systems via TIS and newly created or updated care plan data from other C3-Cloud components like C3DP and PEP, as HL7 FHIR®[7] resources in compliance with the latest interoperability standards, so that it can be easily integrated with additional health IT systems when necessary. In C3-Cloud, the extensible and scalable open-source onFHIR.io Secure Repository[8] is used as the HL7 FHIR® Repository. onFHIR.io, is fully compliant to FHIR DSTU2, STU3 and R4 specifications and implemented on top of MongoDB noSQL database. An authorized user or system can use native FHIR API, i.e. Restful interfaces to store/query/update/delete patient data. It is not possible to access any resource in the secured repository without first acquiring a valid access token. The authorization flow is fully compliant with the Smart App Authorization specification, which is based on the well-known OAuth 2.0 specification[9] as supported by C3-Cloud Security and Privacy Suite (SPS) module.

4.2.4. Security and Privacy Suite

The Security and Privacy Suite (SPS) is responsible for authentication and authorization of the care team members, while they are managing personalized care plans of patients and ensuring that all data exchanged within and across C3-Cloud software components is encrypted and properly auditable.

As explained above, in the C3-Cloud architecture, the patient's electronic health records received from the local EHR systems via the TIS, patient reported observations from the PEP, and the care plan of the patient managed through C3DP, are all managed in the C3-Cloud FHIR Repository. Hence, each of these client apps, i.e. TIS, PEP and C3DP needs to be authenticated and authorized to access (read, write, and update) patient data to the C3-Cloud FHIR Repository, via the functionalities provided by SPS. All such operations need to be logged for ensuring accountability via SPS. In the following we can summarize important features of SPS:

- C3-Cloud SPS Server provides services for user registration, privacy policy management and endpoints defined in the OpenID Connect 1.0 standard to perform authentication and authorization (Authorization Endpoint, Token Endpoint, etc.). By implementing the OpenID Connect API, it serves C3-Cloud Identity Provider (IdP), which is the default IdP when the IdP of some users (e.g., social care workers) of the pilot sites cannot be integrated within the scope of the project. SPS enables authentication of the care team members into the C3-Cloud applications in two ways: i) via their already existing accounts (e.g., username-password) provided by the local authorities by integrating with the existing Identity Provider (IdP) systems of the pilot sites; and ii) by creating C3-Cloud specific user accounts for those users whose IdPs cannot be integrated with the SPS, for example, the social care workers. The SPS Server also manages the C3-Cloud Access Control Policy Store.
- C3-Cloud SPS Manager is a web application for representing the functionalities of C3-Cloud SPS Server with the following user interfaces: single sign on UIs, policy management UI, client registration UI, user registration UI and audit viewer UI.
- SPS serves an Audit Record Repository as a FHIR repository that maintains audit trail records implemented as FHIR AuditEvent resource. Thanks to C3-Cloud FHIR Repository's automatic auditing functionality, audit trail records are kept for each operation on patient data. C3-Cloud project has implemented an open source Audit Viewer component as a single-page web application that enables viewing and filtering FHIR STU3 based audit events. It is available on

[7] The main standard adopted by the repository is the Fast Health Interoperability Resources (FHIR) standard published by Health Level Seven (HL7). Please see https://hl7.org/FHIR/ for more information about this standard.

[8] HL7 FHIR® Based Secure Data Repository, https://onfhir.io/ , available at GitHub under GPL license: https://github.com/srdc/onfhir .

[9] https://oauth.net/2/

GitHub under Apache 2.0 Software License: https://github.com/C3-Cloud-eu/audit-event-viewer.

4.3. Referenced deliverables and milestones

Deliverables listed below can be found on C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D6.1	C3-Cloud Technical Interoperability Implementation Guidelines and Open Source Toolkits	6	WARWICK
D6.2	C3-Cloud Semantic Interoperability Platform	6	INSERM
D6.3	Open Source Privacy and Security Toolkits for the C3-Cloud Architecture	6	SRDC
D9.3	Test and Evaluation Report for C3-Cloud Components	9	empirica

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS4	C3-Cloud Software Components Available and Tested	5, 6, 7, 9	INSERM

4.4. Lessons learnt

- The C3-Cloud solution was implemented at three very different pilot sites but with much time consuming, interoperability work on the fly. Starting with a very well defined use case, having access to the information models of the different pilot sites, knowing exactly the coding systems they use (and hopefully will use all along the project) is very important to deliver quickly a first prototype of the system that is not only theoretical but usable in a real-world setting.
- Pilot sites have quite different information models, terminology systems and compositional aggregations to represent data. Any component that needs to integrate with these systems will therefore have several dependencies on these. An in-depth understanding of the systems used at a site is needed to build and populate any interoperability module with the appropriate and relevant clinical concepts and mappings.
  For instance, the Structural Mapper generates JSON encoded FHIR resources and the semantic mapping is based on a pre-filled registry containing, for each concept, the corresponding code(s) for each site's terminology, and the code used as reference by C3-Cloud. The registry had been continuously updated, via a dedicated service method, during the time of the project. This required dedicated expert resources at the time of the implementation since multiple codes can be specified for a single concept if the used terminology has several codes corresponding to the concept (narrower-than relation) and also since multiple terminologies are used as reference, in order to match each concept exactly. This requires a common understanding and a strong collaboration.
- Completely synthetic mock data delivered by a pilot site does not sufficiently describe data for development of interoperability tools. Gaps and inconsistencies exist within the data meaning additional information is needed to fully define the data available.
- There is the possibility, especially for long term trials or use, that coding systems may change, meaning new mappings need to be developed and supported to allow sites to continue to take advantage of the clinical decision support functionality.

4.5. Recommendations

- Time should be spent during the project to achieve a strong and true semantic interoperability within the multidisciplinary consortium. It can be defined as a specific task at the beginning of the project, with continued co-production when needed. To complement the outputs of use cases, data dictionary, and start-of the art review of technical solutions, additional tools such as focus groups, show rooms, training, roleplay could be proposed to achieve further interoperability within teams.
- The intended functionality, including queries, limitations and implications, of interoperability modules, such as the semantic mappers and technical interoperability suite, should be reported early on so target sites know what is required in terms of data that needs to be shared.
- Follow-up, one to one, sessions with pilot sites should be scheduled during the development phases of a project, to review data and information provided by pilot sites. This allows all parties to check consistency and data coverage of extract samples and mapping information.
- Semantic interoperability systems developed should support mappings from multiple coding systems to the internal coding system and should be easily updatable in case new coding systems are introduced. If new coding systems are introduced during the lifetime of a product, pilot site systems should ideally support dual coding, saving both the old coding system code and the new one for each record during the migration period, to allow for a smooth transition.

5. CLINICAL DECISION SUPPORT SERVICES TO SUPPORT PERSONALISED CARE PLAN DEVELOPMENT AND MONITORING

5.1. Background

The roles of clinical decision support (CDS) services are mainly, to propose treatment regimes according to the evidence-based guidelines for individual chronic conditions and to reconcile multiple treatment plans, while soliciting consolidations for the different treatment regimes proposed by different treatment plans. For this reconciliation, different CDS services can be employed in parallel to:

- perform risk assessment and stratification of candidate elderly people for inclusion in integrated care programmes;
- propose treatment regimes according to evidence based guidelines for individual chronic conditions;
- reconcile multiple treatment plans and to suggest consolidations for the different treatment regimes proposed by different treatment plans;
- monitor and detect the duplicate drugs in treatment regimes;
- monitor and detect contraindications across multiple treatment plans due to drug-drug, drug-disease and drug-body part interactions;
- measure the burden of exposure to multiple drugs, by exploiting the principles of pharmacokinetics (e.g., dose) and pharmacodynamics (e.g., dose response, maximal effect);
- suggest the set of risk factors, based on the current conditions of the patient;
- identify disease stage

In C3-Cloud, the CDS services work collaboratively with the Coordinated Care and Cure Delivery Platform (C3DP) to support the development and monitoring of personalized care plan.

5.2. Main results

The C3-Cloud CDS Services are implemented as CDS Hooks API compliant services making use of the HL7 FHIR® resources. This means that the CDS Services are relatively easy to integrate into other systems such as EHR systems when these systems also utilise HL7 FHIR standard. This also enables

easy extension of C3-Cloud with additional external CDS services implementing CDS-Hooks standard[10]. To be able to intelligently propose individualized goals and activity suggestions for the addressed health concerns based on evidence-based guidelines, the C3-Cloud Integrated Care Platform, C3DP, is integrated with the C3-Cloud CDS services via CDS Hooks API. The relevant electronic health records of the patient retrieved from the C3-Cloud FHIR Repository are passed as input to CDS services. Clinical guideline based CDS logic processing these patient specific diagnoses, lab results, medication data enables the selection of individualized goals and interventions for a specific patient based on evidence-based guideline recommendations. Figure 5 shows the CDS Services within the C3-Cloud architecture. The following sections describe the steps in the development of the CDS services.

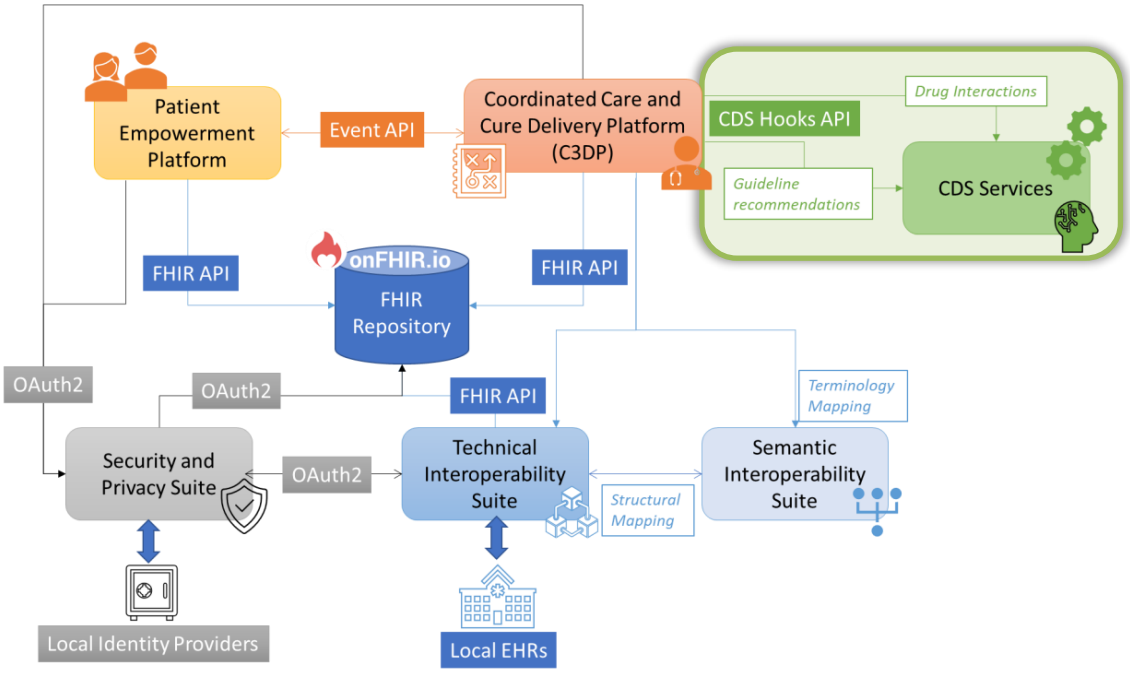

Figure 5: CDS within the C3-Cloud architecture

One of the first tasks was the **identification of clinical guidelines** relevant to the four target diseases of the project (Type 2 diabetes, heart failure, renal failure and depression). The Clinical Reference Group identified the guideline documents that are currently in use in the three pilot regions. There were a number of partially overlapping guidelines in use in all three countries with different audiences and origins. Guidelines are developed by national health agencies, regional bodies and professional societies. While European countries generally share the scientific background and interpretations, there are slight variations in the recommendations. There were no existing computerized guidelines for these four diseases being used with patient specific data in an algorithmic way as proposed in the C3-Cloud project. The English National Institute for Clinical Excellence (NICE) guidelines were chosen to base the common work in C3-Cloud. The analysis work resulted in **43 flowcharts that model the clinical recommendations from the NICE paper-based documents**. In some cases, there are national deviations to the English recommendations, and these have been noted for the consideration of localisations. In addition to the guidelines based on the four diseases of C3-Cloud, the availability and need for some guidance supported by ICT, relating to medication were also analysed. Medication guidance relates to contraindications, interactions, registered hypersensitivity, special concerns for the elderly, and finally, the management of multimorbidity.

[10] http://cds-hooks.org/

In the next step of the CDS services development, these flowcharts were further analysed to specify **implementable technical CDS specifications** by technical experts in close collaboration with the clinical team. Inputs (FHIR resources) and outputs (CDS Hooks cards and FHIR resources) were defined. A decision tree was specified, along with the terminology system binding for the clinical concepts. As an example, Figure 6 shows part of the decision tree for blood pressure management in Type 2 diabetes and hypertension.

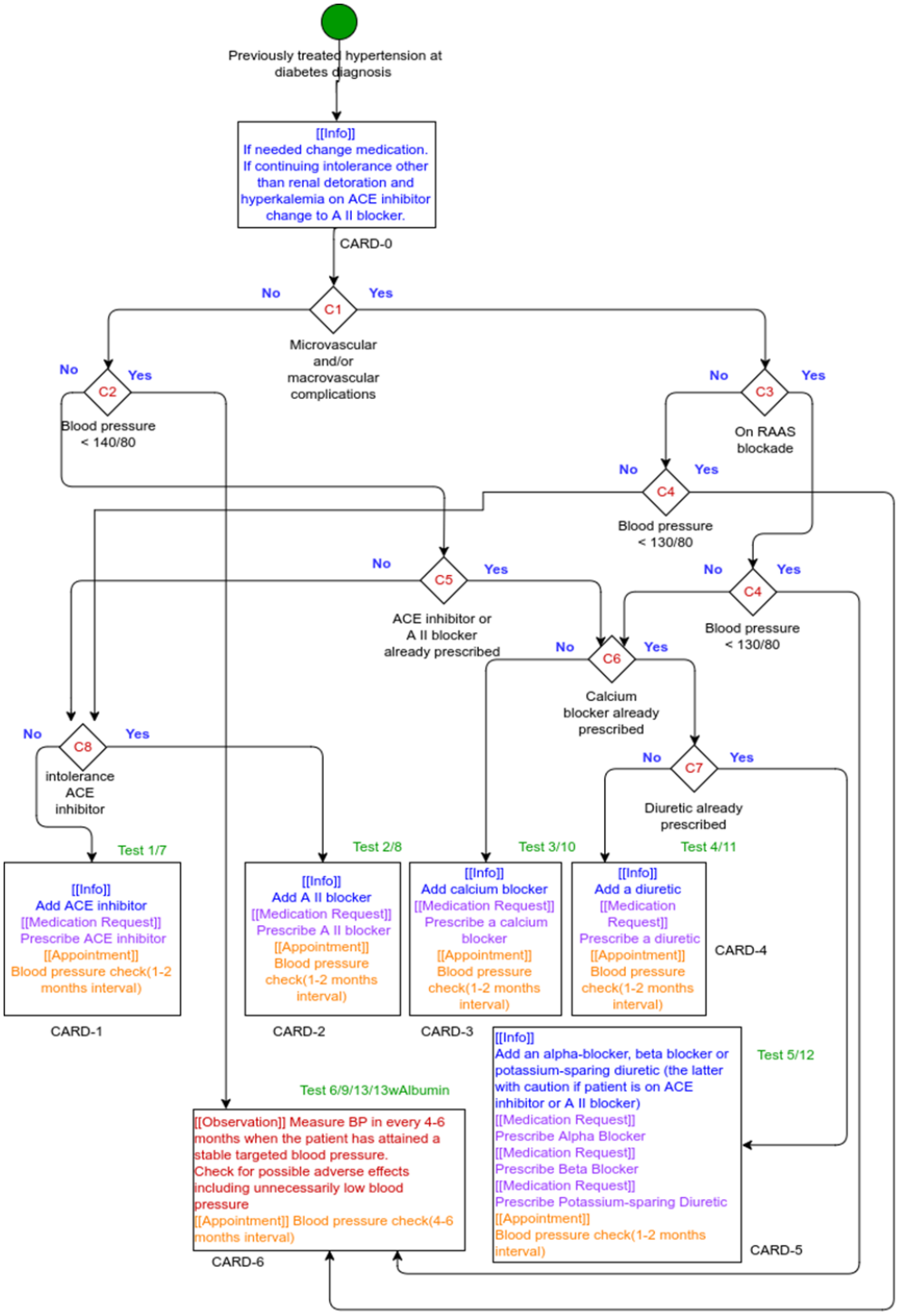

Figure 6: Part of the blood pressure management flowchart

Several types of CDS services have been developed with a total of **31 services**:

1. **GDL2 based CDS services**

These are the CDS Hooks specification compliant computable RESTful services that provide personalized goal and activity (e.g., lab request, referral, self-monitoring task, education material, etc.) suggestions or risk assessments for the patients. **20 CDS services** have been implemented in the Guideline Definition Language 2 (GDL2)[11]:

- 8 Type 2 Diabetes services, implementing 80 clinical rules checking 108 different patient criteria and recommending 119 personalized goals and interventions.
- 4 Renal Failure services, implementing 101 rules, 58 patient criteria and 35 personalized goals and interventions.
- 4 Heart Failure services, implementing ~30 rules.
- 2 Depression services, implementing ~20 rules.
- 2 multi-disease service: drug-disease interaction and lifestyle management.

2. **Mostly static CDS services**
   These 10 services have a simpler decision tree and have been implemented in Node.js.
3. **Reconciliation rules**
   Multimorbidity guideline reconciliation rules were analysed and most were implemented in the existing GDL2 CDS services. Remaining drug-drug and drug-disease interaction rules were implemented as a separate service. **52 reconciliation rules** and **283 rules** were implemented in total.
4. **Drug-drug interaction service**
   A drug-drug interaction service was developed based on NICE British National Formulary (BNF) database that contains 108,600 interactions for 1,009 substances. The service is integrated with C3DP and it be reached remotely from all 3 pilot sites.

The GDL2 CDS services are available on GitHub: https://github.com/C3-Cloud-eu/gdl2-cds-services.

5.3. Referenced deliverables and milestones

Deliverables listed below can be found on the C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D7.1	Evidence Based Clinical Guideline Definitions and Flowcharts for Individual Chronic Conditions	7	ORU
D7.2	Clinical Decision Support Modules for Personalised Care Plan Development and Execution	7	WARWICK
D9.3	Test and Evaluation Report for C3-Cloud Components	9	empirica

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS3	C3-Cloud Improved Models of Care Delivery for Multi-morbid Patients	4, 7	OSAKIDETZA
MS4	C3-Cloud Software Components Available and Tested	5, 6, 7, 9	INSERM

[11] https://specifications.openehr.org/releases/CDS/latest/GDL2.html

5.4. Lessons learnt

- The step from clinical decision support specification to implementation requires a steep learning curve, mainly due to learning the associated technologies and tools, and may be prone to issues.
- Capturing clinical decision support specification in an unambiguous way, amenable to review by clinicians can be enabled by purpose speficic modeling languages. The automatic reconciliation of multiple guidelines requires mature and proven technology in order to be practical. . A semi-automatic approach and process may result in higher confidence in the correctness of the resultant guidelines. is needed.
- Traceability of CDS specification to evidence basis and justification, is needed for validation of the CDS logic, as well as safety compliance of the system.Clinical decision support specification requires review by both an oversight clinical reference group validating with best practice guidelines, as well as end-users who will comment on the practicability of the recommendations.
- Use of open standards such as CDS-hooks enables seamless integration of the CDS engine to the architecture.
- Technology agnostic CDS specification is important for the maintenance and transferability of the specification across multiple demonstrators (and associated clinical scenarios).

5.5. Recommendations

- Co-production between technical and clinical teams is crucial for implementing clinical practice guidelines into computer-interpretable ones, in particular with support from team members with clinical guideline modelling expertise.
- Further research is needed on ontological approaches to computer interpretable guidelines' implementation, including execution engines for such guidelines, to achieve fully automatic reconciliation of guidelines.
- Close co-operation with national and European level evidence and guideline production organizations is needed, for continuity in maintaining and expanding clinical guidelines to support multimorbidity management.
- Validation process between CDS specification and implementation needs to be designed carefully. Support by a tool that will automate some of the more mundane tasks (similar to test driven software engineering) will help eliminate potential errors. preferably
- Future work on Clinical Interpretable Guideline (CIG) modelling languages for CDS is recommended. Clinical decision support can be a powerful tool that will provide a common vocabulary for all stakeholders, to unambiguously co-produce CDS specification. Purpose specific languages can be designed to incorporate constructs that will allow traceability between CDS design, and justification and evidence basis.
- Work on automated reconciliation of CIGs can provide a very useful future avenue that will allow design of more complex services.
- Co-production process to document and link justification of CDS to specification is necessary so that the design process does not create knowledge gaps that will affect the safety and effectiveness of the deployed infrastructure.
- Co-production process to have two rounds of review by CRG and local groups to ensure that the CDS specification encapsulates the requirements of all stakeholders and users, and incorporates local documented and undocumented processes.

6. IMPLEMENTATION OF ONLINE PLATFORM FOR COLLABORATIVE MANAGEMENT OF INTEGRATED CARE PLANS BY MULTIDISCIPLINARY CARE TEAM

6.1. Background

Older age is associated with an increased accumulation of multiple chronic conditions. The clinical management of patients suffering from multiple chronic conditions is very complex, disconnected and time-consuming with the traditional care settings. Integrated care is seen as a means to transform health services to meet these challenges of 21st century, by addressing the growing demand for improved patient experience and health outcomes of multimorbid and long-term care patients. Care planning is a central approach of integrated care, where the aim is to deliver more personalized and targeted care creating shared care plans based on standard care pathways but by clearly identifying the role of each provider, patient and informal care givers in the care process. In the state-of-the-art practices, the multidisciplinary teams (MDT) meet face-to-face to discuss and revise the care plans of several patients at once, at regular time intervals; usually monthly. Individualized care plans are created by manually going over the standard steps of care pathways, i.e. template care plans which are documentation of the optimal management for typical, defined disease patterns. Although implementation of integrated care via these manual processes is already an enhancement over traditional fragmented care practices, C3-Cloud consortium advocates that intelligent collaborative tools can provide significant improvements in the management of chronic diseases.

6.2. Main results

In WP7, we have implemented a Coordinated Care and Cure Delivery Platform (C3DP) that allows collaborative creation and execution of personalised care plans for multi-morbid patients by a multidisciplinary care team (MDT) including GPs, specialists, study nurses, pharmacists, physiotherapists, geriatricians, nutritionists, social care and homecare workers. C3DP is the Web application for collaborative and personalized care plan management by the members of MDT. In the C3-Cloud architecture, C3DP sits at the top of the hierarchy and is directly integrated with all the other C3-Cloud components and indirectly with the local Health IT Systems (EHR/EMR systems, Identity Providers) as highlighted in Figure 7.

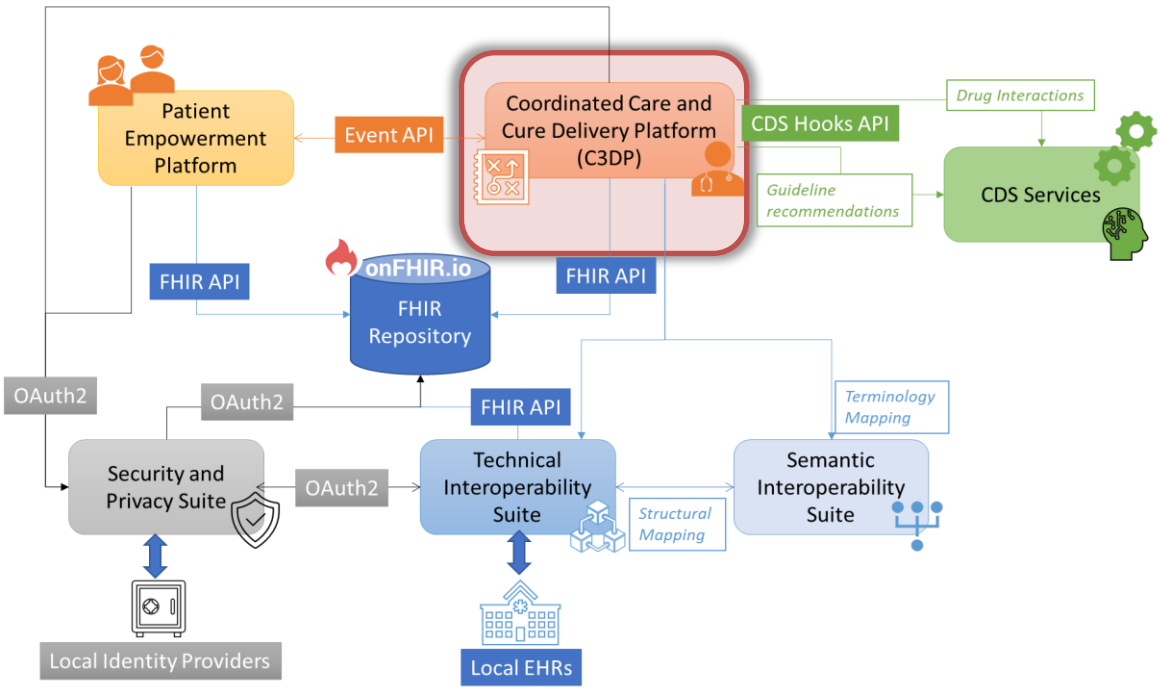

Figure 7: C3DP within the C3-Cloud architecture

The design of the new organizational models to be practiced in proof-of-concept prototypes in the three pilot regions during C3-Cloud study and the guidance for clinical guideline reconciliation for personalized care plans developed in WP4 have been key for the development of Coordinated Care and Cure Delivery Platform (C3DP) in WP7. Both WPs have worked aligned with the aim to improve the care delivery for multimorbid patients; WP4 from an organizational and clinical perspective and WP7 from a technical (software development) one.

The identification of clinical guidelines and the development of flowcharts for individual chronic conditions helped the development of new multi-morbid patient pathways for integrated care, corresponding care plans and new organisational models in WP4. Task 4.2 designed and described the final prototypes to be tested in the three sites in the new C3-Cloud scenario over which the pathways and personalized care plans were built. The new organizational models included the main internal coordination elements and the relationship among all the C3-Cloud components. Throughout the project, Task 4.1 guided on how individual clinical guidelines could be reconciled for the personalised care plan development, which was supported by C3DP and CDS components. A Clinical Reference Group was established in Task 4.1 to link the pilot sites to the technical partners in order to refine the pilot requirements and recommendations for the software developers to improve the user-facing components (PEP and C3DP), elaborate a taxonomy of care plan goals and activities to be used in C3DP, support the development of personalised care plans aligned to C3DP and ensure good usability and accurate guidance to pilot site users, among others.

In the following important features of C3-Cloud Integrated Care Platform C3DP are summarised as main results:

Providing a shared view of patient's medical summary across multiple care providers: C3DP serves as a tool to facilitate clinical thinking and decision making for shared care planning. This necessitates the multidisciplinary care team members to access an integrated patient summary view where the clinician can see all of the conditions and their (planned) treatments from different healthcare providers in one place. To enable this, all the patient data required for care planning are fetched from the C3-Cloud FHIR Repository, the integrated patient record repository, which is continuously updated with EHR data from the pilot sites with the help of the C3-Cloud Interoperability Middleware. C3DP visualizes these data and helps the health professionals to easily manage the integrated care coordination process for multi-morbid elderly patients.

Implementation of international standards in Care Plan Management: C3DP implements the HL7 Care Plan Domain Analysis Model (DAM), and enables health professionals to design a care plan for a patient from scratch by selecting health concerns to be addressed from the EHR of the patient, and setting goals and activities to address the needs of this health concern. This process is formalized as an HL7 FHIR CarePlan resource, which consists of building blocks like Goal and different types of Activity resources.

Personalized care plan goal and activity suggestions: Our platform equips the MDTs with intelligent services to suggest personalized goals and interventions for the care plan of the patient based on the most recent medical summary of the patient and evidence-based guidelines. C3DP is integrated with clinical decision support services to select upon most suitable treatment options in the light of evidence-based guidelines and to schedule and prioritize treatment activities and to detect and warn clinicians about conflicting treatment options and adverse effects.

Patient Empowerment: C3DP enables exchange of the care plan and accompanying educational materials continuously with the patient / informal care givers via HL7 FHIR based integration with the Patient Empowerment Platform (PEP). It enables collection of patient provided data from PEP including feedback on care plan goals and activities, medical device readings, symptoms and patient recorded outcome measures. Same messaging between care team members and patients is also enabled.

Extended features to enable collaboration of multidisciplinary care teams including the patients: C3DP offers a complete suite for integrated care planning with the following additional features: discussions on individual care plan items among MDT members; management of the multidisciplinary team of care (MDT) of a patient; safe messaging among all care team members; a personalised activity calendar for the health and social care workers; real-time system notifications for any update on the care plan or availability of new data.

Easy management and extensibility: C3DP provides several management functions to the administrators such as enrolling health professionals, patients, managing value sets and education materials. C3DP is a generic and extensible care plan management solution. In C3-Cloud, it has been used for the management of four main conditions (type 2 diabetes, heart failure, chronic kidney disease and depression) and associated comorbidities; however, it can easily be integrated with further CDS services for the management of other diseases via updating some configurations only.

6.3. Referenced deliverables and milestones

Deliverables listed below can be found on C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D4.1	Guidance for the Development of New Patient Pathways and Corresponding Care Plans	4	EMPIRICA
D4.2	New Organisational Models for Improved Delivery of Integrated Care	4	OSAKIDETZA
D7.3	Personalised Care Plan Development Platform	7	SRDC
D7.4	C3-Cloud Coordinated Care and Cure Delivery Platform	7	SRDC
D9.3	Test and Evaluation Report for C3-Cloud Components	9	INSERM

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS3	C3-Cloud Improved Models of Care Delivery for Multi-morbid Patients	4, 7	OSAKIDETZA
MS4	C3-Cloud Software Components Available and Tested	5, 6, 7, 9	INSERM

6.4. Lessons learnt

- Developing a single complex integrated system to work in three very different clinical and technical settings is quite challenging. Early demonstrations of initial prototypes to pilot sites proved successful to collect adequate feedback from the pilot sites especially related with particularities of each pilot site.
- Working with realistic care plan examples has eased testing the functionalities of the platform. Through the Clinical Reference Group (CRG) each pilot site provided realistic care plan examples, which have been then represented as HL7 FHIR Care Plan resources. Based on these mock patient data have been created reflecting the realistic care plan stories. The system functionalities and early integration tests have been conducted realistically in this way. This has also facilitated early validation by pilot sites and enabled us to collect early feedback.

6.5. Recommendations

- Testing the system with real but de-identified patient data is highly recommended in future deployment activities with new pilot sites. This may require thorough testing in production environments.
- Organize early validation studies to collect feedback from clinical experts at pilot sites even during iterative development phases.
- Ensure involvement of technical teams of pilot sites which is key for successful integration, deployment and operation.

7. IMPLEMENTATION OF A PATIENT EMPOWERMENT PLATFORM FOR ACTIVE ENGAGEMENT OF PATIENTS AND THEIR INFORMAL CAREGIVERS

7.1. Background

A Patient Empowerment Platform (PEP) acts as the gateway for active participation of patients and their informal care givers including family members to their integrated care management. Multi-morbid patients will be involved in collaborative creation and execution of personalised care plans through the Patient Empowerment Platform, which will enable shared decision making with the multidisciplinary care team (MDT).

The Patient Empowerment Platform provides the following to the patients:

- Gives patients and their informal caregivers a voice in the management of their own care
- Enables messaging between the patient/informal caregivers and the MDT (multi-disciplinary care team)
- Provides access to the up-to-date, integrated care plan and the agreed goals and activities to manage the own health

- Gives access to relevant information and training material specifically chosen for the patient by the MDT
- Allows the patient to share info and data with the MDT (including questionnaire responses, measurements, photos and other observation information)
- Support patients to upload measurement data from connected sensor devices

7.2. Main results

In WP5, the Patient Empowerment Platform has been developed to provide self-management support to educate and train the patient in an interactive manner; actively monitor patient's symptoms; actively participate in setting the goals in their personalised integrated care plan, the aimed time plan, and the list of treatment interventions to achieve these goals; update their progress in achieving these goals; and additional risk monitoring tools such as Activities of Daily Living Index (ADL) to facilitate monitoring of personalised risk factors for patients. Patients and their informal caregivers are able to remotely get in touch with the MDT members through the platform. PEP has been built on top of existing patient empowerment mechanisms and homecare solutions in our pilot sites and the CE Mark certified Medixine Suite product, which provides Web and mobile (phone and tablet) based patient engagement tools. Figure 8 highlights the Patient Empowerment Platform within the C3-Cloud architecture.

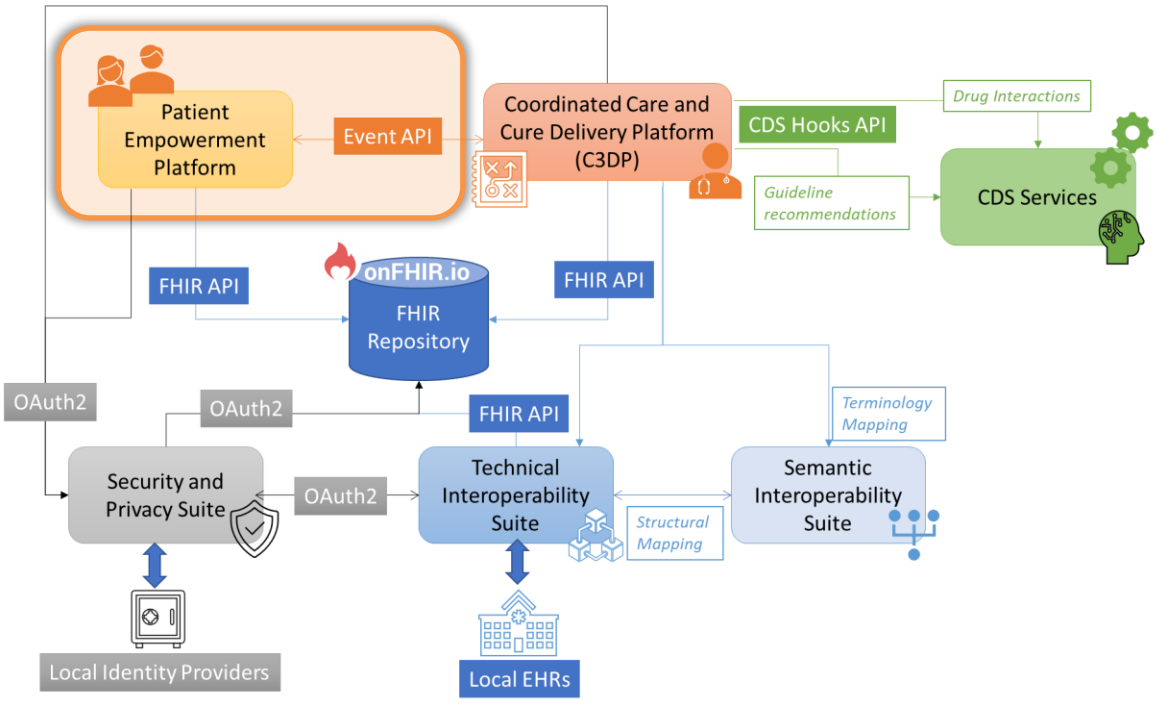

Figure 8: PEP within the C3-Cloud architecture

Training materials have been developed for the patients and their informal care givers to increase patient's adherence and confidence in their care management. These include the introductory training video on the impact and complexity of long term disease and multi-morbidity, the catalogue of existing training programmes, patient support groups and information sources, the C3-Cloud leaflet and the wallet sized project card.

The development of the patient data collection and feedback mechanisms specified for the C3-Cloud solution was completed with two prototypes developed and early integration with C3DP. When iterating the content for patient empowerment with the pilot partners, we made a significant effort to identify what is common in the content for patients for all three pilot regions and what is local to a specific partner. The configurability of the PEP solution allows the local deployments to adapt (for instance the

patient questionnaires, observation types and common info materials for all patients can be managed via the PEP admin tools), but it is very important to find as much common as possible to keep the local configuration management effort as small as possible.

PEP provides access for a patient to the published care plan and its associated information via a web application. Figure 9 shows a screenshot of an example care plan view for a patient. The core PEP functionalities are:

- Care plan access
- Reminders to increase adherence
- Actively collect data related to the care plan activities
- Safe messaging
- Access to relevant self-management material

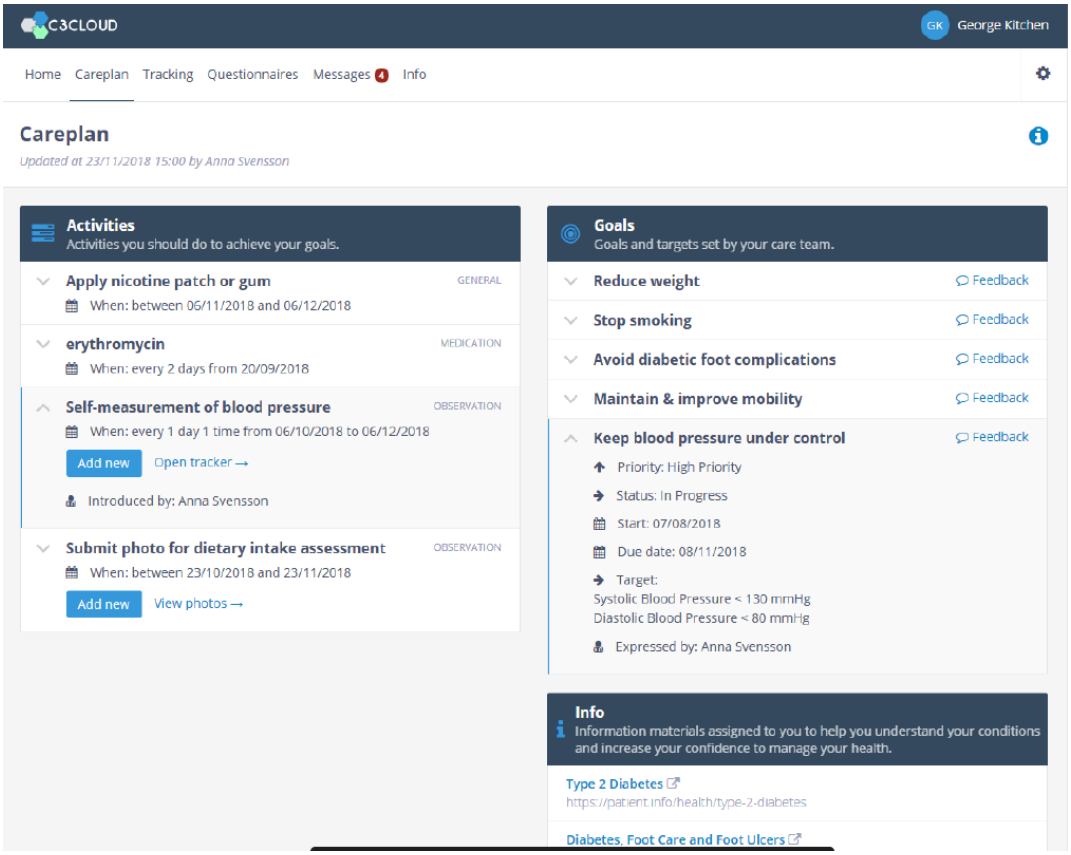

Figure 9: Example care plan in PEP

7.3. Referenced deliverables and milestones

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D5.1	Self-Management Training Materials for Increasing Patient Adherence to Care Plans	5	SWFT
D5.2	Data Collection and Feedback Mechanism	5	MEDIXINE
D5.3	Responsive Multi-Channel Patient Empowerment Platform	5	MEDIXINE

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS4	C3-Cloud Software Components Available and Tested	5, 6, 7, 9	INSERM

7.4. Lessons learnt

- With three different pilot sites and cultures, there is a need to balance a common solution for all pilot regions, but still be able to adapt it locally. It is important for the content for patient users to feel especially local.
- Configurability makes it possible to adapt the common solution locally. Active dialogue between developers and the pilot partners was very important to identify what is common and what is local.
- With differences in user ICT skills, the elderly, multi-morbid patients is a challenging user group for an innovative IT solution. The solution must be easy to use for these patients to be willing to participate.
- There is risk of additional burden to the healthcare professionals if the use of platform is not carefully planned. For the patients, there is a risk of information overload if the care plan is large.

7.5. Recommendations

- Having an integrated care plan supports the provision of personalised information and local content.
- Enabling loved ones to act on behalf of the patient for those who need it, can help with the differences in ICT skills.
- Centralised planning of organisational workflows and the content can help to minimize the burden on healthcare professionals.
- To minimize the risk of information overload, the patients should be given focused views with only minimum amount of information at any one time.

8. DEPLOYMENT AND OPERATIONS OF THE C3-CLOUD SYSTEM

8.1. Background

One of the aims of the C3-Cloud project was developing ICT platforms (Personalised Care Plan Development Platform & Coordinated Care and Cure Delivery Platform) and supporting Clinical Decision Support Modules, in order to enable a multidisciplinary team of health and social care givers to collaboratively create, execute and monitor personalised care plans, through reconciliation of clinical guidelines for individual diseases.

This involved two main strands of work: i) implementation of the Coordinated Care and Cure Delivery Platform (C3DP), which acts as a workflow engine to facilitate organisation, planning, and monitoring of integrated care activities, and to enable flagging of unperformed activities and unmet goals for later follow up within the scope of a personalised care plan, and ii) integration of all C3-Cloud software components that were developed within the project with local Electronic Health Record (EHR) and Identity Provider (IdP) systems of the pilot sites.

In order for the C3-Cloud Pilot application to be deployed in real-life settings a number of steps needed to be carried out: (i) definition of the requirements and the detailed design of the C3-Cloud pilot

application, (ii) ensure data quality and readiness of the pilot sites before deployment and (iii) manage the deployment and operation of the pilot application in real-life settings.

8.2. Main results

The requirements of the C3-Cloud system were achieved by means of detailed use case scenarios capturing the intended use of C3-Cloud, as the basis to extract and elicit requirements. One scenario was developed per pilot site, with the involvement of multidisciplinary team members and patients. From the scenarios, 60 different Pilot Application user Requirements (PAR) were identified and mapped to different required C3-Cloud High Level Components (HLC). The current ICT landscape at each pilot site was also mapped and described, enabling the development of use cases and requirements for the pilot site application in the different regions.

The definition of the deployment requirements of the HLC to be implemented at the pilot sites was described in the High-level Deployment Design of the system. It mapped the components identified in the logical architecture to physical servers and other network devices to create deployment architecture. It included the Application Architecture, Technology Architecture, Deployment Architecture, Physical and Network Architecture and Non-functional requirements:

- The Application Architecture is a high-level view of the layers, an example if given in Figure 10 for the Osakidetza pilot site.
- The Technology Architecture represents the frameworks and technology used in each layer. It specifies for each of the HLC: the Development platform, Web Server, Application Server, Database Server and Messaging Server.
- The Deployment Architecture depicts how the software is packaged and installed and describes the resource requirements needed to deploy it. It involves resource sizing in a physical environment, which includes computing nodes in an intranet or Internet environment, CPUs, memory or storage devices. Strategies differ from Windows (Patient Empowerment Platform) to Docker (rest of the components).
- The Physical and Network Architecture defines and describes the hardware resources and communication infrastructure. Each module is deployed only in one machine at a time. They include a reverse proxy and load balancer on top of the modules as a single entry point.
- The Non-functional Requirements (system qualities) are persistent qualities and constraints of the system that ensure the usability and efficacy of the entire system to satisfy internal business, user, market needs, or regulatory or standards agencies. They provide guidance on hardware configurations for performance, availability, scalability, and other related quality of service (QoS) specifications.

This design was adapted and refined according to the final HLC and Pilot Sites requirements based on security and privacy protection policy and distribution model at each site and reviewed before the deployment per pilot site.

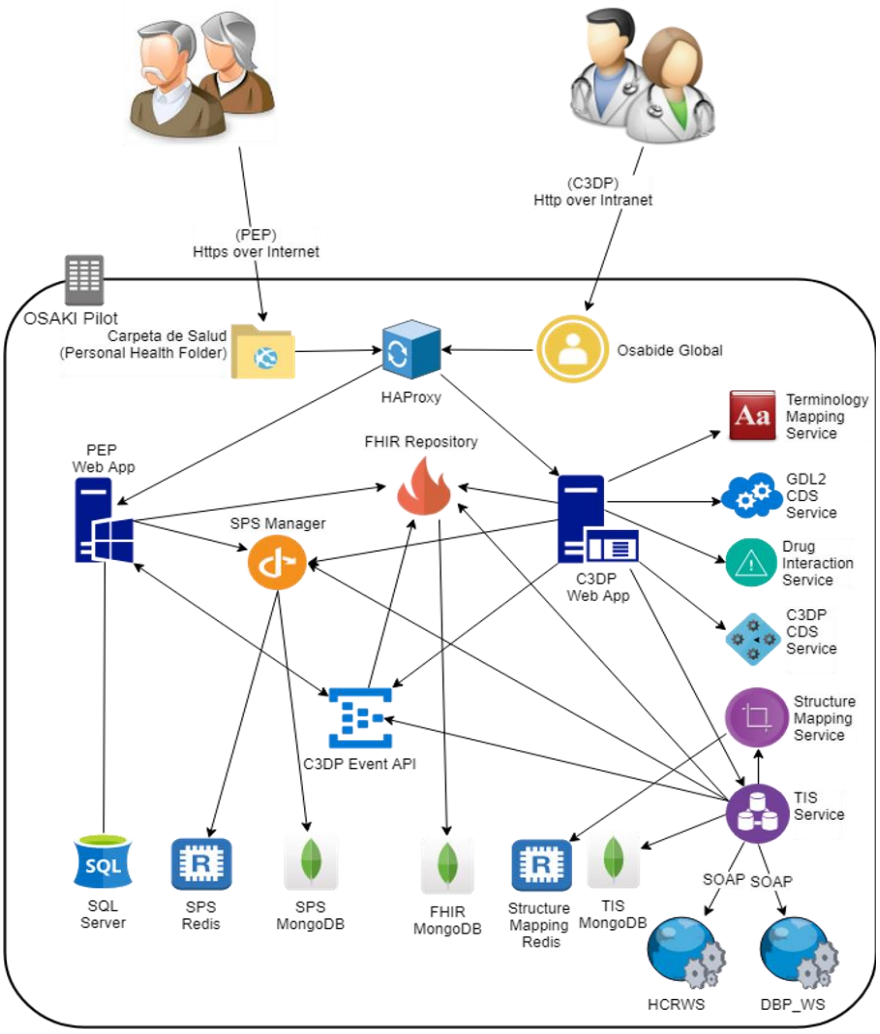

Figure 10: OSAKIDETZA pilot application architecture

In order to facilitate the deployment of C3-Cloud application in real-life settings and operations, pilot sites first needed to prepare C3-Cloud servers for hosting pilot applications. This preparation involved the following activities:

- Following the integration and component testing, technical partners finalised software features based on testing and evaluation feedback and built the final release of C3-Cloud software ready to be deployed.
- Pilot sites acquired and prepared the hardware servers, installed operating systems and database software according to the physical architecture design.
- Technical partners and pilot sites agreed on the domain names of all installable components. Pilot sites registered the domain names in DNS service and acquired SSL certificates for Internet facing components.
- Pilot sites set up required network services such as SMTP provider for sending emails, and open network ports necessary for component installation.
- Pilot sites prepared their patient data API services, described below, and identity providers and made them available in the pilot infrastructure.
- A private Docker registry at was set up for C3-Cloud so technical partners could push Docker images to the registry from developer machines and pull images to pilot servers during installation.
- Every technical partner signed a one-to-one non-disclosure agreement (NDA) with pilot sites and applied for VPN accounts in order to access the pilot servers remotely.

- Technical partners tested VPN connections and made sure all installation dependency was satisfied in pilot servers.

Close collaboration between the technical partners and pilot site IT teams ensured the proper installation and configuration of pilot IT infrastructure and the integration and deployment of 17 C3-Cloud software artefacts, produced by the 7 high-level components in South Warwickshire, Basque Country and Region Jämtland Härjedalen.

Necessary for integration with pilot site systems was configuration of the TIS component, implementing the technical layer of interoperability. TIS provides a generic ETL framework independent of any particular EHR data exchange protocol. To integrate specific EHR data sources, an ETL task was built for that data source using the TIS framework. In the scope of C3-Cloud, TIS integrated the three pilot sites through their respective APIs for patient data access. Table 1 summarises the data exchange mechanisms used by each pilot site.

Table 1: Pilot sites data exchange API

Pilot Site	*EHR Data Exchange API*	*Description*
OSAKI	CDA Web Service	The web service is a SOAP service, which returns the document of Summarized Clinical History of a patient in HL7 CDA R2 format. The CDA document contains the patient's demographics, conditions, medications, procedures, allergies, etc.
	DBP Web Service	Similar to the CDA service, this is a SOAP service which returned patient observation data, vital signs, test and immunisations
RJH	Cambio Open Services - Diagnoses	The REST service returns all diagnoses for a patient. The selection can be filtered with reference to time period.
	Cambio Open Services – Medical notes	The REST service returns all journal entries for a patient. The selection can be filtered with reference to time period.
	Cambio Open Services – Laboratory chemistry	The REST service returns all laboratory response chemistry for a patient. The selection can be filtered with reference to sampling time.
	Cambio Open Services – Drugs list	The REST service returns all pharmaceutical list for a patient. The selection can be filtered with reference to time period.
	Cambio Open Services – Patient	The REST service returns demographic data for a patient.
SWFT	EMIS data extract	The patient data extract is a CSV file generated from EMIS reporting service. EMIS is a GP system in SWFT. The extract contained patient demographics, conditions, lab tests, vital signs, medications, vaccinations, allergies, procedures and encounters. The extract is updated on a weekly basis.
	Lorenzo/GAP data extract	The data extract is a CSV file generated from Lorenzo/GAP. Lorenzo is a patient administration system in secondary care and community care. GAP is a community scheduling tool in community care. The extract is updated on a weekly basis.

Pilot sites provided two environments, staging and production. Ensuing industry best practice, pilot applications were fully tested in a staging environment with anonymised multi-morbidity patient samples before being replicated to the production system. An agile approach was used to continuously integrate and deploy components as soon as they were ready. Once the staging environments were tested and accepted in the three sites, production environments were deployed and tested by clinical and

administrative personnel. Issues in both Staging and Production environments were identified and resolved by technical partners in collaboration with pilot sites, including changes to features and updates to support idiosyncrasies in production data.

After finalizing the testing, training was arranged for healthcare professionals at sites and the study using the C3-Cloud system was started. Live use of the system commenced in November 2019 in all three pilot sites. Details of testing and enhancements made to the C3-Cloud components during this period were documented in Deliverable 9.5. Any requests for changes to the components made after the start of the study were carefully considered. In preparation for the end of the study, a closure plan for the C3-Cloud study and associated systems was developed to document the processes needed to safely and effectively manage the shutdown of both systems and operations and include notification of users, archival/transfer of data, archival of docker containers and removal of access rights and accounts, with processes detailed in the closure plan being followed to decommission software components and related assets.

8.3. Referenced deliverables and milestones

Deliverables listed below can be found on C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D8.2	Design of the Implementation of the Pilot Application Scenario	8	KRONIKGUNE
D7.4	C3-Cloud Coordinated Care and Cure Delivery Platform	7	SRDC
D8.3	Deployment of C3-Cloud Pilot Application	8	WARWICK
D9.5	Interim Evaluation Results for the C3-Cloud Pilot Application	9	EMPIRICA

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS4	C3-Cloud Software Components Available and Tested	5, 6, 7, 9	INSERM
MS5	Coordinated Care and Cure Delivery Platform - Integrated System and Pilot Application Ready for Deployment	7, 8, 9	SRDC

8.4. Lessons learnt

- Active communication between pilot sites and technical partners were crucial to make sure the challenges were well understood and actions are taken in time to address them. Dedicated one-to-one meetings and/or regular team meetings were scheduled every one or two weeks to review the progress and adjust plan based on the site's own circumstances.
- GitLab issue tracking tool was used to manage the issues identified during testing and to support operations during the pilot study. It was used by technical partners and pilot sites. It allowed categorization of issues which helped to prioritize work.
- The signature of Data Processing Agreements (DPAs) between pilot sites and technical partners facilitated that technical partners provide support during the operation phase.
- Any delay in completion of C3-Cloud component development and integration, impacts on the deployment process. The readiness of each component and its integration has to be assured before the deployment starts.

- The testing has ensured the system is enough robust and reliable to be used by HCPs and patients during the study.
- Making C3DP available to all pilot sites and technical partners from the very early days of the project facilitated gaining feedback and improving the system in advance. Yet, testing with real data and real end-users revealed several unnoticed issues or brand new feature requests.
- As the entrance point for all professional users, whenever there is an issue in any C3-Cloud component, this is most of the time detected via C3DP. Therefore, it is very important for C3DP to have traceability functions available to the users.
- The semantic interoperability mapping tools required validation schemas to ensure data was not corrupt and appropriate information was fed back to user.
- Defined concept codes for conditions needed to cover as many historical concepts as possible to ensure information was not missed.

8.5. Recommendations

- Testing of prototype systems should take place as early as possible to ensure additional features or unnoticed issues are identified early even though pilot sites may want to have testing once all components are integrations are in place. Where software is being tested in a technological research setting, issues not critical to trial operations need to be accepted to avoid delaying trial start and workarounds need to be provided to avoid issues during trials.
- Processes for managing changes to reflect other components are essential for maintenance and ensuring consistency between components and their interfaces/functions.
- Test scripts are essential for providing a summary of typical scenarios, e.g. for CDS services, and for ensuring all aspects of a system are tested systematically between changes.
- Test data needs to mimic inconsistencies found in production data for robust development.
- Data displayed to patients will want to be reviewed and filtered by HCPs so this should be built into patient facing systems by design.
- Well defined processes for importing data are required if not importing via an API to avoid data corruption or incompatibility issues and the capability of API functions exposed by source systems needs to be communicated early on to ensure necessary functionality to handle them is built into the components being deployed.
- Regular feedback from testing at sites is required for efficient issue resolution.

9. ACHIEVING INTEGRATED CARE COORDINATION – RESULTS FROM C3-CLOUD

9.1. Background

In WP9 we tested the C3-Cloud components (T9.1 and T9.2), planned for the evaluation and the technology trials (T9.2 and T9.3), developed training material and procedures (T9.4) and evaluated the use, acceptance and impact of the C3-Cloud components and the pilot technology trial (T9.5).

In D4.3 we developed updated guidance for the development future (I.e. beyond C3-Cloud) development of integrated multi-morbidity care pathways and care plans, based on lessons learned from the C3-Cloud development and its technology trial.

9.2. Main results

The evaluation plans have been prepared and documented in a research protocol (D9.2 and journal paper under review). The main research question is: “Is the use of a personalized ICT tool that facilitated care planning, treatment optimization and patient self-management acceptable to patients with multiple long-

term conditions and their team of health professionals?". Figure 11 gives a summary of the four phases of the evaluation.

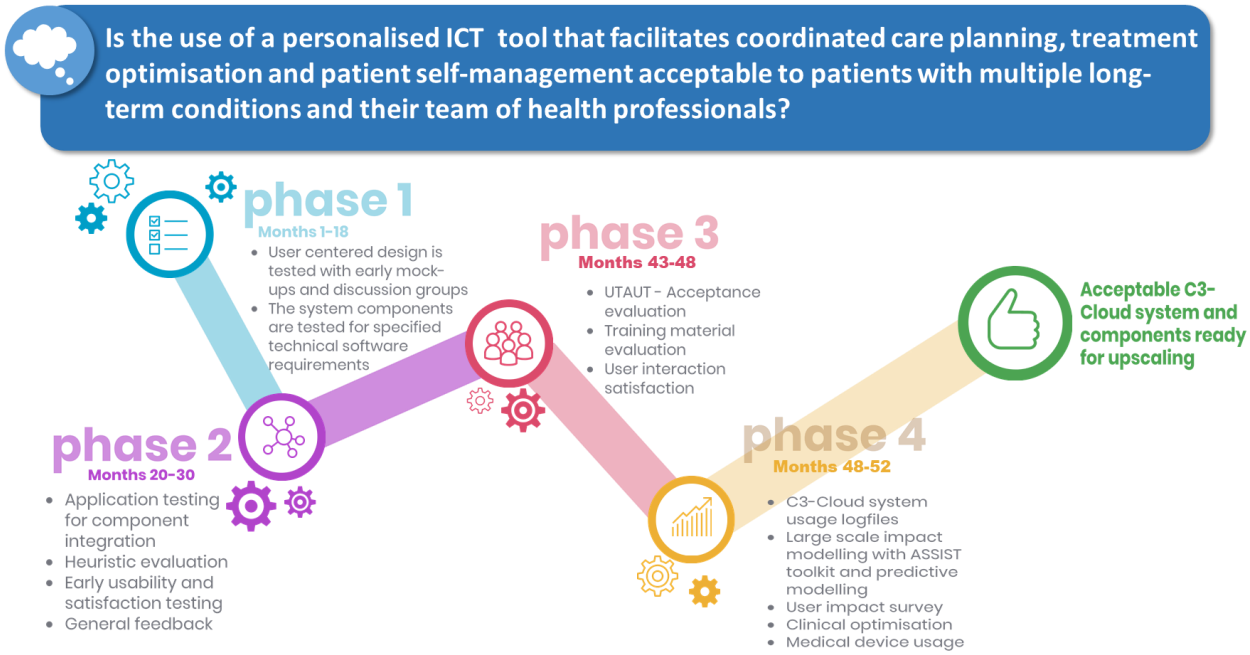

Figure 11: Evaluation phases

In Phase 1, user centered design using mockups and discussion groups was tested. Also, clinical users tested if the system complied with their clinical and technical requirements. In Phase 2, the integration of all C3-Cloud components and the user experience was tested by means of heuristic evaluation, early usability tests and user a satisfaction survey. During these two phases we learned that users found the solution very promising already during the early development phase. They believed that the suggested care plan goals and activities were meaningful and the operation on the platforms was intuitive.

During and after the first two phases, the C3-Cloud development partners worked on implementing the feedback that was received. The C3-Cloud components have been tested and the test results were reported in D9.1. The evaluation criteria were defined in the research protocol in D9.2 and first tests were carried out and reported in D9.3. That was followed by the completion of the deployment of the C3-Cloud components carrying out the technology trial from November 2019 to April 2020.

For Phase 3, the fully deployed solutions were tested with users in Sweden, Region Jämtland Härjedalen (RJH); United Kingdom, South Warwickshire (SWFT); and Spain, Basque Country (BC) with a total of 126 healthcare professionals (HCPs) and 230 patients. We surveyed the acceptance, evaluated user training material, and evaluated the user satisfaction with the C3-Cloud platforms. Phase 4 involved analysing C3-Cloud usage patterns with data generated during the trial as well as developing impact scenarios if C3-Cloud were used at scale. Budget impact analysis and cost-benefit analysis methods were used for the impact modelling and for sketching scale-up scenarios.

Extensive user training material and training plans including technology trial guidebooks and C3-Cloud component technical guide books were developed and reported in D9.4. The interim test results, user enrolment and the planning of the impact modelling were reported in D9.5. The final results of user acceptance, satisfaction, usefulness, the budget impact analysis and the cost-benefit based impact modelling (ASSIST method) were reported in D9.6, showing overall acceptance of the C3-Cloud platforms and general scaling up potential (data basis had some limitations as explained in D9.6).

A monitoring tool was developed in WP9 based on standard operating procedures from T4.3. Regular discussions and updates to this tool were used to update the guidance for the development of new patient pathways and corresponding care plans as reported in D4.3.

We faced some challenges during the technology trial, including delays in finalizing the development and deployment in the pilot sites; patient recruitment issues; and the impact of the COVID-19 pandemic. Consequently, our users' experience with the C3-Cloud platforms was short and compromised. We have a limited data basis for the evaluation and the determination of significant resource use differences when comparing control patients with the C3-Cloud patients was difficult.

Despite this limited data basis, the following results are summarized for Phase 3:

- A rich set of training material and manuals was developed during the project. Users described the core training material overall trustworthy and easy to understand. Given the volume of user training material and supporting documents, it could have been expected that some users wished it would have been more concise.
- The analysis of evaluation surveys shows further, that HCPs indicated the platforms were generally rather easy to become skillful at, that they consider them useful for their job and the platforms fit well with the way they work and the services they provide on a daily basis. In addition, the organisations they work for were supportive of the C3-Cloud technology.
- Our surveys also showed that patients were slightly more positive than negative on whether to use the Patient Empowerment Platform (PEP) in the future, while they indicated that it was rather not worth the effort involved in using it. This shows that patients do see the potential of the C3-Cloud system, yet they could not be fully convinced of its use just during the trial. That finding was slightly different for HCPs who wanted to use C3-Cloud in the future and believed that it was worth the effort involved in using it. These responses show the potential of the C3-Cloud system and that it can be a useful and powerful system to improve patient care.
- HCPs do rather not believe that C3-Cloud will enhance their productivity just yet and they could not put the system to full use during the trial. That can be explained by fact that some HCPs used several systems in parallel to C3-Cloud and others experienced technical issues during usage that prevented them from using it to its full potential. The impression of "decreased productivity" is detrimental to what the C3-Cloud envisaged for HCPs and it should be carefully reinvestigated in a follow-up trial whether these statements hold or if their origin lies in the shortened trial period and the COVID-19 situation with a high workload and burden on professional staff. The latter may have turned HCP perceptions to negative opinions on the professional C3-Cloud platform.

In Phase 4, a discrete event simulation (DES) model was used to represent mathematically the natural history of C3-Cloud patients' health conditions. This allowed performing a budget impact analysis to generate economic healthcare resource consumption models (costs per patient and month) for the following 7 years. The significantly different cost categories determined included primary care consultations with general practitioners (GPs) and nurses; telephone contacts between patients and nurses; nurse home visits; and accident and emergency (A&E) unit visits. The ASSIST cost-benefit method was the last evaluation method that was applied in Phase 4, aimed at sketching the economic scale-up scenarios for the pilot sites, using a cost-benefit analysis and merging this with the DES results.

We first identified stakeholders who are involved or affected by C3-Cloud implementation, comprising patients and their informal caregivers, GPs, nurses, call center staff, hospital staff, the healthcare payer and software developers. We identified relevant positive and negative impact indicators along the categories "financial impacts", "resource use impacts" and "intangible impacts". Costs included for instance C3-Cloud development costs; forgone income from fewer GP consultations; time spent on training or inconvenience using the new system. Benefits included for instance Time saved during GP consultations; less reimbursement due to fewer GP consultations; or improved satisfaction at work. "Fewer GP consultations" is both a cost and a benefit. This is based on the way we set up the analysis and illustrates a typical benefit shift. Fewer GP consultations may be a cost to the primary care organization, but a benefit to the institution that reimburses such consultations.

After performing the full impact modelling, we found that the three regions vary regarding their overall cumulative socio-economic return (SER) figures for the stakeholder groups and their systemic socio-economic return. Interestingly, the general direction has shown similarity in all three pilot sites (Figure 12).

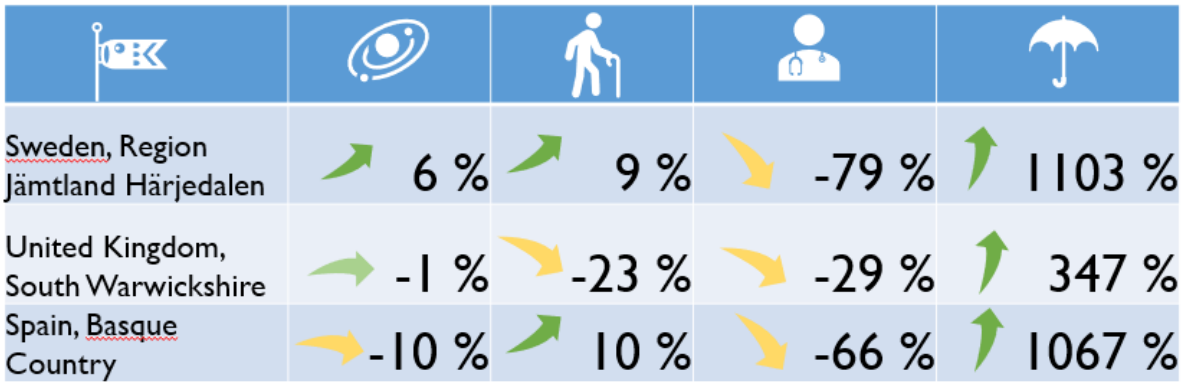

Figure 12: Overall socio-economic return for the whole service system (systemic SER), for patients, for primary care and for the payer

Patients and their informal caregivers have an intermediate perception of the system and their costs and benefits are rather equalling out. The Healthcare professionals have a rather large negative SER; however, this translates only into marginal costs in absolute terms (i.e. a couple of ten thousands €). Healthcare organizations are the losers in terms of SER. This is explained largely as in the current models they pay for HCPs training time on C3-Cloud, medical sensor devices (i.e. weight scales and blood pressure meters, and they have forgone income for instance from avoided GP and nurse consultations. It can be debated if this is indeed a loss in income, as it is largely dependent on the reimbursement schemes given in the pilot regions. Also, a reduction in GP and nurse consultations will in effect liberate their time which they could spend to provide better quality care. As a secondary effect, we could then see increased HCPs work satisfaction and patients may feel better cared for. Thus, if fewer consultations would not go along with reduced reimbursement for the health care providers, their SER could be more positive.

The great winner in the model, under given assumptions, will be the payers that cover costs for general healthcare provision. Be that the Ministry of Health, a health insurance, or the NHS. The Payers save large amounts of money with a highly positive SER, ranging from 347% in South Warwickshire to 1103% in Region Jämtland Härjedalen.

9.3. Referenced deliverables and milestones

Deliverables listed below can be found on C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D9.1	Functional and Non-functional Testing Criteria for C3-Cloud Components	9	EMPIRICA
D9.2	Qualitative and Quantitative Evaluation Criteria for C3-Cloud Pilot Application	9	EMPIRICA
D9.3	Test and Evaluation Report for C3-Cloud Components	9	INSERM

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D9.4	User Training Materials and Preparation Outcomes	9	KG
D9.6	Final Result of Evaluation and Modelling Large-Scale Impact of the C3-Cloud Pilot Application	9	EMPIRICA
D4.3	Updated Guidance for the Development of New Patient Pathways and Corresponding Care Plans	4	EMPIRICA
D4.4	Guidelines for Management of Changes in the Models of Care Delivery	4	EUROREC

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS6	Availability of Final Validated C3-Cloud Solution, Business Plan and Guidelines	1, 2, 4, 9	EMPIRICA

9.4. Lessons learnt

- Ethics boards in the different pilot site regions had different degrees of requirements for documentation. Our research evaluation protocol underwent several iterations for instance in RJH and SWFT, while it was less complicated at BC. This is time consuming and a risk to the trial starts, as ethics boards meet irregularly or for instance on a monthly term only. The timely start of pilot site technology trials would have been crucial to obtaining the data that was foreseen for the impact modelling.
- This goes hand in hand with the recruitment of patients which has fallen far below our expectations. Initial literature research suggested a positive patient response rate around 80%. What we have seen in the trials was rather around 10% with extra efforts to reach even that mark.
- The survey return rates may have been low due to lengthy surveys and generally a C3-Cloud usage frequency below our expectations. For future surveys, a way to contact and track survey responses anonymously and from the outset should be implemented to remind those trial participants to return their survey who had not done so.
- Due to the short duration of the trial, it was difficult to determine potential cost and benefit impact indicators for the several stakeholder groups that were involved or impacted from C3-Cloud. For future impact assessments, a use case workshop is suggested discussing in detail with key experts from the pilot sites, the impacts that the service implementation will have on specific stakeholder groups. This was done with selective experts bilaterally in the pilot sites yet a workshop format could have cross pollinated ideation.

9.5. Recommendations

- We recommend repetition of the evaluation technology trial after a thorough IT implementation and testing phase in a period that is less stressful for HCPs and patients (e.g. a period when COVID-19 is under control and staff can focus on the work involved in the trial).
- A dedicated period for patient recruitment should be planned which should be short and intensive, thus well-planned. This is because patients will be set off if several months pass between recruitment and the trial start. Patient IT support during the trial must be accessible to patients as easy as possible (“one-stop-shop”) as to avoid dropouts and resolve issues effectively and efficiently.

- The trial should last 18 months as to be able to observe health care resource thoroughly. Patient inclusion criteria could be stretched from mild and moderate conditions to include also severe conditions (if the CDS and patient characteristics / diseases support this). In addition, a follow-up trial could focus also more on the clinical impacts to evaluate clinical impact as well (e.g. health condition improvements or delay of deterioration, Quality of Life improvement).

10. THE FUTURE OF C3-CLOUD

10.1. Background

As we mentioned in Section 2, C3-Cloud has set out to a number of objectives in order to challenge the burden of multimorbidity. C3-Cloud proposes new patient pathways and organisational models for addressing multi-morbidity, complemented with innovative set of ICT tools for improved provision of patient-centred coordinated care services to elderly patients. Our solution will have impacts at multiple levels, ranging from improvement in clinical outcomes to strengthening the European industrial position in ICT products.

10.2. Main results

The C3-Cloud Exploitation and Route to Impact Framework has followed a stream of activities aiming to transform the project idea into technology and market-ready products/services, aiming to generate revenue into future commercialisation and incorporation activities, as well as scientific/knowhow assets and strengths for the consortium as a whole and its partners. The dimensions of the C3-Cloud Exploitation and Route to Impact Framework includes: commercial and incorporation exploitation; health and social care practice exploitation; industrial exploitation; research exploitation, both in terms of published outcomes, research pollination and future research agenda; education exploitation; open access to selected assets and results (open source repository); and standardisation & policy exploitation, in terms of influencing best-practice in digitally enabled integrated (coordinated) care (both at national and European level).

As the C3-Cloud components were technically mature, one of the aims of the project was to establish an exploitable integrated care solution. The EU Innovation Radar has recognized four of the C3-Cloud innovations as “Tech-Ready”. The project had tasks specifically focusing on the exploitation of the project and its continuation as a business. A series of activities and reports gradually identified exploitable elements, routes for exploitation, impact, and intellectual property of C3-Cloud and its dependencies on partners. These activities culminated with the production of the final exploitation and business plan, setting the scene and identifying the steps after the end of the project. The two reports complement each other, the former identifying the potential of the project to exploit its results, and the latter identifying the interaction of a follow-up commercial unit with potential customers.

The exploitation report produced the following results:

- Identification of exploitable assets, based on the contributions of the project; for example, definition of the clinical guidelines for each condition as a Clinical Decision Support System.
- Mapping of exploitable assets to architectural components and deployment modules. As C3-Cloud was structured around its architecture, it is expected that the architectural modules will be the products to offer.
- Identification of the functionality of the C3-Cloud family. This defined the functionality of each product, and ultimately the overall capability.
- Market analysis of the areas of relevance to C3-Cloud. Market analysis allowed to understand how C3-Cloud can be positioned within the market, and provided an estimate of the demand for such services. This has also provided evidence for the demand used in the business plan forecasts.

- SWOT analysis, identifying the strengths, weaknesses opportunities and threats for C3-Cloud in general, as well as the C3-Cloud family of products.

The business plan produced the following results:

- Specified the C3-Cloud Partnership Ltd as the business unit that will exploit the results of the project.
- Identified the products and services that will be offered to the customers, and prepared the information as it would be presented to the customer (product sheet).
- Specified the legal form and governance structure of the C3-Cloud Partnership Ltd.
- Defined a revenue, profit and cost model for the business.
- Developed a cost model based on previous costings of the C3-Cloud products.
- Provided a marketing analysis using the four Cs approach (Customer, Cost, Convenience, Communication).

A number of activities have also been identified, along with an expected timeline, which will need to be followed, to lead to the incorporation of the C3-Cloud Partnership Ltd.

10.3. Referenced deliverables and milestones

Deliverables listed below can be found on C3-Cloud project website.

Deliverable Number	Deliverable Title	WP Number	Lead Beneficiary
D9.6	Final Result of Evaluation and Modelling Large-Scale Impact of the C3-Cloud Pilot Application	9	EMPIRICA
D4.3	Updated Guidance for the Development of New Patient Pathways and Corresponding Care Plans	4	EMPIRICA
D4.4	Guidelines for Management of Changes in the Models of Care Delivery	4	EUROREC

Milestone Number	Milestone Description	WP Number	Lead Beneficiary
MS6	Availability of Final Validated C3-Cloud Solution, Business Plan and Guidelines	1, 2, 4, 9	EMPIRICA

10.4. Lessons learnt

- The technical partners on the project had different demands and intentions regarding their intended exploitation based on their academic or commercial status. Business models for future exploitation or commercialization of C3-Cloud assets needed to take into account opinions of all partners to make the final business plan suitable for the whole consortium.
- Exploitation can be through a number of routes, such as commercial, social or political, through industry, research or education. All exploitation avenues should be explored within such a project as each will have a differing impact and return based on the asset being disseminated/exploited. C3-Cloud has achieved a comprehensive exploitation in terms of commercial and incorporation exploitation; health and social care practice exploitation; industrial exploitation; research exploitation, both in terms of published outcomes, research pollination and future research agenda; education exploitation; open access to selected assets and results (open source repository); and standardisation & policy exploitation, in terms of

influencing best-practice in digitally enabled integrated (coordinated) care (both at national and European levels)

- C3-Cloud is a flexible, modular architecture that can be customized according to the needs of each customer.
- Flexibility of C3-Cloud can be a competitive advantage, as most systems expect customers to adapt on their operations rather than the system to adapt on the operations of an organization. C3-Cloud is flexible enough to achieve this, and as a partnership C3-Cloud is small enough to achieve this.
- Flexibility of the architecture may result in unpredictability of the exact cost for new customers.
- Local care giving organisations will have tacit requirements that will not be revealed until the early stages of deployment.
- Local IT practices are not standardized and may have a variable effect on deployment. Issues such as firewalls, IT approval procedures, and accessibility of the system from users (e.g., terminals).
- C3-Cloud has achieved a very successful set of exploitable assets and technology, which have been recognized by the EU Innovation Radar. In terms of market size, the European e-health industry has leading positions in emerging fields, such as the market segments of telehealth/telecare, electronic healthcare records, clinical decision support systems and self-management technologies for patient empowerment (including devices and sensors), in which the C3-Cloud technologies and innovations are centrally positioned.
- C3-Cloud is relevant to a number of stakeholders including EHR vendors, and care giving organisations. However, at a first instance the first customers for C3-Cloud are expected to be care giving organisations, which would like to transform their service into integrated care.
- C3-Cloud exploitation and business goals should work in tandem with the objectives of individual partners, and not be in competition.
- The C3-Cloud partnership will need to be sustainable and not rely on significant external (to the consortium) funding source, which may have goals not in line with those of the partners.
- The C3-Cloud partnership would like to offer benefit to the community in addition to its commercial side.

10.5. Recommendations

- Completing a SWOT analysis for all exploitable components is useful for identifying possible future avenues for exploitation and helps to formalise the strengths and weaknesses of a product, assessing it against the wider market. This can then also inform marketing strategies in the future. Exploitable assets, whether tangible or intangible, should be identified as the project nears completion to inform what future exploitation activities are suitable.
- A thorough market analysis, covering all possible market segments a developed product can apply to help in developing projections for possible market share and profitability of an enterprise formed.
- Developing a business canvas helps formalise and identify possible market segments and value propositions of an exploitable asset. This also helps identify key activities, resources and partnerships needed to achieve a sustainable enterprise.
- Highlight the customize-ability of C3-Cloud to customers, and its adaptability to multiple clinical scenarios.
- Offer a cost model to customers, so that they can understand that higher degree of customization may incur a higher expense.
- Document service and clinical requirements clearly and unambiguously, so that there is clear consensus with the customer on what needs to be delivered. Furthermore, provide high quality traceability to specification and test cases. This can also server as evidence for compliance for the customers' local requirements.
- Provide a rapid development deployment, even with a skeleton functionality. This will allow to understand and de-risk local constraints such as IT firewalls, authentication methods, and approval processes.

- Provide focused perspectives for each stakeholder of the system, who may affect its procurement and deployment. Different stakeholders will be interested in different types of information such as clinical evidence, and evidence for cost savings.
- Include all stakeholders in the requirements process, making sure that the perspectives of the end users and the commissioning unit are represented, as they may not be the same.
- Provide a cost a revenue model that incorporates the business models of the project partners and does not undermine their business interests.
- Adopt a revenue and staffing model that allows the partnership to operate without significant overheads needing high upfront investment.
- Adopt an ethically responsible profit model, in addition to offering freely available content. An ethical profit margin will allow the partnership to grow whilst offering benefit to the community.

11. RESOURCES

11.1. Project information

- Project website: https://www.c3-cloud.eu
- EU CORDIS project record: https://cordis.europa.eu/project/id/689181
- OpenAIRE project record: https://explore.openaire.eu/search/project?projectId=corda__h2020::7fcd7f267ffcc860816802b3cbaea5ee

11.2. Pilot sites

Beneficiary Name	Contact Person	Country	Logo
Basque Country • Institute for Health Services Research Kronikgune (KG) • Servicio Vasco de Salud (OSAKIDETZA)	Esteban de Manuel *edemanuel@kronikgune.org* Antonio de Blas *antonio.deblasdeblas@osakidetza.eus*	Spain	kronikgune institute for health services research Osakidetza
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11.3. Other project partners

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