C3-Cloud

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

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

D9.5 INTERIM EVALUATION RESULTS FOR THE C3-CLOUD PILOT APPLICATION

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EXECUTIVE SUMMARY

In preparation of this deliverable, all project partners were heavily involved in advancing the C3-Cloud system and making it safe to use for the technology trial. The technology trial start has been delayed for several reasons: (i) continued updates due to the pilot sites' consideration of what an acceptable system us (with pointing out high-priority issues that needed resolving); (ii) the decision of the consortium to have a high-quality system that is closer to a clinical system than to a staging system and (iii) operational delays in the study preparation (e.g., the organization of trainings and clinic visits at the sites).

The technology trial has been prepared with 420 patients and 62 healthcare professionals recruited to the trial at the moment of writing this deliverable. It was originally envisaged that this deliverable would also present already structured information on the evaluation of the C3-Cloud platform. As the technology trial has just started in November 2019, the process of recruitment is still ongoing. Therefore, this deliverable contains detailed information on the improvements that were made towards the C3-Cloud system. Also, we compiled a detailed report on the recruitment of technology trial participants and gathered unstructured feedback from some of the participants that have started using the C3-Cloud system already.

The research protocol has been developed early in the project (D9.2). After that, feedback from the local ethics boards has been received at multiple instances which needed reflection in the research protocol, including changes to the system, the research conduct procedures and inclusion of historic control patient data, as well as several iterations of the translation of survey questions.

Over the last year, we have seen that a complex system such as C3-Cloud needed extensive, i.e. more than anticipated, testing during development but also after deployment of the solution to the staging environment. Pilot site managers were pushed by their healthcare professionals that they should only release a safe and usable system for the technology trial. Despite knowing that this is a technology trial, most clinicians are very busy and wanted only to use a system that is of high quality and near to a product.

We have also worked on the method and the technical approach towards the phase 4 impact modelling with Osakidetza's predictive modelling which will be combined with the ASSIST tool (cost-benefit modelling), which is described in chapter 7. Finally the pilot site managers describe their early plans or hopes for post-project deployment and scaling up the usage of C3-Cloud in their region or even nationally.

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1. BACKGROUND, PURPOSE AND STRUCTURE OF THE DOCUMENT

WP9 is responsible for the evaluation and impact assessment of the complex technical, organizational and clinical nature of the C3-Cloud components and pilot trials. A research protocol was initially developed in Task T9.1 and presented in deliverable D9.2, which is submitted for publication. The first evaluation layers/phases have been completed in Tasks T9.2, T9.3 and T9.4 and first results were presented in deliverables D9.3 and D9.4 respectively.

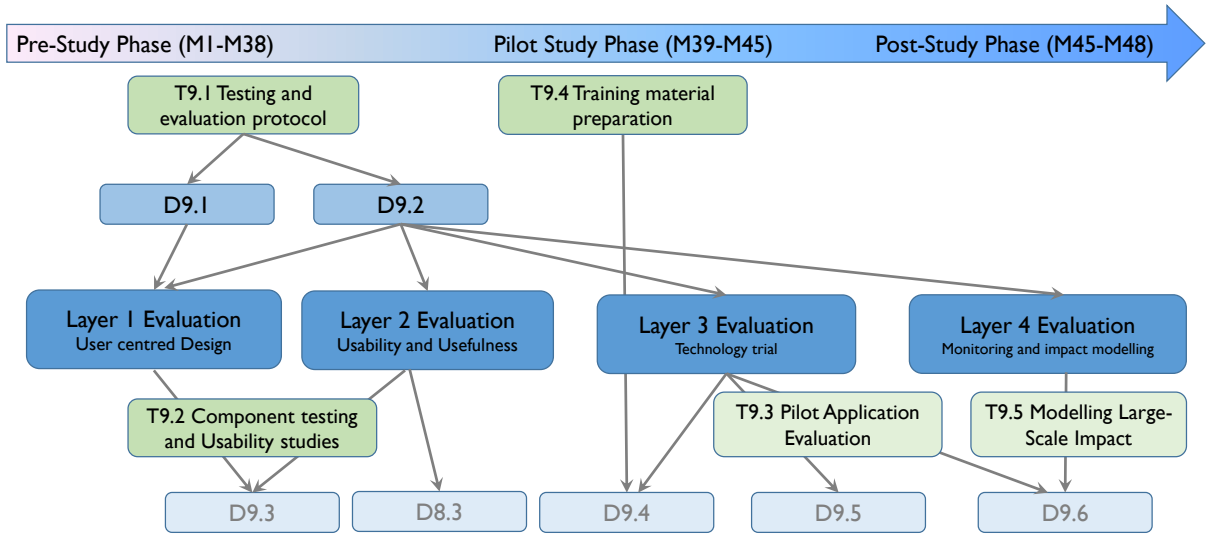

Figure 1: Interrelation between tasks, deliverables and the technology trial

This deliverable D9.5 builds on the experience gained during the previous work and presents the lessons learned until now and the evaluation results obtained so far from the Tasks T9.3 and T9.5. Task 9.3 concerns the pilot application evaluation with evaluation phases 3 and 4 and T9.5 concerns the large-scale impact modelling.

The purpose of deliverable D9.5 is to report on the activities towards the technology trial and, as far as possible, already describe testing results of the C3-Cloud system during deployment in the three pilot sites. The evaluation phases that included in T9.3 and T9.5 are presented in Table 1.

Phase	Evaluation Layer	Description
Pre-study phase	Phase 1: user-centred design (T8.1, T8.2, T3.2, T3.3)	Involvement of stakeholders, including care givers and patients in the design of the C3-Cloud components (e.g. functionality, content provided, language used, level of detail, user-friendliness) through requirements gathering and development of use cases.
	Phase 2: Usability and usefulness (T9.1, T9.2)	This phase provided feedback to T7.4 to inform the technical partners on the usability of the C3-Cloud software components to reconfigure and update the C3-Cloud components. The evaluation followed the testing and evaluation protocol defined in T9.1.
Pilot study phase	Phase 3: Technology trial (T9.3)	Involving 150 patients, their informal caregivers and 52 MDT members during the technology trial, phase 3

Phase	Evaluation Layer	Description
		evaluates the user experience and satisfaction with the C3-Cloud system, its usability and the training material developed in T9.4.
Post-study phase	Phase 4: monitoring for impact modelling (T9.5)	With the involvement of all 420 patients, their informal caregivers and 62 MDT members, phase 4 evaluates acceptability of the C3-Cloud system. It prepares the modelling of the large-scale impact of C3-Cloud implementation after the technology trial by obtaining data on healthcare resource usage and usage of the C3-Cloud system.

Table 1: Overview of evaluation phases

The deliverable includes the following chapters:

- A summary of the changes to the research protocol over time
- A report on the deployment testing of the C3-Cloud system and following improvements to the system
- A report on the recruitment of study participants
- Early, unstructured feedback from the healthcare professional training
- The approach towards the large-scale impact modelling tool
- Early deployment and scaling-up plans for the three pilot sites

1.1. Issues and Achievements

Issues: This deliverable D9.5 was postponed: The enrolment report and the report on the first evaluation surveys were envisaged for this deliverable. At the second periodic review meeting, the delay of deploying the live C3-Cloud system in the pilot sites has been discussed. It became apparent the critical assessment and testing through clinical and project management staff in the sites is crucial to deploy a software that is safe and ready to use. In addition, pilot site health care professionals and experts indicated that they will not pilot a software that has not been thoroughly quality tested in a staging environment before. Initially the trial start was planned earlier, with the submission of D9.5 scheduled for M40 (August 2019). The trial start was much later than originally planned which causes delay to conduct the first (i.e. baseline) evaluation surveys with C3-Cloud users. To allow sound reporting on what has been done in the meantime until pilot starts, a postponement of this deliverable to 30 November 2019 was requested and granted. The late trial start however is the reason that we cannot deliver structured evaluation results in this deliverable.

Achievements: The pilot sites and technical partners have developed and tested thoroughly the C3-Cloud system, which is now ready for use in the trials. In this process we implemented changes to the research protocol based on ethics committees' requirements. Despite issues with very low response rates to the trial recruitment, the pilot sites spent considerable time on mitigation actions and we managed to already include 273 patients to the trial across all three sites, with approx. 236 more patients that we expect in the next weeks. We have developed the approach towards the impact modelling tool and developed a set of indicators that we will be using for the modelling. In this context, the early deployment and scale-up plans have been discussed with the pilot sites and these were written up in chapter 8.

1.2. Abbreviations and Acronyms

Acronym	Definition
API	Application programming interface
ASSIST	The ASSIST toolkit - a socio-economic cost benefit analysis method
BC	Basque Country (pilot site)
BP	Blood pressure
CDS	Clinical decision support
CDSM	Clinical decision support module
CF	Cardiac Failure
CHD	Coronary Heart Disease
CIC	Corporate Identification Code
CNS	Community Nursing Services
COPD	Chronic Obstructive Pulmonary Disease
CSV	Comma separated values
CVD	Cardio Vascular Disease
DES	Discrete Event Simulation
DOA	Description of Action
DRG	Diagnosis related group
EHR	Electronic health record
EMIS	Egton Medical Information Systems
EMR	Electronic medical record
EPR	Electronic Patient record
FB	fractional bias
FHIR	Fast Healthcare Interoperability Resources
FV	Fractional variance
GFR	glomerular filtration rate
GP	General practitioner
HC	Health Care
HCP	Health Care Professional
HF	Heart Failure
HISA	Health Information Service Architecture
HLG	High level goal
ICD	International classification of disease
ICT	Information and Communication Technology
ITK	Interoperability Toolkit
KG	Kronikgune
MDT	Multi-Disciplinary Team
NHS	National Health System
NMSE	normalized mean square error
NYHA	New York Heart Association
PEP	Patient Empowerment Platform
PHR	Personal health record
READ	UK general practice Read codes
REC	Research ethics committee
RF	Renal failure
RJH	Region Jämtland Härjedalen
SIS	Semantic Interoperability Suite

Acronym	Definition
SPS	Security and Privacy Suite
SRDC	Software Research and Development Consultancy
SWFT	South Warwickshire Foundation Trust (pilot site)
TIS	Technology Interoperability System
UTAUT	Unified Theory on the Acceptance and Usability of Technology

2. CHANGES TO THE RESEARCH PROTOCOL OVER TIME

The research protocol presented in D9.2 has evolved over the duration of the project. Specifically, the following aspects were amended:

- Control patients will not be contacted for qualitative evaluation surveys: Despite our efforts, it was not possible to obtain ethics approval to contact control patients directly. However, their anonymous data on healthcare resource use will be used for the predictive modelling in T9.5. Historic control patient data from electronic health records (EHRs) will be used from different doctor cohorts / care centres in February 2020. No randomization will be done for the selection of control patients. Information retrieved will be on health care resource consumption. To ensure that data cannot be traced, the data extracts will not include demographic descriptors and identifiers. Data entry of resource utilization dates will be manipulated automatically and randomly within a determined range (+-30 days) for each data entry. The project partner Osakidetza developed an MS Excel based tool for data anonymization, which will be used by the pilot sites before transmission of the anonymized data sets to Osakidetza for analysis.
- The qualitative participant surveys and data extracts will be anonymized, as required by the pilot sites' ethics committees. As a result, we cannot link pre-trial and post-trial measurements.
- The technology trial time planning was revised a few times to re-align with the system development, deployment and testing. While this has negligible impact on the qualitative surveys, the validity of the predictive modelling will be reduced due to a shorter study period and less patient-clinician contacts that may occur in the shorter trial period.
- Osakidetza revised the power calculation for the discrete event simulation based on real-world data from their pilot site in the past years, which resulted in a reduced number of intervention patients needed for the predictive modelling. Originally (in the proposal), the plan was to involve 100 intervention patients at SWFT and 250 patients at both RJH and BC (600 total). This was reduced to a total of 420 intervention patients as an observation goal (i.e. patients that are still in the trial at the trial end and have not dropped out earlier) across the three pilot sites.
- During the recruitment period, keeping patients motivated to participate in the trial was very difficult. Reasons will be elaborated in the following chapters. As a result, we added the age range 55-64 to the inclusion criteria to allow for a larger cohort from which patients were recruited.
- All questionnaire (survey) items were translated from English to Spanish and Swedish. In this process, the original phrasing was reviewed and items that were no longer needed due to above changes were removed.

3. TESTING AND IMPROVEMENTS OF THE C3-CLOUD PILOT APPLICATIONS

The C3-Cloud Pilot Application has been extensively tested as an integrated solution in a controlled testing environment at the three deployment sites. This ensures functionality of the system and to maximize patient safety during the live technology trial. Initially, the C3-Cloud clinical reference group has been involved in this process, for instance, to review the Clinical Decision Support specifications, the activities and goals in the care plan, the definition of blood battery tests and their presentation in care plans.

Since the start of the deployment phase (as reported in deliverable D8.3), the pilot site managers and local clinicians tested the systems iteratively and reported their issues and feedback, using the GitLab issue tracking tool. The issues were categorized using labels: *high-priority, pending-testing, awaiting new deployment, C3DP, CDSM, Cambio, FHIR, Not for study, OSAKI, PEP, Pending future Development, RJH, SIS, SPS, SRDC, SWFT, TIS, bug, common, concept, configuration, discussion, documentation, enhancement, integration, Medixine, production, staging, suggestion, terminology, testing, usability*. Discussions on these issues took place during weekly and bi-weekly teleconference calls and communications via GitLab as well.

With over 300 issues handled, this section summarises the types of issues and requests made and to illustrate the significant amount of work that was done to ensure a high-quality system. For each of the main components of the C3-Cloud systems, we highlight key improvements that have been made ahead of the operational phase of the pilot study.

Table 2 shows the number of issues/updates, their type and whether they involve individual sites of all sites. Note that some issues/updates might appear in multiple categories.

Issue Type/Site Involved	All Sites	BC	RJH	SWFT
Bugs		3	5	2
Functionality (including integrations)				
Care planning	10	13	6	25
Clinical decision support	9	13	6	23
Patient empowerment		3	2	1
Terminology/Semantics		2	19	5
Interoperability		5	6	3
C3DP-PEP		5		2
C3DP-SIS	1	5	3	11
CDSM-SIS	4	5	1	
CDSM-TIS		1		
C3DP-CDSM	8	3	2	7
C3DP-SPS			2	3
C3DP-TIS		1	1	
TIS-SIS		4	1	2
Translation/Language	1	17	2	
Future development	3	3		5
Other (e.g. clarifications)	3	15	6	24

Table 2: Number of issues resolved and updates to the system

3.1. Key Enhancements in the Coordinated Care & Cure Delivery Platform (C3DP)

C3DP is the one and only C3-Cloud software component that is used by all health and social care workers in the C3-Cloud pilots and it is integrated with all other C3-Cloud components. It is the entrance point for all professional users so that whenever there is an issue in any C3-Cloud component, this is most of the time detected via C3DP. Therefore, more than half of the 300 issues in the C3-Cloud issue tracker are directly or indirectly related with C3DP. SRDC as the leader of C3DP has not only solved C3DP issues, but also provided debugging support to leaders of other components.

C3DP has been made available as a public demo to all C3-Cloud partners since September 2017 (M17) and was successfully deployed to staging environments of all 3 pilot sites by the end of October 2018 (M30) and to production environments in March 2019 (M35). It was tested heavily and several times in iterating sessions by all 3 pilot sites in between. Hundreds of feedbacks were provided to SRDC in this duration, which included some bugs, missing translations, improvement requests and new feature requests. SRDC has analyzed all the feedback and created the corresponding tickets in its own issue tracker and finally updated C3DP to resolve these issues. This has been a very time and resource consuming process but, in the end, it contributed a lot to improving the C3DP further and making it more stable. Almost all critical issues were detected and resolved for C3DP in this time frame. These have been explained in earlier activity reports. However, due to delays in some other components and in important data integrations, testing with real data and real end-users took place only after this time and as expected, this process revealed further issues including again bugs, improvement and new feature requests. Therefore, this section summarizes key enhancements that have been implemented in C3DP in this period of intense testing with real data and real end-users:

- A great majority of the update requests by the pilot sites were related with missing codes or clinical concepts that need to be matched as inputs of the CDS services. When faced with real data coming from the EHRs, the pilot sites noticed that the terminology codes they provided earlier in the semantic mapper sheet and hence being used for semantic interoperability were incomplete at times. This has led to continuous update of holistic profile with new concepts and especially terminology codes on the C3DP side. Most of the time, SRDC has also led the update of the semantic mapper sheet and informing the CDS implementer partners when relevant by identifying the clinical concept and the associated CDS service to be updated. In some cases, these processes even ended up with update of CDS service specifications as explained in the dedicated CDS services section below.
- The second highest number of enhancements were related with translation improvements. In some cases there were missing Spanish or Swedish translations, and in some other cases the pilot sites requested a better translation after seeing the data in full context. Overall, C3DP translations have been updates tens of times in this duration.
- Medical summary screen related enhancements:
    - Medical summary page was updated to display only the latest of each distinct patient record according to clinical terminology codes or titles, due to the fact that some real patient data contains more than 1000 records and repetition of a single condition around 300 times. It is still possible to see the whole history when clicked on an individual record.
    - It turned out that Osakidetza EHR services cannot provide datetime information for lab results; only date. However, they still want to see the measurements in the correct order, when synchronization is done a few times on the same day. In order to overcome this challenge, C3DP was updated to sort patient data in the medical summary not just according to observation date but also the insertion time at the FHIR repository.
    - It was observed that care barrier data are usually missing in EHR data, so it is now possible to add care barriers manually via medical summary screen. This has been implemented as an exception.

  - Further updates were done to interpret extra fields in the FHIR resources for richer display in the medical summary screen, due to the fact that medical data is not always consistent in real EHR data, especially among pilot sites.

- CDS integration related enhancements:
  - There had been several problems related with goal and activity recommendations that are supposed to be provided by CDS services, when tested with real patient data. It was very hard to understand the reason when some CDS services were not providing expected response, or any response at all. In order to facilitate debugging, SRDC first did an update in C3DP to display the code and code-system attributes for each coded element in medical summary and CDS required data sections. More importantly, SRDC implemented a new debug interface for all CDS interactions that shows the input and output of all CDS Hooks services. Thanks to these efforts, issues such as mismatching terminology codes or unaccepted lab result units were identified and resolved more easily by CAMBIO, WARWICK, INSERM and SRDC.
  - The collated responses of CDS services were not displayed altogether when one of the calls to the CDS services were failing. This has been updated to skip the failing response(s) and display the ones that can be processed correctly.
- Care plan creation and editing related enhancements:
  - SRDC implemented a mechanism to prevent publishing of tens of care plan update events. This used to be a problem especially while a care plan is created from scratch and several new goals, activities and education materials are created. A new publish button for care team members to inform the other care team members and patients has been introduced.
  - Improvements were implemented in major disease selection and hence assignments to high-level goals and CDS services while creating a care plan from scratch or updating it later, to better handle complex cases like several codes being available for chronic kidney disease.
  - There are defined expiration times for different types of data, e.g. 3 months for vital signs, 18 months for laboratory results, and these can change per pilot site. It was later decided to allow all active medications for import into the care plan by discarding the expiration time for medications.
  - A new patient activity and measurement, self-measurement of fluid balance, was defined and introduced in C3DP upon the request of Osakidetza.
  - The dates of matched records are also displayed along with their titles/codes in the CDS required data sections.
  - Updates were implemented in the display of dropdown lists with several options for being able to show all alternatives and easy filtering at the same time.
  - There have been updates in some laboratory result units for different sites. C3DP also allows prioritization of different units per site now.
  - Upon request of RJH, it is now possible to use comma and dot in the same way in decimals, which are used for providing some laboratory results manually if necessary.
  - The location fields (e.g. for appointments) support now both pre-defined locations and free-text entry at the same time.
  - There have been several rounds of updates of pre-defined education materials in all pilot sites.

  - SRDC completely changed the PDF extraction process for care plans. The current version is much more lightweight than the former. Some translation updates were done as well in the PDF content.

- Administrator functionality related enhancements:
  - It is now possible to refresh the semantic code mappings of the clinical concepts in the holistic patient profile via a button in the admin user interface, which calls the SIS semantic mapper service at the background for individual code mappings.
  - A bug in batch messaging functionality for the patients was fixed.
  - There have been major and critical improvements in evaluation data extraction, which provides a snapshot of all the care planning data in C3DP for the whole population according to evaluation data requirements in an excel document. This feature and the excel document outcomes were tested in a few rounds in collaboration with the WP9 evaluation team, until it answered all the requirements.
  - Upon request of SWFT, a new help menu dedicated to administrator users was implemented.
- PEP related enhancements:
  - SRDC implemented a new mechanism to dynamically update the view in the browser in real-time (i.e. without the need for refreshing the page) when some new data is provided via PEP (e.g. questionnaire response, observation).
  - SRDC and MEDIXINE have implemented a user friendly and simple way of goal feedback exchange from patient to care team members.
- Security and privacy related enhancements:
  - Upon request by pilot sites, it is now possible to suspend user accounts of care team members via Security and Privacy Suite (SPS).
  - SMTP accounts were set-up in SPS in collaboration with pilot sites to be able to send password renewal links and user account approvals via automated emails.
- Miscellaneous enhancements:
  - The display and filtering of all patients in the system has been improved to solve the problems that sometimes used to occur in paging of results.
  - After finding the chance to observe the system in operation, SRDC has realized some performance improvements such as reducing the number of HTTP requests in the summary pages and limiting the number of matched resources to latest five for each clinical concept that is required by any CDS service.

3.2. Key Enhancements in the Clinical Decision Support Modules (CDSM)

3.2.1. Addition of codes for conditions to CDS rules

Evaluation of the CDS services revealed that conditions imported into C3DP, which would normally be expected to trigger CDS suggestions were not doing so. It was found that the terminology codes for these conditions were not identified during the design phase for the CDS services. To rectify this an export of all historical conditions for consented participants was obtained from the affected site and based on this historical data in the EHR, missing codes were identified. In conjunction with a clinician, these codes were then mapped to existing concepts in the semantic mapper (or new concepts were added if no equivalent already existed) and added to the relevant CDS services to ensure all equivalent diagnoses to those specified at the design stage were captured and recognised by the CDS.

3.2.2. Addition of input validation schema

During testing it was revealed that a lot of data needed by the CDS rules were corrupted* causing the CDS engine to return an error. In order to prevent this from happening an input validation schema was implemented. This feature provides the following benefits:

- Ensure that there are no corrupt data* in the input provided to the CDS engine
- If corrupt data* exist in the input, provide a meaningful feedback to users and technicians regarding which data specifically are corrupted and what the expected form should be.

* Corrupt data refers to data that are:

  - Missing important information such as dates, units, terminology, codes etc.
  - Not based on international standards or according to the standards decided on this project

3.3. Key Enhancements in the Patient Empowerment Platform (PEP)

Much of the feedback received was related to how the integrated care plan created by the multi-disciplinary team (MDT) in C3DP is displayed to the patient and the informal caregivers. The main page contained too much detail and was changed to provide a more compact summary of the plan, in which the number of goals, activities and guidance materials assigned to the patient are shown to the users. Some changes were also made to the care plan detail page fine-tuning how the information available in the care plan data is shown.

A section with active tasks was also added to the main page. This section displays data collection tasks like completing questionnaires and registering measurement values. It only displays uncompleted tasks and a task is hidden when the patient completes the task. This makes it easier for the patient to know when the patient is expected to do something in the system.

The care plan feedback functionality was changed to allow patient to give feedback on the goals and the progress using a free-text field and a 3-level mood using smileys (sad, neutral, happy).

The health professionals expressed also the need to hide some goals from the patient as they would be too clinical and not clear for the patient. C3DP added a Boolean toggle to record whether to display the goal to the patient or not. In PEP only goals marked for display are shown in the user interface.

These and other changes made to C3DP required some changes to the structure of the care plan FHIR. The PEP displays were updated to handle these changes. Some minor changes were made to the FHIR data written by PEP to make it easier to consume the data in C3DP (e.g. meta tag added).

3.4. Key Enhancements in the Semantic Interoperability Suite (SIS)

During test and evaluation, issues related to structural mapper were mainly due to the gap between live production data and the test patient data provided during development of the tool. Each site implementation of structural mapper was in need of updates to correct mapping error coming with new patient data mainly due to new use case not seen during development stages.

Further updates included:

- Some issues were about the development of specific mapping for specific terminology codes.
- Some improvements were also made about MedicationStatement generation dosage mapping specially for RJH site.
- Some filters were made to ignore some data that were not usable for the project.
- Some minor bugs about Date, Numeric values were also treated.

3.5. Key Enhancements in the Technical Interoperability Suite (TIS)

3.5.1. Update to support changes to patient record before last import

A limitation of the original TIS design was that, while it allowed information to be pulled from the EHR, there was no functionality which reconciled this information with data already in the C3-Cloud FHIR repository. This meant that only data after the last import could be added and any changes to old data would be lost. TIS was enhanced to allow import of the complete history of a patient from the EHR and by comparing differences between the import and the data in the FHIR repository, update or delete items already in C3DP where it had changed. This enhancement allowed C3DP to accurately reflect the data in the source EHR eliminating the risk that decisions would be made on incomplete or incorrect data.

As part of the change, TIS needed to be updated to support pagination through the FHIR query response to allow the full history of the patient to be retrieved before import for comparison with the data from the source EHR. This, however, introduces a new risk in that as the whole patient record is retrieved, as the patient record grows, the time taken to retrieve this data would increase leading to a timeout on the C3DP side. This would need to be addressed if the system were taken beyond the prototype/trial stage.

Additionally, due to the changes made to support the previous enhancement, TIS was further updated to allow changes to the Patient FHIR resource. This meant that corrections or updates to names, dates of birth, addresses and demographics, including ethnicity etc. could be captured in C3DP, further reducing the risk of decisions made on incorrect data and allowing the tracking of participants if their contact details changed.

3.5.2. Multiple updates to support import of additional data items

During evaluation by HCPs in preparation for the trial, field codes for items imported from site EHRs changed or new fields were requested by HCPs. This was supported by updating the configuration in TIS to request new fields, for API based calls, or supporting changes to field orders in CSV uploads. Additional changes to the structural mapper and C3DP allowed these new items to be properly mapped and displayed in C3DP. For usage beyond the trial updating configurations for source data mapping should be supported to quickly allow for updates in source systems to be addressed without the need for technical support or new deployments.

Among the updates made, metadata around diagnoses and procedures were added. This provided more information to HCPs in C3DP, such as dates of diagnosis and periods for episodes of care, as well as additional information for CDS services to tailor rules based on diagnoses with a particular recency.

3.5.3. Update to support time and period cut-offs for historic data import

Related to the changes needed to support updates to the patient record. TIS was enhanced to allow import of all data 3 years from before the first import, to allow historical data to be captured in C3DP. However, this presented a new issue where, if the system at a hospital had changed in the last 3 years, such as the coding system migrating or a change affecting the reliability of older data, this would cause confusion for HCP users. To combat this, the TIS import script was enhanced to allow customisation of dates/periods of history to import for each data type. For example, an administrator can specify that conditions from the last 3 years should be imported but medications should only be imported from 01/01/2017.

3.5.4. Updates to the import process and execution log page

During testing and evaluation, many errors were discovered in TIS imports due to live production data not mimicking the test patient data provided during development; fields being filled differently or required attributes missing, text-based fields where coded values were expected etc. To ease the import and debugging process for admin users in TIS some usability enhancements were made.

Import scripts were updated so that, for imports of multiple patients, the import process would continue to the next patient if an exception or error was encountered rather than aborting the import entirely. This would allow the rest of the patients to be successfully imported leaving only patients with errors in their data to be investigated.

To support debugging, the Task Execution Log page has been updated to display full error stack traces to enable administrators to quickly provide logs to technical partners rather than having the partners log into live systems or have the administrators run terminal commands or check long log files.

The Task Execution Log page was also updated to allow sorting of the logs by date to ease searching for log entries.

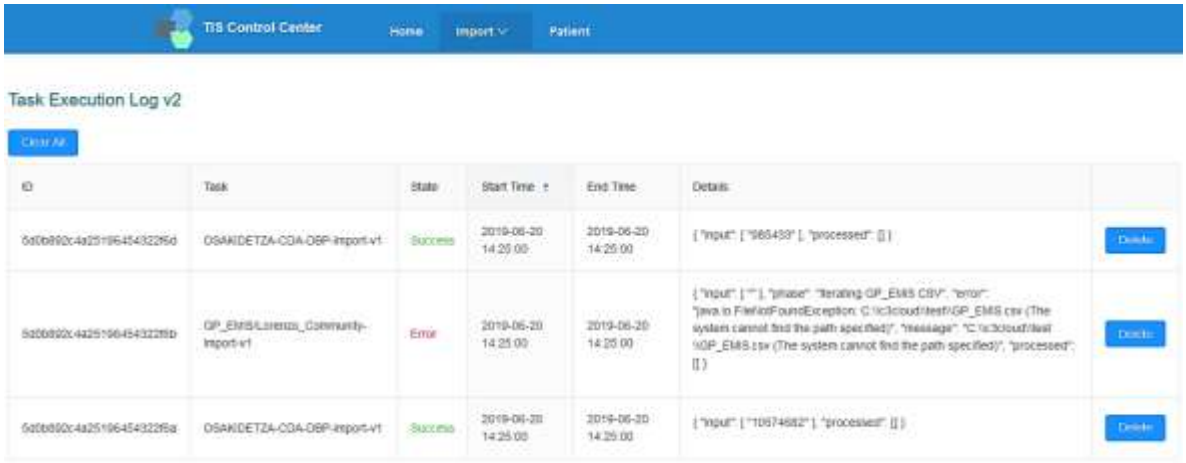

Figure 2: Task Execution Log page

4. ENROLMENT REPORT

It was planned initially that the recruitment period for patients starts 3 months before the launch of the pilot test (i.e. July – September 2018) to allow sufficient time for the identification of eligible participants and obtaining informed consents, while also keeping the time-period between recruitment and piloting start as short as possible. Due to delay of the deployment in the pilot sites, the time span between the identification of the first eligible participant and actual study start prolonged up to 12 months.

MDT members were contacted individually by pilot site managers using convenience sampling, taking into account their individual profiles and willingness to participate. This non-probabilistic sampling involves the sampling of MDT members that are nearby. It aimed for a total sample size of 62 across the three pilot sites.

For the iterative evaluation phase 3 and phase 4, we defined the patient number that we need to observe based on power calculations as the "observation goal", which is 420 patients total. As a number of patients may withdraw their participation during the technology trial, we added a 25% dropout margin to the observation goal, summing up to 526 patients to be recruited for the piloting trial participation (the "recruitment goal"). We anticipated that a number of patients that were approached for participation, would decline from the outset. Accordingly, the number of patients that were approached for participation (the "approaching goal") was set to 16% larger than the recruitment goal, summing up to 610 intervention patients across the three pilot sites. The number of comparator patients whose resource consumption data will be monitored anonymously will match the intervention patient numbers at each pilot site. Patient recruitment has proven very difficult due to various reasons that are elaborated per pilot site below. Table 3 to Table 6 show the efforts that the pilot sites have put into recruiting the largest number of patients possible. Both SWFT and RJH approached more than twice the number of patients for trial participation than originally planned. BC has a slightly different process where the MDT members will recruit the patients once they were trained. Thus the number of consented patients as presented here is not the final number and we expect an additional 290 patients to be recruited.

Across all three pilot sites, 1,183 patients were already contacted and we consented 275 of 420 patients (BC final number is pending).

All Pilot Sites		
Intervention patients	**Planned**	**Actual**
Approached	610	1183
Recruited	526	293
Consented by Nov 2019	420	273
Additional participants expected to be recruited	0	236
Gender distribution (female/male)		
MDT members	**Planned**	**Actual**
Consented	62	168
Comments	Additional 236 patients are expected to be recruited at BC when MDTs were trained.	

Table 3: Number of trial participants across all three pilot sites

South Warwickshire Pilot Site		
Intervention patients	**Planned**	**Actual**
Approached	70+18+14 = 102	241
Recruited	88	25
Consented by Nov 2019	70	20
Additional participants expected to be recruited	0	0

Gender distribution (female/male)	35/35	7/13
MDT members	**Planned**	**Actual**
Consented	16	16
Comments	3 GPs, 2 practice nurses, 4 dieticians, 2 diabetes specialists, 5 district nurses, 1 heart failure nurse	

Table 4: Number of trial participants at SWFT

Basque Country Pilot Site		
Intervention patients	**Planned**	**Actual**
Approached	175+44+35 = 254	250
Recruited	219	To be confirmed
Consented by Nov 2019	175	11
Additional participants expected to be recruited	0	236
Gender distribution (female/male)	50/50	To be confirmed
Comments	Additional 236 patients are expected to be recruited shortly before and during the trial start (when MDTs were trained). Approx. 5 patients per GP are expected.	
MDT members	**Planned**	**Actual**
Consented	16	88
Comments	48 GPs, 40 primary care nurses.	

Table 5: Number of trial participants at BC

Region Jämtland Härjedalen Pilot Site		
Intervention patients	**Planned**	**Actual**
Approached	175+44+35 = 254	692
Recruited	219	223
Consented by Nov 2019	175	203
Additional participants expected to be recruited	0	0
Gender distribution (female/male)	50/50	91/112
Comments	3 patients deceased during study trial delay. Another 12 patients withdrew their consent before trial start. 3 patients moved to other areas, 1 patient moved to special housing, 1 patient no longer fulfils the inclusion criteria.	
MDT members	**Planned**	**Actual**
Consented	30	30
Comments	MDTs include 20 doctors, 10 nurses.	

Table 6: Number of trial participants at RJH

4.1. Enrolment report Region Jämtland Härjedalen

From electronic health records, social security numbers were retrieved for patients identified with the use of specified search terms at a number of health care centres (Frösön, Lugnvik, Zätagränd, Ripan, Odensala, Torvalla, Krokom, Föllinge and Backe) with a total population of approximately 54,000. General inclusion criteria were an age of at least 55 at November 1st, 2018 and being alive in the first week of July 2018. General exclusion criteria were living in a nursing home, having an address "care of", and age >95 years. An eGFR below 30 was an exclusion criterion. No ethical approval had been obtained to screen all EHRs. Thus, realistic search strings were constructed to try to identify more severe heart failure (NYHA III-IV) and more severe depressions. Having had >3 appointments during the last

12 months with the diagnosis cardiac failure or equally for depression was taken as an indication of more severe disease and thus considered as an exclusion criterion.

The following search strings used were:

(1) Diabetes type 2
(2) Diabetes + renal failure
(3) Diabetes type 2 + cardiac failure
(4) Diabetes type 2 and depression
(5) Diabetes type 2 and ATC
(6) Cardiac failure + renal failure
(7) Cardiac failure + depression
(8) Cardiac failure + ATC
(9) Renal failure + depression
(10) Renal failure + ATC

Diagnosis were retrieved from autumn 2017 to June 2018. The search strings 1, 2, 3, 6, 9 and 10 from the list above all requested an additional eGFR of 30-59. The following ICD-10 codes were used for patient screening.

Condition	ICD-10 / ICD-9 Jämtland Härjedalen
Type II Diabetes	Diabetes = E11 Diabetes with RF= E11.2 or I13.0 Diabetes with complications = E11.8P
Renal Failure with eGFR/ GFR 30 – 59 (measured or estimated glomerular filtration rate)	RF = N18.9 or I12.0 or I13.1 or N19.9 or N19.-P or N18.2 to N18.5 Hypertension +RF+ CF = I13.2 was also used if supported by an eGFR of 30-59 and then interpreted as renal failure. This diagnose was not used for identification of cardiac failure.
Heart Failure in compliance with NYHA I-II (New York Heart Association classification of heart failure)	CF= I50 or I11.0 Diabetes with CF= E11.2 or I13.0 Hypertension +RF+ CF = I13.2
Mild or moderate depression in adults	Depression = F32.9 or F32.1 or F33.1 or F32.0 or F32- or F33- ATC codes included were the groups N06A or N06AX. A diagnosis of depression was considered superior to ACT code and made inclusion possible also in cases with treatment from NO6AA.

Table 7: ICD-10 and ATC codes used for patient screening at RJH

A total of 692 patients were eligible and an online random generator (http://slump.nu/) was used to select the planned number of participants to invite.

The consent rate in ages 65-75 was approximately 25% while in older ages only some 10% consented. Due to this, in order to increase the number of consented patients, all 692 were invited. Also, patients aged 55-65 with the same inclusion criterions were included, this after a new search in October. Together with the previous 692 invited we ended up with a total of 1017 study invitations. The consent rate in these younger ages were found to be lower than in ages 65-75, again around 10%. In total 223 patients consented to participate but under the waiting time for study start, three of them were deceased and 10 withdrew consent.

The RJH technology trial went live with the first patient on 18.11.2019. Until the writing of this deliverable, 70 patients have received their C3-Cloud multimorbidity care plan already via the patient

platform and a total of 190 patients is expected by the end of November, quickly getting to the full cohort of 203 patients.

4.2. Enrolment report South Warwickshire

In SWFT, it was agreed that the trial would be run in a single practice – Rother House Medical Centre in Stratford-upon-Avon - and that the participating patients would be recruited from their list of ~13,600 patients. HCPs would be recruited from both Rother House and SWFT.

Prior to the start of the study, SWFT estimated in the Description of Action (DOA) that there were approximately 400-500 potentially suitable patients who might benefit from the system. Therefore, SWFT committed to recruiting 250 patients (evenly split between an intervention and a control group). However, due to concern being expressed by the pilot sites about the achievability of their recruitment targets and the ethics boards veto saying that we cannot contact control patients, the numbers were reduced and the parallel control group patients will not be involved in the evaluation surveys.

As a result, in the most recent version of the Research Protocol (v3.2), SWFT made a revised commitment to approach a minimum of 204 patients, with the hope of recruiting 88 patients to the intervention branch.

The initial cohort of patients were identified from the Rother House's EMIS system by an experienced research nurse using age and a pre-agreed set of disease codes Table 8. The records of these patients (approx. 400) were then reviewed by the GPs against the more detailed inclusion/exclusion criteria.
In order to identify potentially suitable patients for the trial, Rother House Medical Centre ran a report on their EMIS system using the pre-agreed codes for the 4 targeted conditions (Table 8).

Condition	READ Codes: South Warwickshire
Type II Diabetes	Type 2 Diabetes: C10F** (including all codes below in the code tree)
Renal Failure with eGFR/ GFR 30 – 59 (measured or estimated glomerular filtrati on rate)	K05* (Chronic renal failure) and all codes below in the tree. 1Z1* (chronic renal impairment) (including all codes below in the code tree)
Heart Failure in compliance with NYHA I-II (New York Heart Association classification of heart failure)	C58* (including all codes below in the code tree) 420300004 (NYHA Class I) and 421704003 (NYHA Class II) classification will be an individual check by a GP
Mild or moderate depression Depression in adults	Anxiety with depression – include all. (Read Code: E2003) Depression NOS – include all. (Read Code: Eu32z-1) Depressive episode, unspecified – include all. (Read Code: Eu32z) Endogenous depression – include all. (Read Code: E112-4) Reactive depression NOS include all. (Read Code: Eu32z-4) Chronic depression – include all. (Read Code: E2B1) Recurrent depression – include all. (Read Code: E1137) Endogenous depression – recurrent – include all. (Read Code: E113-1) Low Mood – include all. (Read Code: 1BT-1)

Table 8: READ codes used for patient screening at SWFT

The list of patients obtained was then screened by the GPs and was reviewed against all of the lower level selection criteria. This process reduced the list of potentially suitable patients to 241. In January 2019, the recruitment pack was sent by Rother House to 241 patients (37 patients more than the agreed minimum). Due to resource constraints within the practice, and to comply with data protection regulations, it was agreed with the Research Ethics Committee (REC) that patients who were interested in taking part would be asked to return a 'Consent to Contact Form' to the SWFT based C3-Cloud project team in a pre-paid response envelope. The team would then contact patients who expressed an interest to discuss the study further, and if appropriate, arrange for them to sign a Consent to Participate form. Patients who were not interested in taking part were not required to respond.

The uptake was relatively poor with only a small number of patients returning a Consent to Contact Form. To try and increase the update, a reminder letter was sent approximately one month after the initial recruitment pack, as agreed with the Research Ethics Committee. This yielded a very small number of additional responses (total at this stage = 47 or 19.5%). It was not felt appropriate to send another reminder, especially as a small number of patients had already expressed dissatisfaction about being contacted a second time and asked for reassurance that they had been removed from the contact list. The practice also reported that some patients were quite negative about the study when they attended for routine appointments. A full set of recruitment statistics are shown in the table below.

	Total	**%**
Total Number of Patients Approached	**241**	**100**
Total number of patients who did not respond at all	165	68
Total number of patients who specifically declined straight off	29	12
Total number of patients who returned a Consent to Contact Form & will not take part (later found to be ineligible)	18	7
Total number of patients who returned a consent to contact form & will not take part (declined at a later point)	3	1
Total number of patients who returned a consent to contact form but after agreeing to take part did not return a consent to participate form	5	3
Total number of patients who returned a consent to contact form & have already consented take part	21	9

Table 9: Patient recruitment numbers at SWFT

The primary issue, which is out of the control of the practice or project team, is that the vast majority of patients contacted (165 or 68%), did not respond at all even after a reminder letter was sent. A further 29 or 12% also took the time to formally decline involvement (which they were not expected to do). This obviously meant that 80% of the patients were lost to recruitment from the outset.

Of the remaining 47 patients who returned a consent to contact form, 3 reconsidered and declined involvement. A further 18 could not be considered further for recruitment as they were later found to be ineligible, e.g. patient had been identified as suitable in error, conditions had resolved, their health had deteriorated, they had moved into a nursing home etc.

Therefore, SWFT are not able to meet the minimum number of patients (88) and have only recruited 21 patients. It should be noted that SWFT did not realise that the uptake would be so low until the recruitment started, especially as more patients than the minimum had been approached initially (241). In research, it is very difficult to predict how successful recruitment will be, especially in a study such as this where there is no real precedent.

The first trial patient has been seen at Rother House Medical Center on 11.11.2019. SWFT has seen 10 patients by 15.11.2019 and the remaining 10 patients will be seen until the end of November.

Some of the mitigating actions that could potentially have been taken to increase patient numbers include:

- Engagement of additional practice(s) to broaden the pool of potentially suitable patients. However, SWFT only ever committed to recruiting a single practice in the DOA and by the time the recruitment issues were appreciable, it would have been too late to engage 1 or more additional practices. Furthermore, to recruit 88 patients, working on the basis of the 10% uptake rate achieved so far, SWFT would need to contact at least 880 patients. On the basis that 241 patients were identified from a single practice with a large patient list, it would be necessary to engage at least 4 practices. This would not be achievable as SWFT would not have the budget available to pay more than 1 practice for their involvement and also separate data extracts would need to be developed at each practice, resulting in additional cost and mapping work for the technical partners. Furthermore, the SWFT project team would not be resourced to manage the project in this number of practices.
- GPs should have contacted the patients initially – it could be argued that the uptake rate might have improved if the patients were telephoned directly by their GP in the first instance rather than being sent a letter. This theory is potentially predicated on the patients owing a 'duty' to the GP/practice which could be considered unethical. More importantly, the practice would not have been resourced to telephone 241 patients as this is an extremely time-consuming activity.
- Give patients who agree to take part more focused attention and support during the study to increase the intensity of their participation and enhance the richness of the study data. However, this might be considered to be an additional intervention and the study should be based on clinical relevance and 'normal' clinical care not artificial enhancement.
- The rather narrow inclusion criteria may have been offset to a small extent by reducing the lower age limit from 65 to 55+.
- Reduce the payment to Rother House in light of the lower numbers so that the funds can be re-distributed within the project. This would jeopardise SWFT's involvement in the study as the practice may refuse to participate, particularly as there is no way to predict the burden that will be placed on the practice during the trial.

4.3. Enrolment report Basque Country

A preliminary list of candidate patients who met the study inclusion and exclusion criteria was produced in Basque Country at the beginning of the initial recruitment period (November 2018). This was supported by the Osakidetza unique database (OBI), which enables data extraction and analysis system. The initial list of candidate patients was created from primary care physician quotas who had agreed to participate in the intervention. The search involved the patients of the general practitioners taking part in C3-Cloud. Once these healthcare professionals gave their consent, the search of patients was made through database screening of the set of patients of their quotes. The list identified each patient with his/her unique Corporate Identification Code (CIC) in the Healthcare System. Then, each healthcare professional reviewed his/her own list of patients. Inconsistencies with inclusion/exclusion criteria that were not documented in the local EHR (Osabide) were identified and rectified. The process produced a modified list of eligible study participants.

Primary care healthcare professionals contacted (via phone or face-to-face meetings) the selected study candidates of the updated list to explain the nature of the study, the objectives of the evaluation and the expected role of the participants. This first contact came with support materials (project information sheet and informed consent sheets). If the patient decided to participate in the first meeting, the informed consent could be signed and collected. If the patient decided to take more time to think about joining the study, a second contact was scheduled by the healthcare professionals.

The first round (November 2018) was launched once the age-range was modified to >55 as inclusion criteria and involved the patients cared by a total of 67 GPs from 14 health care centers from 7 Integrated Healthcare Organizations (ICOs), OSIs in Spanish: Alto Deba, Araba, Barrualde-Galdakao, Debabarrena, Donostialdea, Ezkerraldea Enkarterri Cruces and Tolosadea. According to the inclusion and exclusion criteria, the following ICD-10 search strings were used for the patient screening:

Condition	ICD-10 / ICD-9 Basque Country
Type II Diabetes	Diabetes = E11 Diabetes with RF= E11.2 or I13.0 Diabetes with complications = E11.8P
Renal Failure with eGFR/ GFR 30 – 59 (measured or estimated glomerular filtrati on rate)	RF = N18.9 or I12.0 or I13.1 or N19.9 or N19.-P or N18.2 to N18.5 Hypertension +RF+ CF = I13.2 was also used if supported by an eGFR of 30-59 and then interpreted as renal failure. This diagnose was not used for identification of cardiac failure.
Heart Failure in compliance with NYHA I-II (New York Heart Association classification of heart failure)	CF= I50 or I11.0 Diabetes with CF= E11.2 or I13.0 Hypertension +RF+ CF = I13.2
Mild or moderate depression in adults	Depression = F32.9 or F32.1 or F33.1 or F32.0 or F32- or F33- ATC codes included were the groups N06A or N06AX; NO06A

Table 10: ICD-10 and ATC codes used for patient screening at BC

In the first round, more than 2,500 patients were identified as eligible. Primary healthcare professionals selected a first round of patients planned to invite. Initially 45 patients accepted to join the study. Due to the extra time needed for the C3-Cloud component development and integration with local sites, the completion of final deployment, including also the recruitment, had been postponed. C3-Cloud system is going to be used in real clinical practice which has set the performance requirements threshold much higher than planned. After this period, several GPs have withdrawn to participate due to personal and other reasons and the current participating GPs have asked to update the eligible list of patients as their health status may have changed significantly. In October 2019 an updated list has been produced with a total of 2,419 eligible patients. At the time of writing this deliverable, seven patients have consented to participate and currently the recruitment process is actively ongoing. The official trial start (first HCPs using the systems with their patients) was 8.11.2019 and the full patient capacity will be reached approximately at the end of December 2019.

4.4. Enrolment lessons learned for future recruitment plans

Initially, enrolment difficulties have been encountered because of local ethics committee requirements. More specifically, the UK pilot was initially considered as a clinical trial, instead of a technology trial. Clarifications were needed and a number of iterations of the ethics approval followed to resolve open issues which resulted for instance in the exclusion of control patients from the qualitative surveys for the evaluation phases 3 and 4.

Contacting patients in the first place was burdensome at SWFT, where the ethics board allowed only to contact patients via post. Only if they replied with written consent allowing SWFT to contact them further, we could inform them about the technology trial and invite them for participation.

Due to low response rates from patients who were invited for trial participation, much more patients than originally planned were invited. In the age ranges younger than 65 and over 75 the consent rate was lower than expected. Feedback received indicates that this may be due to reduced IT-literacy (false or true impression) among participants aged >75 and reduced interested or lack of time among participants aged <65. In consequence, we extended the inclusion criterion “age” to patients aged 55-64. This allowed us to recruit four additional patients at the SWFT pilot site and 22 in RJH (where 109 additional patients in this age range were invited). In BC the first screening for eligible patients was already with the extended age range so that additional patient numbers as a result of the added age range could not be determined.

A few patients died in the period after giving their consent and before the trial started and thus the delay in the trial start prevented them from participation. Some patients, on first contacting them, were out of the country and wanted to be contacted again later and shortly before the trial start, which was difficult to follow up with. Additionally, healthcare professionals did not want to sign consent for participation too early in case the members in their clinical teams changed until trial start.

Some of the main factors affecting the low uptake rate are thought to be:

- **Technology trial with older subjects**. Older people are likely to be less comfortable with IT. That said, it was hoped that this would be less of a problem in the area targeted for instance at SWFT, as the GP practice is in an affluent area with a well educated patient base with higher than average IT literacy & technology usage. Furthermore, patients who stated that they were not comfortable with IT were generally not encouraged by the option to involve a friend, family member of carer, and some patients said that they did not have anyone to call on. A small number of patients declined as they specifically said they don't like IT and prefer face to face interaction. Even some of the patients that have started on the trial were very nervous when they first saw the system.
- **An updated set of inclusion and exclusion criteria was defined after the original numbers were agreed in the DOA** which will have impacted the number of suitable patients available. In particular:
    - The severity levels of the 4 conditions were reduced, e.g. inclusion of mild to moderate RF, HF and depression and the exclusion of Type 1 diabetes. The pilot sites original estimation of numbers would have been predicated on the inclusion of all disease severity levels. More clarity is needed here in future proposals. However, patients with severe conditions were excluded based after advice from the clinical reference group: as more severe conditions need additional clinician time and also additional guidelines were needed to include in the guideline reconciliation, this was not considered feasible with given resources during the project lifetime.
    - Exclusion of patients in a nursing/residential home and patients who have other conditions which affect their ability to provide informed consent or to use the system.
- **Over-optimistic about the predicted numbers**. Numbers were estimated prior to the start of the study and a formal case note review was not carried out before the numbers were agreed in the DOA. This is an important learning point from the research.
- **Underestimating the percentage of patients that denied participation from the outset**. Based on a desk research, we expected that approximately 16% of all contacted patients would deny participation. It turned out this number was much larger and varies between 75%-90% at SWFT and RJH (numbers were unavailable for BC).
- **Information provided may have been too difficult to understand:** although efforts were made to ensure that the information provided to patients about the study in the recruitment pack was simple, it may not have been simple enough. Patients may even have overestimated the level of input that would be required or the complexity of the study without seeking clarification. There was a requirement to balance the volume of information provided with not overloading the patients or discouraging them from reading it.
- **For SWFT: Possible inaccuracies in the way that diagnoses are coded in EMIS**: this may mean that the EMIS search was not able to reliably identify all relevant patients or some patients may have been identified as suitable but prove not to be suitable following case note review. There are no other sources available in the practice to identify suitable patients, e.g. multi-morbidity diseases registers.
- **Ethics Committee restrictions:** the project team were not permitted to put pressure on patients to participate, to offer inducements or to sell the potential benefits of the study to any great extent. The team did not get permission to contact and survey control patients about their view on their multi-morbidity care plans.
- **Use of the term 'multi-morbidity':** some patients may have been put off by the use of the term 'multi-morbidity'. One patient stated they felt that the term had negative and worrying overtones. Other patients did not see themselves as the targeted patient group as they did not

understand the term “multi-morbidity”. Some patients were not aware of their conditions and were put off from being contacted through the project team.

5. MEDICAL DEVICES FEASIBILITY STUDY PREPARATION

Medical sensor device usage and connected device usage is envisaged to be evaluated with a patient sub-set at the RJH pilot site. Patients will be individually selected from the group of patients at the discretion of local clinicians and based on their diagnosis. The testing serves to evaluate the technical possibility of including sensor and connected devices as an integral part of the patient care and planning.

11 weight scales, 16 blood pressure devices and 16 Motorola G7 Play Smartphones were purchased through Warwick, tagged and shipped to RJH. RJH purchased UK to EU converters for the USB charger plugs. The RJH IT team installs a data SIM card, the Medixine hub android application and establishes the Bluetooth pairing between the sensor devices and the Smartphones. Consequently, the hubs are registered in the Medixine Suite and the sensor kits will be assigned to specific patients once identified. Patients will be advised through their caregiver on how to use the sensor devices and will perform home-based weight and blood pressure measurements during the trial period. The measurement timings will be determined when their care plan is set up and can be reviewed anytime on the patient empowerment platform.

The outcome on the medical devices study will be reported in D9.6 with the aim to:

- demonstrate interoperability and data fusion between the PEP and the C3DP, so that clinicians can see data entered via from the devices to the PEP and in the C3DP via the FHIR repository.
- Show that data fusion includes data from EHR via TIS
- Report on frequency of use of medical devices and the PEP and to potentially show increased use of sensor devices by elderly patients
- Evaluate if having access to patient self-measurements in C3DP can be or is used for improved patient management and care planning
- Evaluate the experience and use of clinical devices among patients and health care professionals.

The medical devices feasibility study is only being done at RJH as the recruitment challenges lead to the decision to focus the medical devices feasibility study on a small subset of patients in the Swedish pilot site together with a few general practitioners for the feasibility study. This is to ensure allocation of devices to participants and the required support during the study.

6. TOWARDS THE INTERIM EVALUATION RESULTS

Table 11 presents the plans for the surveys that we will use to evaluate the C3-Cloud components and their usage. Table 11 presents in black letters the surveys that will be sent to trial participants shortly after their first training on the C3-Cloud system (approximately late early December 2019) (Table 11, column "Survey"). Each survey entails 1 or more specific questionnaires (Table 11, column "Questionnaires"). We will report in detail and in a structured manner on each of the surveys in the final WP9 deliverable D9.6. The subchapter below offers however already early, unstructured HCP experiences on the system, after their initial training.

Survey	Questionnaires included in the survey
First survey for patients – Survey for all patients	M43 UTAUT patients (acceptability of C3-Cloud)
Second survey for patients	M45 UTAUT patients (acceptability of C3-Cloud)
Detailed survey for 50 patients (number 1) – survey for 150 phase 3 patients	M43 Patient Questionnaire (usefulness of C3-Cloud for care planning and empowerment) M43 QUIS7 Patients (Usability questionnaire) M43 Patient Material Output (Evaluation of training material) (video, information leaflet, wallet card)
Detailed survey for 50 patients (number 2) – survey for 150 phase 3 patients	M45 Patient Questionnaire (usefulness of C3-Cloud for care planning and empowerment) M45 QUIS7 Patients (Usability questionnaire) M45 eCCIS patient (System satisfaction questionnaire) M45 Patient Material Outputs (Evaluation of training material), (Leaflets and web pages as well as peer support groups)
First survey for MDTs – survey for all MDTs (phase 3 and 4)	M43 UTAUT MDT (acceptability of C3-Cloud) M43 QUIS7 MDTs (Usability questionnaire)
Second survey for MDTs - survey for all MDTs (phase 3 and 4)	M45 MDT Questionnaire (usefulness of C3-Cloud for care planning and empowerment) M45 UTAUT MDT (acceptability of C3-Cloud) M45 QUIS7 MDTs (Usability questionnaire) M45 eCUIS MDT (System satisfaction questionnaire)
First survey for informal caregivers	M43 eCCIS informal caregivers (System satisfaction questionnaire)
Second survey for informal caregiver	M45 eCCIS informal caregiver (System satisfaction questionnaire)
Survey about sensor device usage for patients	M45 Device usage patients (feasibility study to show usage of data from multiple sources)
Survey about sensor device usage for MDTs	M45 Device usage MDTs (feasibility study to show usage of data from multiple sources)

Table 11: List of questionnaires per specific survey

6.1. Unstructured HCP feedback from the training sessions

Healthcare professionals have already received training about the C3-Cloud system in SWFT, BC and RJH. Their general feedback is very positive. They appreciate the system, find it easy to use and intuitive and think that has real potential to help with the management of multimorbid patients. What

they have seen until now appears robust and reliable which enables their willingness and confidence to use it over the technology trial and possibly in the future. In unstructured, informal evaluation talks with HCPs, they made already comments about:

- Inconsistent terminology on some of the pages.
- It was unclear who would receive referrals to other HCPs and how.
- The possibility to schedule periodic appointments automatically
- The option if a HCP can be informed when the patient has seen their care plan in the PEP
- The option if a HCP or patient can know if messages sent through the system were received and read by the recipient.
- In C3DP and PEP, they would like to see Medication displayed separately to other activities, e.g. measuring BP, walking etc. The patients were finding it difficult to separate their medications from tasks in PEP and asked if they could have a medication section in PEP.
- The possibility to include not only allergies but also intolerances, as this was considered important information that should not be missing.
- The GPs did not like working with the high level goals (HLG) at the top of the screen. Given how little time they have to see patients, they would not be able to keep moving between the different screens. They would prefer to have a single CDS dataset, especially as a lot of the medical data is duplicated across multiple HLG screens.
- GPs feel that they would only be able to use the C3DP functionality if it was somehow integrated as a module within their existing clinical system. Clinicians are not likely to use several systems at once.
- A GP asked if there was a way of identifying which medications are on repeat prescription but not currently being taken. One of the patients yesterday was questioning why she could see a particular medication in the list when she wasn't taking it at the moment. It was because she has a repeat prescription for it but only requests it when she needs it.
- Several healthcare professionals have indicated that a mobile app version of C3-Cloud would be desirable in their every-day practice.
- The screen navigation: users can navigate between different goals and activities, while in practice the "show all" button is really what would be used most of the time. Is would be preferably thus to have goals and activities linked or synchronized more logically and displayed next to each other. Baseline measurement and target (goal) measurement could also be displayed on one page for comparability.
- The data capture process could be more intuitive. E.g. hitting a button to "set a goal for the patient" could lead you automatically through a sequence of steps to complete needed information. The current setup requires users to select from three different "add" buttons (for "goals", "activities" and "educational material"). It is then not clear where to take the next step and the user gets lost on the system. While typing goals, the activities to reach them could already be suggested instantly.
- Medical device linked to the system for home-based self-measurements should remind patients to take their measurements. This could improve the monitoring of patient parameters over time series a lot.
- It will be interesting to observe the uptake of systems such as C3-Cloud in the future, with patients that are less used to technology. Current users that are interested in the system are also willing to be trained. But patients and HCPs that are less interested in the technology, need a systems that is very easy to use.
- A major benefit of the system is that GPs can see in the care plan what the goals or activities or measurements the other HCPs have set.

7. THE APPROACH OF THE LARGE SCALE IMPACT MODELLING TOOL

The increasing prevalence of chronic diseases mainly because of an aging population has led to a profound change in the paradigm of health care. In OECD countries the 15% of the population were 65 years old or more in 2010 and expected to reach 22% by 2030[1]. Life expectancy of elderly has also increased significantly where people at age 65 will expect to live for 21 years on average for women and 17 years for men[2]. Older age is associated with an increased accumulation of multiple chronic conditions3. More than half of all older people have at least three chronic conditions and a significant proportion has five or more [4,5.] Chronic diseases are the main reason for poor health and restricted activity, affecting over one third of Europe's population and accounting for 70% of healthcare expenditure in Europe[6]. Therefore, health systems have changed in perspective, and health care organizations previously concerned mainly with treating acute problems are now focused on a continuum-of-care approach [7].

The natural history of multimorbidity is characterized by frequent transitions between stable and unstable states over time and the clinical management of patients is much more complex and time-consuming than those with single diseases[8]. This generates the need to organise the care around the patient and not around the disease [9,10]. Poly-pharmacy induced is also an important factor that leads to a significant cost in the health system. In this context, C3-Cloud project was launched to develop an integrated patient-centred care and cure ICT infrastructure, considering the realities of multimorbidity and poly-pharmacy and taking into account the medical, technological, organisational and socio-economical challenges of creating a collaboration environment for all of the stakeholders involved in the holistic continuum of care.

The objective of this work is to develop the economic evaluation of C3-Cloud intervention taking into account all the stakeholders involved to help decision makers to decide on further using the application. As at this stage of the project there is no data available form C-3-Cloud, the specific objective is to develop a prototype of the modelling in a format capable of being merged with ASSIST.

7.1. Predictive modelling

7.1.1. Design

The C3-Cloud intervention will be deployed in 3 European regions with diverse health and social care systems and ICT landscapes: South Warwickshire (United Kingdom), Basque Country (Spain) and Jämtland Härjedalen (Sweden). The economic evaluation will be disaggregated for each stakeholder group, taking into account patients, informal caregivers, health care system, social care system, pharmacies and industry. For that purpose, an innovative tool will be used merging predictive modelling developed in the CareWell project by Osakidetza and the cost-benefit assessment framework ASSIST developed by Empirica. In order to gain reliability and validity, the predictive modelling will be used to represent mathematically the natural history of the disease[11,12]. This will allow to foresee in the long term the healthcare resource consumption and to obtain per month the unit costs of different resources involved. After that, these unit costs will be used as inputs in ASSIST, where thanks to its comprehensive perspective will foresee the economic impact for each stakeholder. The combined application of both approaches will enable a symbiotic realisation of their complementary strengths while reducing their limitations.

The target population are multimorbid patients over 65 years old with at least 2 of 4 chronic diseases between diabetes (type 2), heart failure (NYHA I-II, first stages), renal failure (eGFR/GFR 30-59, no need for haemodialysis) and depression (mild/moderate). Patients with most severe diagnosis are excluded from the analysis as well as patients admitted in nursing homes. The data needed will be obtained from the pilot sites databases and, if it will be necessary, from the literature.

So, as patients care will be personalised and adverse effects of poly-pharmacy more controlled, the initial hypothesis is that patients will have less destabilization phases. This will reduce the informal

caregiver or social caregiver dedication time. In the same way, hospital resource consumption will have a decrease, as same as contacts with A&E services and hospitalization. For its part, the better control of adverse effects of poly-pharmacy will impact on drug prescription, generating a reduction on drug consumption and pharmacy billing. On the other hand, as new ICT platform will be developed, it demands an initial investment and it will generate a periodic maintenance or operational cost.

7.1.2. Variables of the study

The evaluation of the C3-Cloud program will be developed measuring the change in the resource use profile for each stakeholder. The information necessary to develop the predictive modelling relating to control and intervention group will be obtained from administrative and clinical databases of each pilot sites. This information will include patient and resource consumption data. Patient data is composed by age, sex, diseases, death and dropouts. The resource consumption collected from electronic health records in primary care (PC) will include contacts with PC nurses and general practitioners at healthcare centre, at home or by telephone. In hospital care (HC) contacts with cardiology, endocrinology, nephrology, psychiatry and internal medicine will be taken into account. Besides the contacts with outpatient services, contacts with ambulatory & emergency (A&E) services, hospitalizations and home hospitalizations will be also collected. The drugs prescribed to the patient have to be considered too. For the cases in which data is available, the unit dose, the frequency and the prescribed period will be used. If data is not available, the mean usage dose and frequency will be obtained from the literature. The information about the unit cost of the consultations (PC and HC) in 2017 will be obtained from the accounting systems of the pilot sites. To foresee population projections between 2017 and 2030 databases of national statistics institutes of different pilot regions will be used.

7.1.3. Predictive modelling

To represent the care pathway of the patients involved in C3-Cloud program a Discrete Event Simulation (DES) will be used. This will allow to calculate the evolution of resource consumption from 2017 to 2030[11,13,14]. DES is a flexible modelling method that can represent complex behaviours and interactions between different individuals, levels and environments[15,16]. The model will be built using the software Arena®, a simulation tool property of Rockwell Automation.

Mathematical functions will be obtained developing a parametric survival analysis with the data extracted from the trial. The mathematical functions determine the time until the event occurrence for all the competing risks according to different characteristics (sex, age, etc.), so personal attributes will be assigned to each individual that enters in the model. In this way a list of future events that the individual will go through will be generated. The event that will occur first will be determined according to which is the closest in time. After that, the time to event for that event is recalculated and the event that will occur next will be determined again according to which is the closest in time. This process will be repeated until the patient leaves the model by death or the time horizon of the simulation reaches its end.

The conceptual model will include all the possible pathways and contacts that patients can have. That way all contacts with PC nurse, general practitioner, outpatient services, A&E services, hospitalisation and home hospitalisation will be counted. The drug consumption will be also calculated according to the time that the patients remain in the system. The simulation model will be validated using goodness of fit test.

Once validated the model, the resource consumption for each group will be calculated. The cost of the disease for the control and the intervention groups will be obtained multiplying the resource consumption rate of each group by unit costs. Resource consumption and costs of both groups will be projected in time from 2017 to 2030 using population projections of the national statistics institutes and taking into account the effect of aging population. That way, the unit cost per resource and per month will be obtained until 2030 to feed ASSIST with reliable data.

7.1.4. Development of the prototype

As the results of the control and intervention groups are not still available, a prototype have been developed with data from the Basque Health Service. The C3-Cloud target population have been identified in the corporate data base OBI (Oracle Business Intelligence) and it includes patients with Diabetes Mellitus, heart failure, renal failure and depression alive on the first of January of 2017. Patients with an active diagnosis in 2017, older than 65 years and two of four chronic conditions have been searched according to the trial inclusion. Patients living in a nursing home, patients liable to need palliative care and patients with haemodialysis treatment have been excluded. A sample of 1,854 patients has been obtained and their characteristics were described. The most frequent chronic condition is Diabetes Mellitus. The descriptive analysis of the contacts that those patients had in 2017 with the health system was also performed.

Drug consumption has been measured by recording all the medications prescribed to the target population in 2017. For each prescription Basque Health Service databases contains the Anatomical Therapeutic Chemical (ATC) classification system code, the daily dose, the unit cost, the date of prescription and the date of end of prescription. All this information has permitted to calculate the total medication cost for each patient. Only medication related to the chronic conditions included in the C3-Cloud study has been taken into account. The ATC classification system has been used to classify the drugs according to the organ or system where they act and their therapeutic, pharmacological and chemical properties.

7.1.4.1. Analytic framework description

The prototype presented here is a dynamic multi-cohort model developed using the software Arena® that includes all the prevalent and incident multimorbid patients. Eligible patients at the beginning of the implementation have been considered as prevalent cohort, and they represented the initial target population[17]. New patients who would become eligible for C3-Cloud in the future constitute incident cohorts. Figure 3 shows the conceptual model that includes the possible pathways and contacts that patients can have. As it is shown in the picture, all contacts with PC nurse, general practitioner, outpatient services, A&E services and hospitalisation will be counted. The drug consumption will be also calculated according to the time that the patients remain in the system.

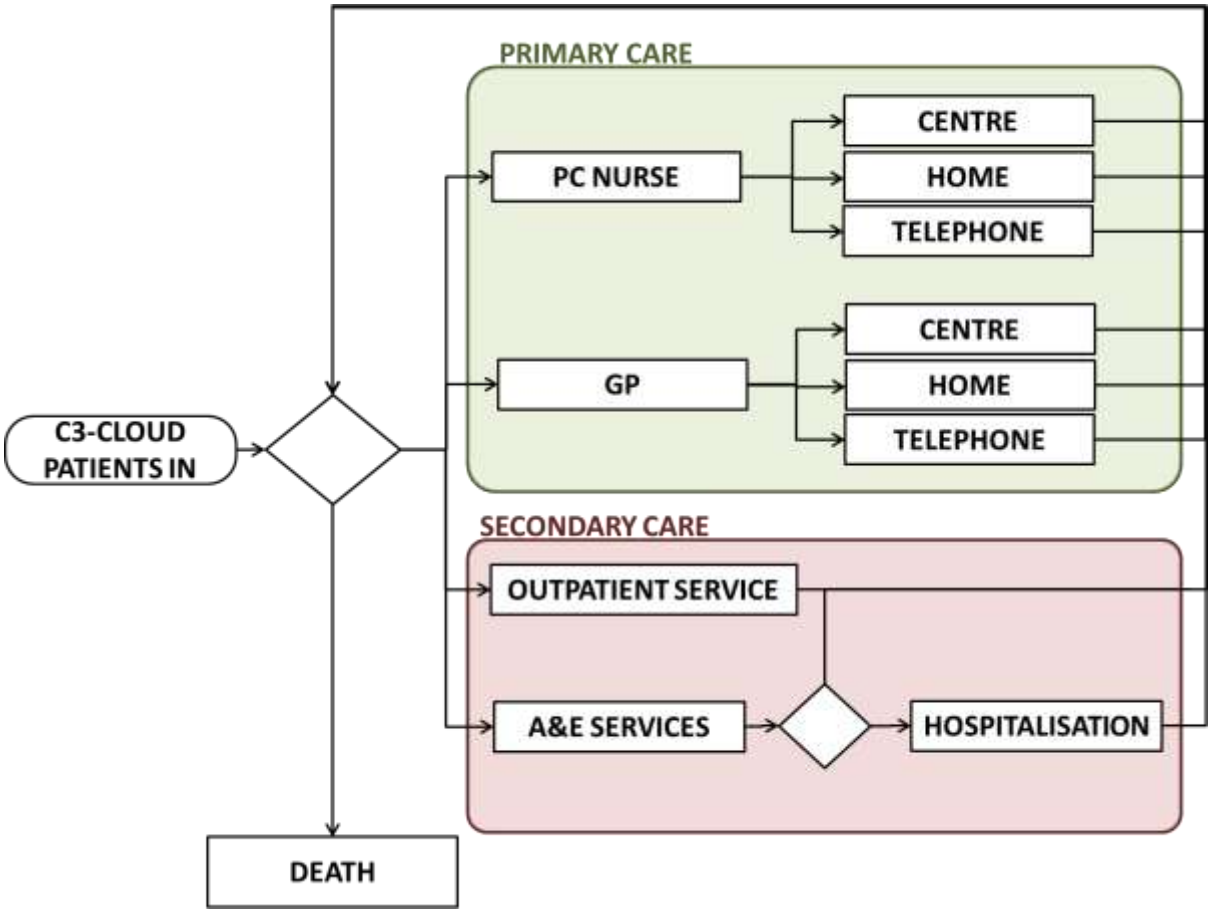

Figure 3: Conceptual model for the analytic framework

When patients are entered into the model their characteristics (age, sex and diseases) are assigned. At the same time, times until the different events (contact with PC nurse, contact with general practitioner, contact with outpatient services, contact with A&E services or death) are assigned according to their characteristics. If the shortest time is time until death or the time horizon of the simulation reaches its end, the patient is taken out of the model.

If the shortest time is time until contact with PC nurse or general practitioner, the type of visit is then assigned according to the obtained probability distributions base on patient's characteristics. Patients can be assisted by the PC nurse or the general practitioner either in the health center, at patient's home or by telephone. After the contact occurrence, the time to event for the next contact with PC nurse or general practitioner is recalculated and assigned to patients according to their characteristics.

If the shortest time is time until outpatient services, the specialist visited is assigned according to the obtained probability distributions base on patient's characteristics. Patients can have a contact with endocrinology, cardiology, nephrology, psychiatry or internal medicine. After the contact occurrence, the time to event for the next contact with outpatient services is recalculated and assigned to patients according to their characteristics.

If the shortest time is time until attendance to A&E services, patients have two ways, they can be discharged or hospitalised according to the obtained probability distributions base on patient's characteristics. If the patient is hospitalised, hospitalisation duration is assigned. After the contact occurrence, the time to event for the next contact with A&E services is recalculated and assigned to patients according to their characteristics.

Once assigned patient's characteristics, the model is ready to clone the target population in order to represent alternative scenarios. The model also can clone the random numbers used for each patient so that the both clones will be exactly in the same settings.

The model outputs are the resource use consumption per month and costs per month disaggregated by each health care resource costs and pharmacy costs.

7.1.5. Input data

All the relevant data about the study population have been obtained from Basque Health Service databases and the statistical analyses needed to obtain different parameters of the model have been performed in Stata (version 13) or R (version 3.3.2). The unit costs used for the prototype can be seen in the Table 12.

Resource	Euros (€)
PC Nurse (Centre)	12.00
PC Nurse (Home)	21.80
PC Nurse (Telephone)	6.00
General Practitioner (Centre)	27.20
General Practitioner (Home)	38.10
General Practitioner (Telephone)	13.60
Outpatient Services (First)	133.09
Outpatient Services (Second)	78.27
A&E Services	168.30
Hospitalisation (Mean per Stay)	2,273.70

Table 12: Unit costs

Prevalence and mortality data by gender and age group have been obtained from the data set recorded in the administrative databases in 2017. The mortality has been adjusted by the incremental death risk of multimorbid patients. Incidence rates by gender and age group have been obtained from the same origin comparing the target population in 2016 and 2017. After that, the incidence has been extrapolated until 2022 according to the population forecast of the Basque Institute of Statistics.

Patient's characteristics (age, sex, diseases and pharmacy cost) must be assigned to each one at the entrance of the model. To assign clinical conditions according to age and sex logistic regressions have been used. To obtain the parameters of those logistic regressions, it has been taken into account also the diseases that patients are subjected to. On the other hand, pharmacy costs have been assigned according to age, sex and diseases that patients have using a logarithmic function obtained from the target population data with a linear regression.

The mathematical functions that define the times until different events have been obtained developing a parametric survival analysis of the data in Stata. The DES model requires considering time in an explicit way. Patients alive or without an event at the end of the study period were categorized as survivors, i.e., as a censored data. In the analysis different distributions have been tested as survival functions: exponential, generalized gamma, log-logistic, Weibull, Gompertz and lognormal. All functions have been adjusted by age group, sex and diseases. The types of function that best fit with the observed data have been selected using the statistical Akaike Information Criteria (AIC)[18,19]After that, the mathematical functions have been used to determine the time until the event occurrence for all the competing risks according to different characteristics (sex, age and disease).

7.1.6. Validation

The validation is a set of methods used to measure the accuracy of the prediction model[20]. In this case, the model has been validated by comparing the simulated event rates with the observed ones in 2017. For that purpose goodness of fit tests has been used with the following statistics[21]: the correlation

coefficient (R), normalized mean square error (NMSE), fractional bias (FB), fractional variance (FV) and the fraction of predictions within a factor of two (FAC2). To validate the model the correlation coefficient and the factor of two must be higher than 0.8, the normalized mean squared error must be lower than 0.5 and the fractional bias and the fractional variance must be between -0.5 and 0.5. The goodness of fit tests have been carried out for different resources differentiated by sex and all the statistics are within the established criteria.

7.1.7. Data anonymization

For the modelling process, anonymized data will be used. This means that each pilot site will use an Excel-based data base to anonymize their data sets before these are transferred to Kronikgune for the modelling. In this data base each record corresponds with one patient but no identification code or ID will be assigned. No additional information, link with the original patient data bases or keys will be kept that effectively allow reversal and re-identification of individuals. The following data entries will be transferred to Kronikgune for the modelling. For each of these data entries, the average unit cost will be determined and used for the modelling.

Age
Sex
Caregiver (Yes/No)
Diabetes Mellitus (Yes/No)
Heart Failure (Yes/No)
Renal Failure (Yes/No)
Depression (Yes/No)
Dropout (Yes/No)
Dropout because of Death (Yes/No)
Dropout Date
Drug Prescriptions (Name)
Drug Prescriptions (ATC Code)
Drug Prescriptions (Dosis)
Drug Prescriptions (Frequency per Day)
Drug Prescriptions (Days)
Nº Contacts with PC Doctor at Centre
Nº Contacts with PC Doctor PC Doctor by Telephone
Nº Contacts with PC Doctor at Home
Nº Contacts with PC Doctor in Total
Contact Dates (PC Doctor at Centre)
Contact Dates (PC Doctor by Telephone)
Contact Dates (PC Doctor at Home)
Nº Contacts with PC Nurse at Centre
Nº Contacts with PC Nurse by Telephone
Nº Contacts with PC Nurse at Home
Nº Contacts with PC Nurse in Total
Contact Dates (PC Nurse at Centre)
Contact Dates (PC Nurse by Telephone)
Contact Dates (PC Nurse at Home)
Nº Contacts with Cardiology
Contact Dates (Cardiology)
Nº Contacts with Endocrinology

Contact Dates (Endocrinology)
Nº Contacts with Nephrology
Contact Dates (Nephrology)
Nº Contacts with Psychiatry
Contact Dates (Psychiatry)
Nº Contacts with Internal Medicine
Contact Dates (Internal Medicine)
Nº Contacts with A&E Services
Contact Dates (A&E Services)
Nº Contacts with Hospitalisation
Nº Days in Hospitalisation
Contact Dates (Hospitalisation)
Nº Days in each Contact Date (Hospitalisation)
Nº Contacts with Home Hospitalisation
Nº Days in Home Hospitalisation
Contact Dates (Home Hospitalisation)
Nº Days in each Contact Date (Home Hospitalisation)

Table 13: Data items to be used in the predictive modelling

As stated, before sending the excel database files that contains patients follow-up and resource consumption data to Kronikgune, these files will be anonymized by each pilot site. To make sure that data cannot be traced, the data extracts will not include any identifiers. Neither will demographic descriptors be used apart from age and sex. Moreover, instead of the exact age of the patients, an age range will be used to ensure the anonymization. Each age range covers a 5 year age-span. In the same way, for each patient, all the resource utilization or contact dates will be manipulated automatically and randomly within a range of ±30 days. This way it will not be possible to trace the data and to link it with the original databases.

To automatically anonymize the database, an excel tool has been created. This template has two sheets. In the first sheet the pilot sites can manually enter the original data to create the original database. In this sheet each row will correspond to a patient and no identifiers or identification codes will be assigned. The second sheet will automatically anonymized the data introduced in the first sheet, converting age to an age range with a 5 year age-span and varying the patients contact dates ± 30 days. Figure 4 shows how the conversion from the original database to anonymized database will look like. This second anonymized sheet will be the one that pilot sites will have to send to Kronikgune by email for later use in the modelling.

Figure 4: Conversion from the original database to the anonymized database.

7.2. The ASSIST approach

ASSIST is an assessment and evaluation tool for telemedicine that was developed in the context of a project funded by the European Space Agency, which ran from 2010 to 2012. It was originally developed for use in the context of telemedicine and telehealth services, specifically to assess the economic viability of telemedicine pilot projects. During the validation phase, ASSIST was successfully applied by five telemedicine projects. A core aim of ASSIST is to facilitate the transposition of a pilot project into routine service operation and to support service providers in achieving a sustainable economic model where service benefits are higher than service costs. In short, it consists of a methodological approach, a service assessment model and a software toolkit to help project leaders, entrepreneurs and start-ups to objectively and rigorously evaluate their solution from an evidence-based multi-stakeholder perspective, i.e. individuals and organisations that are actively involved or passively affected by a service. The tool's assessment process has three steps:

1. Service assessment model setup (the service change is analysed to identify the key components like applicable governance and the reimbursement model, stakeholders and the financial impacts (costs and benefits on the stakeholders).
2. Data collection and monetization.
3. Calculation of performance measure (the main outcome measure is based on the ratio of total costs to total benefits, i.e. including financial costs and benefits, resource costs and benefits and intangible costs and benefits).

The ASSIST tool acts as a cost-benefit data pond from different sources and adjusts for the varying data quality using a Monte-Carlo simulation. Data sources include accounts data from the pilot sites, literature reviews, expert interviews, trial participant surveys and expert estimations.

7.2.1. Suggested indicators for the impact modelling

For the impact modelling approach, options for meaningful cost and benefit indicators are discussed with the pilot site managers. Below we present an initial set of indicators that could be used for the modelling. The definite indicator set may vary per pilot site. The indicators will be used in the ASSIST tool (results to be reported in D9.6) and populated with data from the pilot sites.

For health care provider organizations, such as clinics, the following indicators are suggested and currently under revision with the pilot site managers and local clinicians:

Impact	Description
Average gross annual income of Primary care physicians	
Average gross annual income of Primary care nurses	
Negative impacts (intangible and tangible costs)	**Description**
Staff time spent on service development	Includes all personnel working on the development, testing and implementation of the service.
Staff time spent on training sessions	Includes all personnel receiving training in relation to the new service.
Adaptation time	In addition to the personal, non-economic cost of adaptation, professionals usually also need more time in performing their tasks during a transition period. This is a temporary reduction in productivity and includes time spent on engagement, for defining new working practices, as well as time needed for getting used to new technology and new practices. Once the services become routine, the need becomes zero. This indicator considers working time of professionals, and is thus an economic cost to care organisations.

ICT – software	Includes the new ICT service system under observation or any other software that may be needed in addition to conventional service provision.
ICT – hardware	Includes for instance server costs or medical devices. These have well known market prices
Devices for professionals	Includes all devices used by professionals, as specified by the particular service. Measures are market prices
Extra staff time for service provision to patients – actual time	Includes all personnel working on service provision.
Extra staff time for service provision not related to patients - actual time	Includes all extra time spent by personnel not in relation to an end-user, as an effect of the new service. Time is accounted for using minutes per day.
Forgone income from avoided practice consultations	Avoided consultations by patients / clients at the practice due to the new service leading to a reduction in the income of the organisations.
Forgone unit cost from avoided practice consultations by Multimorbid patients	Avoided consultations by patients / clients at the practice due to the new service leading to a reduction in the income of the organisations.
Forgone income from avoided home visits	Avoided visits to patients / clients due to the new service leading to a reduction in the income of the organisations.

Payment to teleservice provider	Payments to teleservice providers can include all telecare/telehealth services, telecommunications services, hardware, software, and training.

Positive impacts	**Description**
Resource liberation (assessment/planning) for Primary care physicians or nurses	Includes all staff resources saved by personnel in relation to an end-user, as an effect of the new service. Time is accounted for different types of activities, the time saved for them and their frequency of occurrence.
Resource liberation (intervention) for Primary care physicians	Includes all staff resources saved by personnel in relation to an end-user, as an effect of the new service. Time is accounted for different types of activities, the time saved for them and their frequency of occurrence.
Resource liberation (intervention) for Primary care nurses	Includes all staff resources saved by personnel in relation to an end-user, as an effect of the new service. Time is accounted for different types of activities, the time saved for them and their frequency of occurrence.
Resource liberation from avoided home visits - travel cost	This is the financial component of avoiding home visits, quantified by the number of visits avoided and the price of travel
More income from more visits	C3-Cloud services can lead to identification of otherwise undetected demand, as well as shifts between services, where clients / patients visit one type of facility instead of another. For example, a specialist consultation may replace a hospital admission. This brings some extra demand to the specialist care organisation.
Top-up payments from South Warwickshire NHS Foundation Trust and NHS Digital (government org.)	HPOs may receive a financial incentive by payers to reimbursement of extra work caused by the telemedicine service

External financial support for Primary care organisations, e.g. the H2020 funds	Especially at the beginning of a service external financial support can be used for reducing the risk of failure. Support can be received from a number of different agencies like banks or research funding institutions

For payers, the following indicators are suggested and currently under revision with the pilot site managers:

Negative impacts	Description
Extra service use: additional consultations with Primary care organisations	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: additional consultation with Rheumatology department	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: more admissions to Hospital	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: longer stays in Hospital	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: more trips by Medical transportation services	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: earlier institutionalisations in Nursing homes	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: more visits by Community Nursing Services (CNS)	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: more visits by Social care provider	Amount of reimbursement paid by this payer to provider for all additional service use.
Extra service use: more visits by Third-sector provider	Amount of reimbursement paid by this payer to provider for all additional service use.
Payment to Tele Service Centre	Amount of reimbursement paid by this payer to provider for all additional service use.
Top-up payments by South Warwickshire NHS Foundation Trust and NHS Digital (government org.) to HPOs	Direct payments (not part of regular reimbursement) to provider for service use.

Increase in drug costs	Telemedicine can lead to better compliance to treatment, or earlier intervention because of more timely diagnosis. To the extent that this involves medications, the consumption of drugs can increase, causing an increase in the expenditure on drugs. Only the extra bills are considered.
Positive impacts	**Description**
Reduced service use: less consultations with Primary care organisations	Amount of reimbursement saved by this payer from provider for all reduced service use.
Reduced service use: less consultation with Rheumatology department	Amount of reimbursement saved by this payer from provider for all reduced service use.

Reduced service use: less admissions to and shorter stays in Hospital	Amount of reimbursement saved by this payer from provider for all reduced service use.
Reduced service use: delayed institutionalisation in Nursing homes	Amount of reimbursement saved by this payer from provider for all reduced service use.
Reduced service use: less visits by Community Nursing Services (CNS)	Amount of reimbursement saved by this payer from provider for all reduced service use.
Cost saving from shorter sick-leaves (short-term)	Payers can cover the cost of absence from work due to (short-term) illness.
Cost saving from shorter sick-leaves (long-term)	Payers can cover the cost of absence from work due to (prolonged) illness.
External financial support for South Warwickshire NHS Foundation Trust and NHS Digital (government org.)	Especially at the beginning of a service external financial support can be used for reducing the risk of failure. Support can be received from a number of different agencies like banks or research funding institutions
Cost savings from lower drug bills	Better clinical outcomes can be associated with a generally better health condition, a different medication mix, possibly a cheaper one.

For **patients and their informal care givers**, the following indicators are suggested and currently under revision with the pilot site managers:

Impact	Description
Average gross annual income of Multimorbid C3-Cloud patients	Enter an average household or individual income for this group.
Share of Multimorbid C3-Cloud patients working	Enter an average share of people in this group that would usually be working / in employment.
Negative impacts	**Description**
Fee for services	Depending on the business model, clients / patients may be expected to pay for a service out of pocket. The payments may be covering the whole cost of service, or be a contribution on top of payments by third parties.
Contribution to home adaptations	Some applications may require more or less substantial installation and even construction work at the end-user's home.
Inconvenience: training time	Includes all time spent by end-users in relation to training received as part of the new service. Other than for provider organizations, time here reflects inconvenience caused by using the service, rather than a tangible cost item.
Inconvenience: adaptation time	Includes all time spent by end-users getting used to the new service. The indicator reflects both the negative impact of temporary discomfort and scepticism towards change, as well as the extra time spent with the system during the adaptation period, compared to the time spent during routine service.
Inconvenience: extra time for service use spent by Multimorbid C3-Cloud patients	Includes all extra time spent by end-users, as an effect of the new service. Time is accounted for different types of activities, the time spent for them and their frequency of occurrence.
Inconvenience: extra travel time for service use spent by	Includes all extra time spent by end-users for travelling to receive services, as an effect of the new service. Time is accounted for

Multimorbid C3-Cloud patients	different types of activities, the time spent for them and their frequency of occurrence.
Extra travel cost for service use spent by Multimorbid C3-Cloud patients	Includes all extra cost for end-users for travelling to receive services, as an effect of the new service. These can be for private travel or public transport, based on distance traveled and cost per kilometer.
Positive impacts	**Description**
Valuation of intangible benefits by Multimorbid C3-Cloud patients according to eCCIS	Covers overall subjective and intangible benefits of the new service, primarily in relation to user satisfaction. Supported by the questions included in the eCCIS - eCare Client Impact Survey and the eCCIS scoring tool.
Convenience: time saved for service use by Multimorbid C3-Cloud patients	Includes all time saved by end-users, as an effect of the new service. Time is accounted for different types of activities, the time saved for them and their frequency of occurrence.
Convenience: travel time saved for service use spent by Multimorbid C3-Cloud patients	Includes all time saved by end-users for travelling to receive services, as an effect of the new service. Time is accounted for different types of activities, the time spent for them and their frequency of occurrence
Travel cost saved for service use spent by Multimorbid C3-Cloud patients	Includes all cost saved by end-users for travelling to receive services, as an effect of the new service. These can be for private travel or public transport, based on distance traveled and cost per kilometer.
Saved money from contribution to care costs saved by Multimorbid C3-Cloud patients	This includes avoided out of pocket co-payments to health or social care services. An instance where this occurs is when referral to a nursing home can be deferred or avoided because of a home telemonitoring service being effective and sufficient

For **clinicians, nurses and other clinic staff**, the following indicators are suggested and currently under revision with the pilot site managers and local clinicians:

Impact	**Description**
Average gross annual income of Primary care physicians	Enter an average income for one full-time employee without employer contributions to social security
Negative impacts	**Description**
Temporary inconvenience	Health and care professionals, regardless of whether they are users or become providers of telemedicine services, need to be personally involved from the very beginning.
Continuous inconvenience and irritation	Further to temporary effects related to adaptation, professionals can perceive that some old working practices are superior to new ones. Health- and care professionals may feel that they are being watched and judged.
Positive impacts	**Description**
Valuation of intangible benefits by Primary care physicians according	

7.3. Predictive modelling and ASSIST – the merged impact modelling tool

In line with the specific C3-Cloud objectives SO6 and SO8 detailed in the DoA, C3-Cloud will develop a large-scale impact modelling tool for large-scale rollout modelling, by merging the predictive modelling of health care resource use tool (using discrete event simulation, DES) developed by Osakidetza and the cost-benefit analysis tool for innovative ICT services 'ASSIST' developed by empirica. It is used for large-scale impact modelling of the C3-Cloud application by evaluating the estimated/predicted impact of C3-Cloud system. It informs decision making in the management of integrated care and on the expected impact of scaling up the use of C3-Cloud. By merging the tools, we try to improve reliability and validity of the tool as this new tool would incorporate the comprehensive perspective applied by ASSIST and the flexible engine developed in modelling to represent mathematically the natural history of the disease. The conceptual model would include not only the health system but also the complete set of involved stakeholders.

Research objectives for the merger are:

- Evaluation of C3-Cloud service utilization (e.g. number of care plans developed, intensity of use, number of virtual sessions or time use for C3-Cloud activities)
- Evaluation of healthcare resource utilization with C3-Cloud services
- Help decision makers to decide on further using the C3-Cloud application to foster exploitation and innovation.
- Identification of disadvantaged stakeholders that are affected by benefit shifts during change management.

The output of Osakidetza's predictive modelling will be used for the ASSIST modelling. The following data will be added as cost indicators for respective stakeholders or organizations in the ASSIST tool:

- Prevalence of disease cases / i.e. patients in a given region or pilot site at any given month for a 84 months projection. This is based on incidence rates and considers also mortality rates
- The mean number of contacts between the different healthcare professionals (nurses, GPs, endocrinology, cardiology, nephrology, psychiatry, internal medicine, A&E) and their patient) per month/year
- Number of contacts with hospitalization per patient per month and the related unit cost based on days in hospitalization
- Number of days
- Unit cost modelled per month and patient for drug prescriptions, hospitalization and contacts with healthcare professionals

This data input will be based on technology trial data and anonymous control patient data and thus is more accurate than for example expert estimations that are often used with the ASSIST approach. Thus, it improves the validity and reliability of the ASSIST modelling. However, the predictive modelling let the analyst take only one perspective – that from the healthcare system – while the ASSIST model let one take the perspective of each stakeholder affected by or involved in a new service. Combining the two approaches thus makes the results more reliable but broad enough as to identify specific winners or losers of a service introduction. This allows to analyse data and to draw better conclusions for the up-scaling and recommendations towards the potential of the service system.

8. DEPLOYMENT AND SCALE-UP PLANS

The following sub-chapters elaborate on the early, interim deployment and scale-up plans of C3-Cloud for the three pilot sites, based on input in D9.3, presuming it were available on the market post project. This is in preparation for the ASSIST modelling as we identify already indicators that will (in the ASSIST tool) be basis data for e.g. the target population, the care providers and organizations that may be involved or affected by a C3-Cloud service, funding or payment options and scenarios that could be foreseen for C3-Cloud up-scaling.

8.1. South Warwickshire, UK

South Warwickshire NHS Foundation Trust (SWFT) is a vertically integrated healthcare provider, offering acute hospital services to the population and integrated community and children's services across the whole county. Warwickshire ICT Services is a division of SWFT and provides ICT services to all GP practices across the county, as well as to the Trust. This unique support arrangement enables Warwickshire ICT Services to act as an intermediary between acute, community and primary care services across the whole county and serve a total population of 550,000.

Warwickshire has an elderly population of over 20 % (113,000). An estimated 1 in 3 people in Warwickshire are living with one or more long-term conditions. In South Warwickshire this equates to 70,000 people. Currently 12.2% of the total population in Warwickshire is estimated to be living with cardiovascular disease (CVD), whilst 5.6% of the adult population is estimated to be living with coronary heart disease (CHD) and 2.6% with stroke. 7.3% of the population is estimated to have diabetes, and if current trends persist the total prevalence of diabetes is expected to rise to 8.1% by 2020 and 9.1% by 2030.

The total workforce of SWFT is nearly 4,000 staff working across 144 sites. A further 76 GP practices are also supported. SWFT provides nationally recognized innovative services to help patients to stay out of hospital, including a Community Emergency Response Team (CERT) and Discharge to Assess (D2A). In D2A, the Trust utilizes 40 beds in local care homes to assess what a patient's long-term needs are. Building on joint work with social care workers, a new "Trusted Assessment" approach has been adopted, which allows packages of care to be restarted without a full assessment having to be repeated by social services.

Healthcare is funded on a per capita basis through direct taxation. Funding is routed through commissioning organisations who determine what the health priorities are. Some funds are allocated to 'Primary Care' (GPs) and some to 'Secondary Care' (Acute hospital and Community Services). Additional allocations can be made directly from central government and such allocations are spent on the basis of prioritised requirements.

SWFT adopted the "Lorenzo" enterprise Electronic Patient Record (EPR). Initially an administration system, it was expanded in 2015/2016 to include order communications, clinical documentation and electronic prescribing. Lorenzo currently has no 'mobile' capability, so the Trust has deployed the Egton Medical Information Systems (EMIS) Community solution. GP practices across South Warwickshire have moved to a single IT provider which is also provided by EMIS. There is currently no integrated countywide patient record accessible to all relevant agencies and no widespread use of telehealth or telemedicine technologies. SWFT delivers integration between information systems, using a Trust hosted Orion Rhapsody engine, which supports all versions of HL7, as well as numerous other data interchange formats such as email, bulk file import and export, and XML. This is fully HL7 CDA R2 and NHS Interoperability Toolkit (ITK) compliant.

To-be scenarios. The C3-Cloud integrated care solution is currently being piloted at the Rother House Medical Centre in Stratford, South Warwickshire. This Practice has a total list of 13,600 patients and anticipated at the start of the project that between 400 and 500 have complex multiple long-term conditions that could benefit from the C3-Cloud solution. However, out of the 241 patients that were approached, only 20 agreed to take part. These patients will be treated using C3-Cloud (alongside their

existing IT systems and processes) during their normal consultations at the practice and if/when they present to any of the participating healthcare teams within the SWFT hospitals or community.

Although integration with the main SWFT IT systems could not been achieved due to cost and logistical factors, a data extract will be taken from the GP EMIS system, the Trust EPR (Lorenzo), and the Trust community system (Community EMIS) on a weekly basis and uploaded into C3-Cloud. This will reduce duplication of data entry and provide a basic medical summary for the participating patients.

To provide some context for any potential future deployment of C3-Cloud, the illustrations below provide a high-level overview of SWFT's overall IT strategy and plan over the coming years. The C3-Cloud solution would need to be considered in the light of this strategy/plan to ensure strategic, operational and technical fit, but also take account of the relevant procurement regulations.

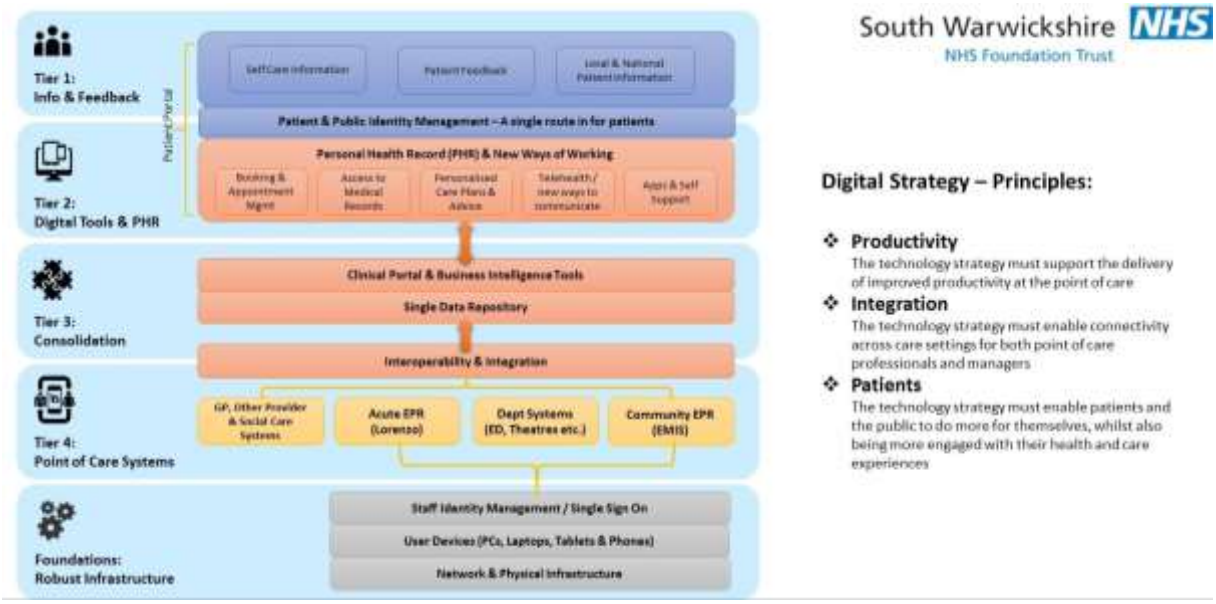

Figure 5: SWFT strategy, priorities and plan 2019/2020

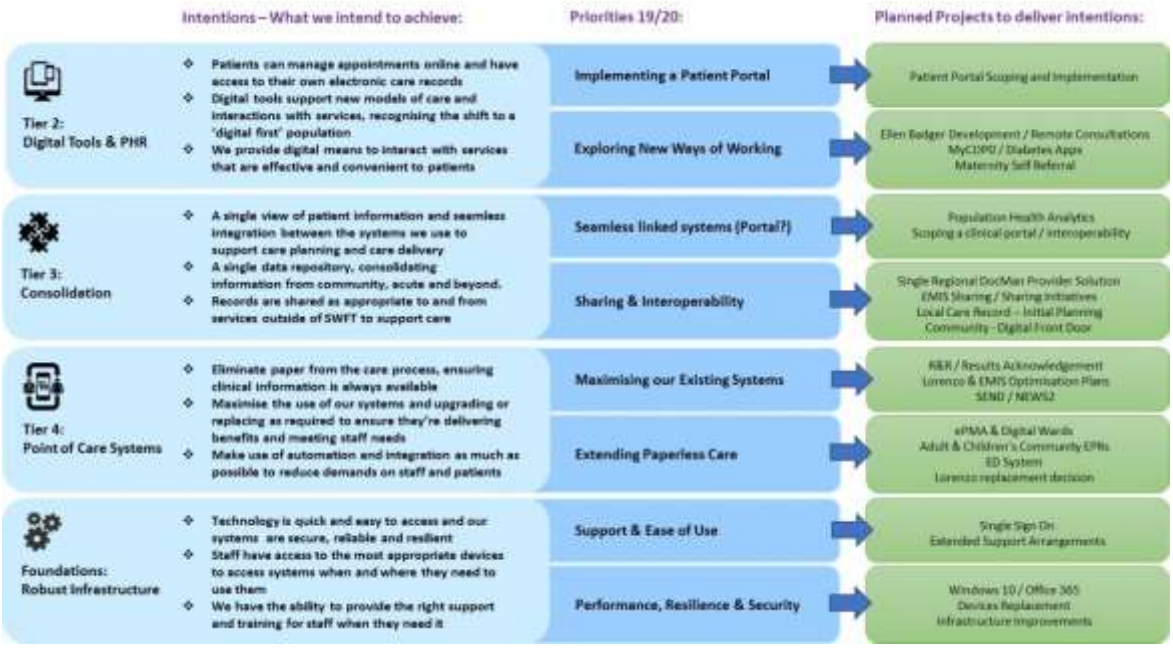

Figure 6: SWFT intentions

Figure 7: SWFT healthcare initiatives alongside C3-Cloud

SWFT is very interested in the usage of C3-Cloud care pathways and care plans for patients with multi-morbidity across primary and secondary care. Poly-pharmacy decision support modules will allow systematically taking into account co-morbidities. Overall, SWFT would like to reduce hospitalization of patients with multiple co-morbidities and increase adherence to treatment and medication regimes.

In consideration of the strategy/plan above, some of the key areas where the C3-Cloud system or it's components could theoretically be considered include clinical portal and patient portal. NHS Policy is to increase patient engagement and provide online access to clinical services and data wherever possible. Local strategy reflects this with an ambition to deploy a patient portal to support the management of patients with complex long term conditions. Similarly, lesson learned from the approach to the shared care plans could be adopted in SWFT.

That said, the intention of SWFT is to review the research generated by the C3-Cloud project, before making any decisions regarding deploying the solution more widely. Furthermore, in line with local and national procurement rules the Trust will conduct a full market evaluation of all potential suppliers to ensure that best value for money is achieved

Any future deployment of the C3-Cloud solution would obviously require extensive engagement with primary and secondary care stakeholders, relying on the ability to demonstrate to care commissioners and other budget holders that there has been a positive impact on patient care with improved outcomes.

It should also be noted that before further deployment within South Warwickshire could be considered a number of activities would need to be carried out. For example, analysing and (where appropriate) implementing feedback from users during the trial, carrying out more thorough testing in a real world environment, widening of the conditions that are covered by the solution, consideration of how to manage the high degree of system integration that would be needed to make a clinical portal successful, especially in the NHS which has a high volume of systems.

8.2. Basque Country, Spain

The Osakidetza, Basque Health System, has a target population of 2.17 million inhabitants. In 2016 more than 21% (>458,000 inhabitants) of the total population was older than 65, more than 28% had one or more chronic conditions and 1.5% of the population had been stratified as complex and multi-morbid. Only considering the patients with multiple chronic conditions, a C3-Cloud system could be used for 128,240 patients and their care planning with reconciled clinical guidelines.

Osakidetza includes 13 Integrated Care Organizations with a unique management team (OSIs), 4 University Hospitals, 7 Regional Hospitals, 2 long-term Hospitals, 3 Integrated Mental Health Networks, Emergencies and Basque Country for transfusions and human tissues. In 2014, the structural staff of Osakidetza consisted of 6.313 physicians, 8,227 GP nurses, 4,022 auxiliary nurses and others (7,245). Chronic Disease Management Programs exist for multi-morbid patients as well as for diabetes, COPD and heart failure. The Active Patient Program (inspired in the Stanford methodology) is used and widely available in the country. The KronikOn program has been developed for empowering multi-morbid patients based on the Stanford methodology. A C3-Cloud system for multimorbidity care planning would complement the current service system nicely.

C3-Cloud service integration into the eminent EHR services (Osabide AP in primary and Osabide Global in secondary care) can be done as is shown with the C3-Cloud technology trial and could be further integrated for instance with the e-Prescription service Presbide, which provides a unique system in both care sectors.

To-be scenarios. C3-Cloud is piloted at five Integrated Care Organizations (OSIs): Alto Deba, Araba, Bilbao-Basurto, Eskerraldea Enkarterri Cruces, and Donostialdea. C3-Cloud is expected to increase the information that patients have access to regarding their health and treatment, by providing access to their personalized care plan. The tele monitoring service will be extended to a wider spectrum of patients and healthcare professionals. The Empowerment Platform will facilitate the collection of self-reported parameters. An integrated C3DP platform enables healthcare professionals to set up care plans for their multimorbid patients directly in the Osabide Global system.

The main customers of a C3Cloud system in Osakidetza include Regional Authorities responsible for health and social care; the healthcare providers (Primary Care Centres / Hospitals); vendors of Electronic Health Record (EHR) / Electronic Medical Record (EMR) / Personal Health Record (PHR) systems. The main users include healthcare professionals and patients with their informal caregivers.

In order to make the C3-Cloud system market ready, it would be desired if the system was extended to cover also additional chronic diseases beyond diabetes, renal failure, heart failure and depression. Also, a bi-directional interoperability with local and regional ICT systems (e.g. appointment scheduling, e-prescription, laboratory orders) is needed.

Key resources needed for initial post-project scale-up include investments to develop the abovementioned system functionalities, with either follow-up projects, new partners or other investors. Also, a C3-Cloud validation study would be the first step to validate and improve the system regarding patient safety, clinical effectiveness and efficiency. Also it would be needed to validate the drug-drug and drug-disease interaction systems.

8.3. Region Jämtland Härjedalen, Sweden

The County Council Region Jämtland Härjedalen (RJH) covers a population of 126,000 inhabitants of which 23% are elderly people (65+). The population is spread over a large area of 53,753 km². A joint project between the County's municipalities and RJH identified 4,930 persons (18% of the 65+ population) to be elderly with comprehensive hospital (>3 hospitalizations/a) or home care needs (>7 out-patient specialist care/a). 3,686 patients are in the national Swedish diabetes register (12.7% of this age group). 85.7% of these diabetic patients also have treated hypertension and 30.8% retinopathy. With

the exception of diabetes, the exact frequency is seldom known. Only considering the patients with multiple chronic conditions, a C3-Cloud system could be used for 3,158 patients and their care planning with reconciled clinical guidelines in RJH.

The County's only hospital is located in the only town Östersund and the most remote healthcare centers are located almost 400 km away, which emphasises the need for ICT supported monitoring and care plans that reconcile medical guidelines across diseases that may have been set up by multiple healthcare professionals spread through the county. Primary care is provided in 28 healthcare centers and secondary care at the hospital. Tertiary care is provided in collaboration with other county councils at a university hospital (Umeå) 450 km away. The hospital has 12 ambulances spread over the county and one helicopter. Social and home care are provided by the municipalities, and the collaboration with the Region's primary and secondary care is well-established.

RJH employs 358 doctors, 922 nurses and 546 nurse assistants. Most of the care of patients with chronic diseases is provided by family physicians in cooperation with district nurses at health care centers. They coordinate the care given at the secondary care level. If patients have a need for care in their homes, a district nurse together with a nurse assistant are provided by the municipality. The doctor from the health care centre and the district nurse from the municipality have regular meetings. Patient education programs and group activities exist for patients of some chronic diseases, e.g. diabetes.

The national website www.1177.se is intended as the patient's first contact point with the care system. The website also includes education and information material. Fully integrated electronic health records are used in all health care centers and at the secondary care level since more than 20 years. The region has recently changed its electronic health care system to Cosmic® by Cambio, a C3-Cloud project beneficiary. Cosmic® is based on pre-European standard Health Information Service Architecture (HISA), supports openEHR archetypes as core information models, and uses HL7 v2 and v3 messages for inter-system communication. Electronic prescription is achieved through Cosmic® and the national data system. RJH allows all patients' access to their records through EHR in 2016-2017.

Municipalities have separate electronic health care systems, presently with no integration to Cosmic. Social care records are kept separately. All caregivers have access to and daily use of electronic health records / home care records. ICD-10 is used for hospitalization and in primary/secondary care; DRG in secondary care. Within home care, wireless telemonitoring is used e.g. to register access by caregivers to the patients' home.

To-be scenarios. Due to many interrelated challenges of the county, there is political, economic and demographic pressure to reform the healthcare chain. The overall wish from both stakeholders and end-users is to develop integrated care, of which C3-Cloud could be one rack-wheel. A beginning shift in care organisation, from primary care and hospital care seen as two separate entities towards a more patient centred integrated care is now seen in RJH. An ambition to have a care integration also with the municipality care is existing, though still distant. Nationally a policy towards a strenghtend primary care is seen.

A crucial premise for post-project deployment and scale-up is a functioning integration with the swedish EHR system. The strategy is to inform about and demonstrate C3-Cloud to the buyers group from the 17 Swedish Regions using Cambio Cosmic. A joint solution for all regions is needed to ensure a succesful deployment. A scale-up would thus need a customer group larger than just RJH. In that regard, the first action to follow up with C3-Cloud post project is RJH's participation in the H2020 ADLIFE project, aiming to advance solutions from the C3-Cloud project regarding diseases covered.

Additional customers could include private healthcare organizations (primary care and hospitals) and private insurances.

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