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

D7.2 Clinical Decision Support Modules for Personalised Care Plan Development and Execution

Work Package:	WP7 Coordinated Care and Cure Delivery Platform
Due Date:	31 December 2017
Actual Submission Date:	21 December 2017
Project Dates:	Project Start Date: 01 May 2016
	Project End Date: 30 April 2020
	Project Duration: 48 months
Deliverable Leader:	WARWICK

Project funded by the European Commission within the Horizon 2020 Programme (2014-2020)		
Dissemination Level		
PU	Public	Demonstrator
CO	Confidential, only for members of the consortium (including the Commission Services)	
EU-RES	Classified Information: RESTREINT UE (Commission Decision 2005/444/EC)	
EU-CON	Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC)	
EU-SEC	Classified Information: SECRET UE (Commission Decision 2005/444/EC)	

Document History:

Version	Date	Changes	From	Review
V0.1	20-11-2017	Template of the document associated to the demonstrator	WARWICK	KG SRDC CAMBIO
V0.2	08-12-2017	Technical requirements of CDSMs (section 2)	WARWICK	
V0.3	13-12-2017	CDSM technical specification (section 4.1 and appendix I)	SRDC	WARWICK
V0.4	14-12-2017	GDL2 and CDS hooks service description	WARWICK CAMBIO	
V0.5	14-12-2017	Guideline reconciliation (section 3)	OSAKI KG	WARWICK
V0.6	15-12-2017	GDL2 and CDS service examples (section 4.2 & 4.3)	CAMBIO	WARWICK
V0.7	15-12-2017	Future plans (section 6)	WARWICK	
V0.8	17-12-2017	Software demo instructions and screenshots (section 5) Addition of annexes, formatting of document	CAMBIO WARWICK	OSAKI KG INSERM
V0.9	19-12-2017	Review comments incorporated	WARWICK	
V1.0	21-12-2017	Final version prepared and reviewed by the Coordinator Team	WARWICK	

Contributors (Benef.)	Lei Zhao, Sarah Lim Choi Keung, Theodoros N. Arvanitis (WARWICK) Rafael Rotaeche, Arritxu Etxeberria, Javier Urraca, Nicolás González, Antonio de Blas (OSAKI) Esteban de Manuel, Lola Verdoy (KG) Mikael Lilja (RJH) Christopher Marguerie, Peter Hutchinson, Phil Goode, Jo Jennings (SWFT) Gokce B. Laleci Erturkmen, Mustafa Yuksel (SRDC) Rong Chen (CAMBIO) Jacques Bouaud, Catherine Duclos, Brigitte Seroussi, Mikael Dusenne (INSERM)			
Responsible Author	Lei Zhao		**Email**	Lei.Zhao@warwick.ac.uk
	Beneficiary	WARWICK	**Phone**	+44 2476574516

EXECUTIVE SUMMARY

WP7 will provide ICT platforms (Personalised Care Plan Development Platform & Coordinated Care and Cure Delivery Platform) and supporting Clinical Decision Support Modules to enable multidisciplinary team of health and social care givers to collaboratively create, execute and monitor personalised care plans through reconciliation of clinical guidelines for individual diseases.

As part of the Coordinated Care and Cure Delivery Platform, Clinical Decision Support Modules will access patient data from different sources to subsequently fuse and analyse all these data, in order to: perform risk assessment and stratification of candidate elderly people for inclusion in integrated care programmes; reconcile clinical guidelines for individual diseases to develop personalised care plans; detect and propose resolutions for guideline clashes; detect duplicate, unnecessary or contraindicating medications; and monitor and detect deviations from the outcome goals set in a patient's care plan. The Task 7.2 concerns the technical specification and implementation of Clinical Decision Support Modules according to the deliverables D7.1 Evidence Based Clinical Guideline Definitions and Flowcharts for Individual Chronic Conditions, D3.2 Requirements Specification of the C3-Cloud Architecture, and the Description of Action. The Task 7.2 started in month 9 (1 January 2017) and has ended in month 20 (31 December 2017).

The deliverable D7.2 is a description of the demonstrator of the C3-Cloud Clinical Decision Support Modules (CDSMs). This document defines the objectives of the task and tools by referencing to clinical guidelines and technical requirements. The document provides also a description of the implementation strategies as well a manual for the tool. The main purpose of the demonstrator and the document is to show the progress of the implementation of CDSMs to implement the use cases in a concrete way. The software demonstration is part of WP7 integrated demo which was given at the project review on 8 December 2017.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

1. DOCUMENT OVERVIEW

1.1. Purpose

The deliverable D7.2 is a description of the demonstrator of the C3-Cloud Clinical Decision Support Modules (CDSMs). This document defines the objectives of the task by referencing to clinical guidelines analysed by the deliverable D7.1 [1] and technical requirements described in the deliverable D3.2 [2]. The document provides also a description of the implementation strategies as well a manual for the software tool. The main purpose of the demonstrator and the document is to show the progress of the implementation of CDSM components to implement the requirements in a concrete way.

1.2. Outline of the deliverable

The report on the CDSM demonstrator is organized as follows:

Section 2 summarizes the basic objectives of the task and tools that must be demonstrated by referencing to task requirements in description of action (DOA) and related deliverables.

Section 3 describes the approach and process we follow to develop Clinical Decision Support (CDS) rules to reconcile clinical guideline definitions for individual chronic conditions identified in D7.1, in order to automate personalised care plan development.

Section 4 details the implementation strategies that were adopted for developing CDS modules and delivering the demonstrator.

Section 5 provides information on how to use the demonstrator with one specific example.

Section 6 addresses future plans to continue the integration work with the other components.

Appendix I provides the complete technical specification of Diabetes Mellitus type 2 related CDSMs.

Annex 1 – 9 provide the complete reconciled rules from the two, three or four diseases (Diabetes, Renal Failure, Heart Failure and Depression) combinations.

1.3. Scope

WP7 will provide Coordinated Care and Cure Delivery Platform (C3DP) to enable multidisciplinary team (MDT) of health and social care givers to collaboratively create, execute and monitor personalised care plans. The supporting Clinical Decision Support Modules enable reconciliation of clinical guidelines for individual diseases, risk stratification, poly-pharmacy management and care plan goal setting and monitoring. As part of C3DP platform, CDSMs will access patient data from different sources to subsequently fuse and analyse all these data, in order to: perform risk assessment and stratification of candidate elderly people for inclusion in integrated care programmes; reconcile clinical guidelines for individual diseases to develop personalised care plans; detect and propose resolutions for guideline clashes; detect duplicate, unnecessary or contraindicating medications; and monitor and detect deviations from the outcome goals set in a patient's care plan. The CDSM implementations will be based on open standards and some of the implementations will contribute to the open source community.

1.4. Context

C3-Cloud CDSMs provide clinical decision support functions to support MDT in the creation, execution and monitoring of integrated care plans for every multi-morbid patient with C3-Cloud C3DP. While the technical mechanisms of C3-Cloud CDSMs are generic and can support a variety of chronic conditions, the C3-Cloud evaluation studies focus on 4 specific chronic diseases and their combinations:

A. Diabetes Mellitus type 2 (DM2)
B. Renal Failure (RF) (including eGFR/GFR 30-59; excluding eGFR/GFR<30)
C. Heart Failure (HF) (including NYHA I-II; excluding NYHA III-IV)

D. Depression (DP) (mild/moderate conditions only)

Patients to be included in the evaluation studies will have at least 2 out of these 4 diseases.

D7.1 surveyed and analysed clinical guideline definitions for the 4 chronic diseases and formalized in the form of flowcharts the care pathways for patients who have a single condition. C3-Cloud targeted multi-morbid patients will have co-existing chronic conditions where individual diseases are interlinked in various combinations. The Task 7.2 expands on the outcome of Task 7.1 and develops clinical guidance on how individual clinical guidelines can be reconciled for the automation of personalised care plan development. CDSMs encode D7.1 flowcharts and the reconciliation guidance into computable CDS rules and provide a standard based service interface to enable seamless integration and information exchange between CDSMs and C3DP. In the conceptual design of C3-Cloud architecture (Figure 1),

- FHIR is adopted as the standard for data exchange between C3-Cloud components;
- Patient data from all sources are transformed and stored in a central FHIR repository which is managed by C3DP;
- The technical implementation of CDSMs will utilize FHIR based open specification and be delivered as CDS Hooks [4] services;
- C3DP fetches patient data from the FHIR repository and calls the CDS services with the fetched data for evaluation;
- CDSMs execute CDS rules and return CDS Hooks Cards.

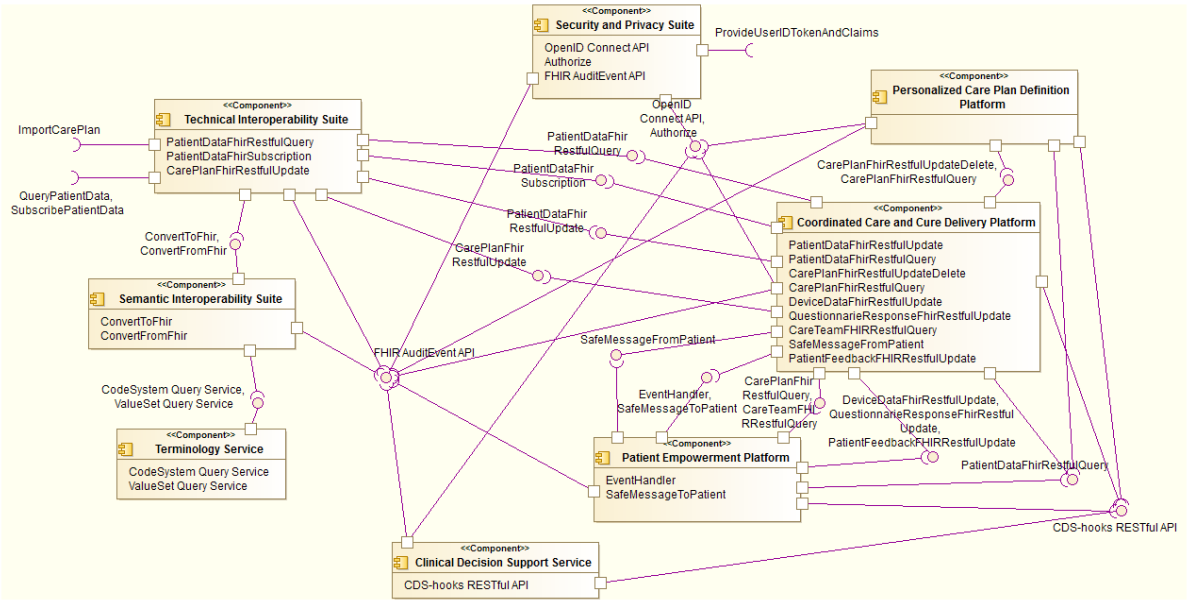

Figure 1: C3-Cloud Component Diagram from D3.3- Conceptual Design of the C3-Cloud Architecture

1.5. Abbreviations and Acronyms

Abbreviation / Acronym	Definition
AII	Angiotensine Receptor II
ACE	Angiotensine Converting Enzyme
API	Application Programming Interface
BP	Blood Pressure
C3DP	Coordinated Care and Cure Delivery Platform

CAMBIO	Cambio Healthcare Systems AB
CDS	Clinical Decision Support
CDSM	Clinical Decision Support Module
CKD	Chronic Kidney Disease
CPG	Clinical Practice Guideline
DOA	Description of Action
DPP-4 inhibitors	Dipeptidyl peptidase-4 inhibitors
DP	Depression
eGFR	Estimated Glomerular Filtration Rate
EHR	Electronic Health Record
FHIR	Fast Healthcare Interoperability Resources
GDL	Guideline Definition Language
GLP-1	Glucagon-like peptide-1
HbA1c	Glycated haemoglobin A1c
HF	Heart Failure
INSERM	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE
JSON	JavaScript Object Notation
KG	Kronikgune
MDT	Multidisciplinary Team
NIC	Nursing Interventions Classification
OSAKI	Servicio Vasco de Salud Osakidetza
PCPDP	Personalised Care Plan Development Platform
QRISK2	Cardiovascular disease risk algorithm
RAAS	Renin-angiotensin-aldosterone system
RESTful	Representational state transfer
RF	Renal Failure
RJH	REGION JAMTLAND HARJEDALEN
Rule ID	Identification number of the Reconciliation Rule
SGLT2 inhibitors	Sodium-glucose co-transporter 2 inhibitors
SIS	Semantic Interoperability Suite
SWFT	SOUTH WARWICKSHIRE NHS FOUNDATION TRUST
DM2	Diabetes Mellitus type 2

2. CDSM OBJECTIVES

CDSM technical requirements and conceptual design were elicited and documented in D3.2 and D3.3. Following the progress of the project, especially Task 7.1, the original requirements and design are refined and extended to support the project objectives and pilot needs. This section defines the objectives of the Task 7.2 and the delivered software tool, by referencing to the original requirements and design in D3.2 and D3.3 and describing their updates.

2.1. Original requirements

The system requirement specification for CDSMs, including functional, non-functional, interface and information requirements, are detailed in D3.2 (section 4.5). The requirements can be summarised as follows:

- The CDS system shall allow to create, view, update and validate the knowledge module of a CDSM.
- A CDSM shall evaluate patient data and produces suggestions based on the knowledge module it embodies.
- CDSMs shall include modules for clinical guideline based diagnosis and treatment suggestions, polypharmacy management suggestions, and risk assessment.
- The patient data for CDS evaluation shall conform to C3-Cloud FHIR profile.
- CDSMs shall be web services and provide API conforming to HL7 DSS standard [5]

2.2. Updated requirements

Due to the fact that T7.1 had not started (Month 5 to Month 8) at the time the requirements for CDSMs were developed (Month 5), the specification of the requirements were general and broad in its clinical scope. Following the development of clinical guideline flowcharts in T7.1, guideline reconciliation guidance in WP4 and evaluation protocols in WP9, a more specific scope of T7.2 is defined. On the other hand, a technical decision has been made in WP3 to adopt FHIR STU3 as the information standard for interoperability. As a consequence, CDS Hooks, instead of HL7 DSS, is chosen as the web services API for CDSMs, because it is an open specification built specifically for CDS on top of the FHIR stack. Based on these development and technical decisions, part of the CDSM requirements are refined as follows:

- CDSMs shall be web services and provide API conforming to CDS Hooks specification.
- CDSMs shall only return information and suggestions on care plan goals and activities.
- CDSMs shall encode the clinical guideline rules described in the D7.1 flowcharts (section 5) for the four non-severe conditions: DM2, RF, HF and DP.
- CDSMs shall encode the guideline reconciliation rules to detect and resolve conflicts between the guidelines for single diseases.
- CDSMs shall encode drug/drug and drug/disease interaction rules for polypharmacy management.

The detailed requirement updates are maintained in WP3 using a requirement traceability matrix.

3. CLINICAL GUIDELINE RECONCILATION

A personal care plan includes a unified care pathway for each patient including all conditions/co-morbidities. This requires estimating the risk, defining clear goals, balancing clinical evidence of benefit and harms and the patient's preferences, a time-based executable workflow of activities towards achieving the respective goals, including the pharmacological treatment.

An uncritical combination of clinical guidelines for separate diseases when treating multi-morbid patients could have contradictions that would increase risk and in some cases even result in unfeasible

treatment. There is a need to support clinicians in decision making in risk assessment, setting goals, choosing activities or pharmacologic treatment to include in a multi-morbid patient care plan.

CDSMs help the clinical decision making during the process of care, providing proactive and data driven decision assistance [6]. A decision support service takes in patient data as the input and provides back patient-specific assessments and recommendations. A service-oriented architecture facilitates implementation of clinical decision support capabilities in a scalable manner. CDSMs require significant resources to develop, curate and maintain large knowledge bases of clinical decision support content. Several functional capabilities have been described for the CDSM. Wright et al. [7] propose the following ones along four axes:

- *Triggers*: The events that cause a decision support rule to be invoked. Examples of triggers include prescribing a drug, ordering a laboratory test, or entering a new problem on the problem list.
- *Input data*: The data elements used by a rule to make inferences. Examples include laboratory results, patient demographics, or the patient's problem list.
- *Interventions*: The possible actions a decision support module can take. These include such actions as sending a message to a clinician, showing a guideline, or simply logging that an event took place.
- *Offered choices*: Many decision support events require users of a clinical system to make a choice. For example, a rule that fired because a physician entered an order for a drug the patient is allergic to might allow the clinician to cancel the new order, choose a safer alternative drug, or override the alert and keep the order as written but provide an explanation.

Within the scope of C3-Cloud, the CDS modules will be developed to be integrated into the C3DP platform. It is necessary to define the type of actions (messages, aids, reminders, etc.) that result in the clinical rules that will be incorporated to the platform and the degree of automatism of their generation.

This section describes the methodology and work plan followed in order to develop the final 52 reconciled rules/algorithms. Single disease decision rules are based on NICE clinical guidelines and described in D7.1 section 5 in the form of flowcharts. The reconciled rules are used together with the D7.1 flowcharts to develop technical specification of CDSMs.

3.1. Context

Clinical decision making in multi-morbid patients (with more than one disease) is a complex task. It can involve many professionals. Evidence based Clinical Practice Guidelines (CPGs) can help as they include the best and up-to-date knowledge that professionals and patients need. Their usefulness increases if they are acknowledged and agreed among the professionals responsible for the care of the patient. However, using different Clinical Guidelines for each individual chronic condition in patients with multiple health problems can lead to adverse effects and polypharmacy. This can cause an unacceptable burden of disease for the patient and his/her family and/or caregivers [8, 9, 10]. Therefore, it is necessary to reconcile the recommendations of the different guidelines.

CDSM in C3-Cloud targets patients over 65, having at least two among these four chronic diseases: diabetes, heart failure, renal failure and depression. It was agreed in Task 7.1 to use the NICE Guidelines as the main source of information. A number of decision making algorithms for the C3-Cloud selected diseases were drawn. They have been the basis for this work. The reconciliation of the selected NICE CPGs for these four conditions, according to the local adaptations collected in D7.1, includes resolving the interactions between them.

3.2. Analysis

The reconciliation of clinical guidelines supports individualized care plans adapted to each person according to their social and family context. These can be updated and modified according to the multiple diseases, changes in the clinical situation of the patient e.g. increasing age, changes to the

patient's selected objectives, progression of the severity of the process, occurrence of medical complications, sum of new comorbidities, drug interactions, etc.

3.2.1. Definition of comorbidity patterns

D7.1 presents logical flowcharts, described in an algorithmic way, for the NICE clinical guidelines targeting the individual diseases of the project. D7.1 algorithms provide information for the target single disease care plans. The challenge is to define how this information (recommendations) is modified when the patient has other co-morbidities. The four selected diseases generate 15 combination patterns, being 11 of comorbidity (Table 1**Error! Reference source not found.**).

Table 1: Comorbidity patterns: 15 different patterns (4 of one single disease) + (6 of two-disease combinations) + (4 of three-disease combinations) + (1 of four-disease combinations).

Single disease	DM2	RF	HF	DP		
Two disease combination	DM2, RF	DM2, DP	DM2, HF	RF, HF	DP, RF	DP, HF
Three disease combination	DM2, RF, HF	DM2, RF, DP	RF, HF, DP	DM, HF, DP		
Four disease combination	DM2, RF, HF, DP					

3.2.2. Interactions, reconciliation and components of Care Plans

CDSM support the reconciliation of care plans and solve interactions in multi-morbid patients (patterns of double, triple or quadruple comorbidity). They propose recommendations in four elements of the personalized care plan:

- Risk assessment;
- Goals;
- Activities;
- Pharmacotherapy.

The reconciliation of evidence based clinical guidelines includes resolving the interactions between them on the four components selected. We propose to follow the proposals of Muth [11, 12] to classify them (Table 2**Error! Reference source not found.**).

Table 2: Types of interactions (modified from Muth [11])

Disease Disease The presence of a disease is a risk factor to develop comorbidity or when it is already, it worsens its prognosis (i.e. RF increases the risk of developing HF but if both are present, HF has a worse prognosis) or both diseases overlap their symptoms (Asthenia as a symptom in a person with heart and renal failure) or may interfere with the diagnosis by altering lab tests results. **Disease to Drug / Drug to disease** The presence of a second disease (i.e. nephropathy) determines some type of contraindication, interaction or dose adjustment in people who need pharmacological treatment (Drug) derived from their index disease (i.e. diabetes) or its complications (i.e. complications Micro / macro of diabetes). Pharmacological treatment of comorbidity (i.e. nephropathy) conditions the evolution of the index disease (i.e. diabetes) **Drug Drug** The use of a drug for the treatment of a disease determines some type of risk with the use of another drug to treat the comorbidity. i.e.: IECAS may increase the side effects of metformin.

3.3. Reconciliation process

The reconciliation exercise aims to analyze the Disease-Disease, Disease-Drug and Drug-Disease between the comorbidities which coexist in a patient. The final aim is to reconcile relevant recommendations for different chronic conditions by identifying the synergies, cautions and contradictions. For Drug-Drug interactions the project seeks to reuse existing databases. Polypharmacy management will use polypharmacy criteria such as STOPP-START, which will also be managed separately.

3.3.1. Methodology followed for reconciliation of guideline recommendations

The method followed was:

1. The primary source of information has been the D7.1 individual conditions flowcharts/algorithms along with sources of information [13] described in the references section. We only considered the recommendations that are relevant for studying the interactions.
2. Selection of the critical issues where interactions can occur and that have to be addressed and reconciled. They include the risk of the patient, setting goals, defining different activities for the care plan or defining the pharmacological treatment. We focused on a few conflicts/constraints, taking into account the effects of the interaction (symptoms, safety, and potential harm).
    - Emphasis was given to [14]:
        - Disease-Disease interaction. There are different types:
            - The presence of a disease is a risk factor to develop a comorbidity or when it is already there, it worsens its prognosis (i.e. RF increases the risk of developing HF but if both are present, HF has a worse prognosis).
            - Both diseases overlap their symptoms (Asthenia as a symptom in a person with heart and renal failure) or may interfere with the diagnosis by altering lab tests results.
        - Disease to Drug / Drug to disease interactions. The interactions can be:
            - The presence of a second disease (i.e. nephropathy) determines some type of contraindication, interaction or dose adjustment in people who need pharmacological treatment (Drug) derived from their index disease (i.e. diabetes) or its complications (i.e. complications Micro / macro of diabetes).
            - Pharmacological treatment of comorbidity (i.e. nephropathy) conditions the evolution of the index disease (i.e. diabetes)
3. Check those selected issues, for possible conflicts between CPG recommendations. Potential conflicts were identified: repetition, wrong sequence or overlaps of activities, contradictory goals, location inconsistencies alternative options, constraints, potential treatment synergies (either beneficial or harmful), outliers, and inconsistencies within pairs of pathways. The aim was to choose among several alternative options).
4. Reconcile CPG recommendations to try and mitigate the conflict or inconsistency by modifying them according to available knowledge (select, removal, merge, substitution, modify with extra input and output).
5. Develop the reconciled rules, according to a pre-established format including context and purpose of the rule, description, trigger, input and output (see below the complete CDSM definition rule template in the work plan section). Work was divided between the three pilot sites. Each one organized a clinicians' expert group that reconciled a set of patterns of comorbidities.

6. Peer review and consideration of local issues. All proposed reconciled rules were reviewed by the other pilot site expert clinicians and local issues included, if necessary. Any changes proposed were discussed by the clinicians of the three pilot sites. A common rule was agreed. Local issues are taken into account in the CDSM implementation.
7. Final reconciled rules were defined and written.

3.3.2. Work plan

Identification of all potential interactions. **A table with all algorithms providing recommendation of the four NICE guidelines reviewed in D7.1 was created. Algorithms (identified by the numbers provided in D7.1) were organized according to the pattern of comorbidities (first column) and elements of the care plan addressed: severity and stage classification, Interventions on lifestyles and self-care, pharmacological treatment and follow-up plan (first row) (**

1. Table 3). Work was divided amongst the three clinicians' expert groups of each pilot site. They selected those algorithms to be reviewed according to the multi-morbidity scope of the C3-Cloud project and criteria such as relevance, severity, effectiveness or irreversibility of options.

Table 3: Set of rules that help decision making in four components of the personalized plan, for each of the 11 patterns of comorbidity.

PATTERNS	Severity and stage classification	Interventions on lifestyles, training and self-care	Pharmacotherapy	Follow-up plan	Notes/ Observation
Diabetes 2	5.2.3 (Blood Pressure Management) 5.2.4 (Cardiovascular risk Assessment) 5.2.12 (Gastroparesis) 5.2.13 (Neuropathic pain) 5.2.14 (Autonomic neuropathy) 5.2.15 (Diabetic foot problem) 5.2.17 (Diabetic kidney problem) 5.2.19 (Eye disease)	5.2.1 (Education) 5.2.2 (Dietary advice)	5.2.3 (Blood Pressure Management) 5.2.4 (Cardiovascular risk Assessment) 5.2.8 (Initial Drug treatment) 5.2.9 (First and second intensification of drug treatment) 5.2.10 (Insulin based treatment) 5.2.11 (Insulin delivery)	5.2.6 HbA1c target 5.2.7 (Self Monitoring Blood Glucose)	
Renal Failure	5.4.9 (Cardiovascular prevention)	5.4.4 (Lifestyle and Dietary advice)	5.4.8 (2, 3 and 4) (Blood pressure treatment) 5.4.9	5.4.6 (Referral criteria) 5.4.7 (frequency eGFR control)	
Heart Failure	5.3.3 (Fluid overload)	5.3.1 (Lifestyle)	5.3.2 (Management summary)	5.3.5 (Referral criteria) 5.3.7 (Monitoring)	

PATTERNS	Severity and stage classification	Interventions on lifestyles, training and self-care	Pharmacotherapy	Follow-up plan	Notes/ Observation
Depression	5.5.1 (Classification Assessing depression and its severity)		5.5.2 (Treatment of persistent mild to moderate depression) 5.5.3 (Moderate (and Severe) Depression) 5.5.4 (Treatment of complex and severe depression) 5.5.6 (Antidepressant Treatment)	5.5.5 (Organization / Coordinated Care)	
Diabetes and Renal Failure	5.4.8.2 (Blood pressure treatment in CKD with Diabetes) 5.4.9 (CV prevention and treatment)		5.2.3 5.2.4 5.2.8 5.4.8.2.		5.2.6(1)
Heart Failure and Depression	5.2.2(sum) 5.3.8	5.5.2(3)		5.5.4.	
Diabetes and Depression		5.5.2(3)	5.2.13 (Gastrop: antidepressant 5.2.14 (Tricyclic)	5.5.4.(3)	
Diabetes and Heart Failure		5.5.2(3)	5.2.8 5.2.9 5.2.11 5.2.14	5.5.4.(3)	5.2.10 (2) 5.10.11(2) 5.3.2.(3) 5.2.6(1)
Renal failure and heart failure	5.4.9		5.4.8.1.(Blood pressure treatment in CKD without diabetes mellitus)5.4.8.3(RASA: Renin-Angiotensine System Antagonist, K^+)	5.3.7	
Depression and renal failure		5.5.2(3)		5.5.4.(3)	
Diabetes, Renal Failure and Heart Failure	5.4.8.2 (Blood pressure treatment in CKD with Diabetes) 5.4.9 (CV prevention and treatment)		5.4.8.2 5.2.3 5.2.4 5.2.8 5.2.9 5.2.11 5.2.14 5.4.8.1 5.4.8.3	5.3.7	5.2.6(1) 5.2.10 (2) 5.10.11(2)

PATTERNS	Severity and stage classification	Interventions on lifestyles, training and self-care	Pharmacotherapy	Follow-up plan	Notes/ Observation
Diabetes, Renal failure and Depression	5.4.8.2 5.4.9	5.5.2(3)	5.2.3 5.2.4 5.2.8 5.4.8.2. 5.2.13 5.2.14	5.5.4.(3)	5.2.6(1)
Renal Failure, Heart failure and depression	5.2.2 (sum) 5.3.8 5.4.9	5.5.2(3)	5.4.8.1. 5.4.8.3	5.5.4.(3) 5.3.7	
Diabetes, depression, heart failure	5.2.2 (sum) 5.3.8	5.5.2(3)	5.2.13 5.2.14 5.2.8 5.2.9 5.2.11(2) 5.2.14	5.5.4.(3)	5.2.6(1) 5.2.10 (2) 5.10.11(2)
Diabetes, Renal Failure Heart Failure and Depression	5.4.8.2 5.4.9 5.2.2 (sum) 5.3.8 5.4.9 5.4.8.2 5.4.9	5.5.2(3)	5.2.3 5.2.4 5.2.8 5.4.8.2. 5.2.13 5.2.14 5.2.9 5.2.11(2)	5.5.4 (3) 5.3.7	5.2.10 (2) 5.10.11(2) 5.3.2 (3) 5.2.6(1)

(1) Old, frailty: relaxed HbA1c target
(2) Not specifically stated but HF (decompensate) may be a contraindication for metformin
(3) Consider comorbidities (general recommendation)

This table summarizes the different algorithms derived from the clinical guidelines.

2. **Reconciliation of the recommendations.** A template was developed with the information required to have the complete rule definition, needed to build the CDSM. The items included are:
    - *Rule ID*: Identification number of the rule.
    - *Context*: Clinical context of the CDS rules, such as target disease combination, stages in clinical process, relevant clinical activity, decision making point, etc.
    - *Purpose*: Purpose of the CDS rules, e.g. for treatment suggestions, poly-pharmacy detection, risk assessment, lifestyle.
    - *Description of the purpose*: It explains the problem to be addressed: what, who (responsible actor), where (location/setting), when (timeline), etc.
    - *Type of purpose*:
        - Classify in Risk assessment, Goals, Activities or Pharmacotherapy
        - For Goals and Activities the FHIR Care Plan categories are provided.
    - *Clinical condition*: Diseases to be reconciled (i.e. diabetes and renal failure)

- *Concept/codes*: Key clinical concepts relevant for the rule execution. The precise meaning of each concept is needed. Standard terminologies can be used to describe care actions and conditions (e.g. SNOMED CT, ICD10, ATC, LOINC, etc.)
- *Rule description*: Detailed description of the CDS rules/algorithm in the format "if…then…else" statement.
- *Trigger*: Condition of the CDS rules, the events that cause a decision support rule to be invoked, i.e. when the rules should be triggered.
- *Input*: What input are needed by the rules? The data elements used by a rule to make inferences. E.g. patient age, gender, blood pressure, medication list, etc.
- *Output* : What kind of output should the rules produce? The possible actions with the offered choices a decision support module can take. Examples include alert (safe, caution, contraindication), reminder, medication suggestion, care plan goal/activity suggestion, risk report, showing a guideline, or just text information.
- *Reference*: Source of information, i.e. source of the rules, such as D7.1, NICE. The more specific, the better, e.g. page or section number. When the original guidelines flowcharts do not provide all information needed, we made some assumptions based on related guidelines, consensus or common sense (that was noted).
- *Notes*: Any other information that helps implementation.

The timeline followed for the reconciliation of guideline recommendations was:

1) A draft first version of two-disease reconciled rules was developed by clinicians from the three pilot sites according to present distribution.
2) Draft versions of two-disease reconciliation were peer-reviewed by the other clinical partners.
3) Final versions of two-disease reconciliation were agreed and produced.
4) A draft version of three-disease and four- disease reconciliation was created.
5) Draft versions of three- and four- were peer-reviewed by other clinical partners from the three sites.
6) Final versions of three- and four- diseases reconciliation were defined (consensus).
7) Final versions were written to be used by the technical partners in the CDSM construction.

3.4. Results

Altogether, 52 reconciled rules were defined:

- 50 rules for the two-diseases combination (Annex 2-7)
- 1 rule for three-diseases combination (Annex 8)
- 1 rule for four-diseases combination (Annex 9)

For the three- and four-diseases combinations, most of the interactions were covered in the 2 diseases reconciliations. All relevant rules could be found in the pair reconciliation's and all rules remained unaltered by an introduction of a third disease.

4. CDSM IMPLEMENTATION STRATEGIES

This section describes the process being followed for CDS modules implementation in the project. As discussed in section 3, on the basis of the outcome of T7.1, clinical experts from all three pilot sites develop guideline reconciliation rules to resolve conflicts resulting from guideline combinations for multi-morbid patients. The technical team analyses the flowcharts in D7.1 and the reconciliation rules, groups relevant flowcharts or rules into coherent modules, expands the natural language description into formalized implementable decision-making flowcharts, and develops detailed technical specification to describe the service input and output parameters for each CDS module. Finally, the formalized decision-making flowcharts are encoded in Guideline Definition Language (GDL) version 2 [15] and, based on the technical specification, each CDS module is implemented as a RESTful web service following the CDS Hooks specification. It is a complex process and there are around 40 modules in total. In the following sections, we will use the blood pressure management module from DM2 guideline as an example to explain the implementation process.

4.1. CDSM technical specification

The technical specification of a CDSM formalizes the CDS logic in the form of a decision-making flowchart similar to that of D7.1 but with much more detail useful for implementation. The specification also describes the input and output of the module using CDS Hooks defined constructs, for example information and suggestion cards. In CDS Hooks, each CDS service can return any number of cards as output. Cards provide a combination of information (for reading), suggested actions (to be applied if a user selects them), and links (to launch an app if the user selects them). Section 4.3 describes more details of CDS Hooks.

As end users of the CDS service, the clinical partners at the three pilot sites give valuable feedback and suggestions to the development of the specification of each module. One important aspect of the feedback is to help the technical team to identify computable decisions from non-computable ones. For a CDS service, its required input parameters may not always be available from the local EHR systems (one example is “possible risk for hypoglycemia” which is not recorded in RJH system). In such cases, the clinician who is using the C3DP system will have to make an assessment and provide the missing value for the parameter manually in order to invoke a CDS service. If, however, there are too many such manual steps taking place in the decision flow, it is preferable to present the guidance as non-computable information cards instead of computable suggestion cards, so clinicians will simply read the guideline as textual information and update the care plan manually using C3DP. If an entire D7.1 flowchart comprises only information cards, the information contained in the flowchart will be included in a care plan template and presented directly from C3DP rather than consulting a remote CDS service.

It is noted that D7.1 flowcharts do not have one to one mappings to CDS modules. Some of the flowcharts in D7.1 are closely related to each other and can be grouped into a single coherent CDS service. For example, D7.1 flowcharts 5.2.8, 5.2.9, 5.2.10 and 5.2.11 are grouped into one CDS module “Drug Treatment for Blood Glucose Management”. See Appendix I for more details.

The development of CDSM specification follows an iterative progress. The first iteration is based on D7.1 flowcharts for single disease only. In subsequent iterations, guideline reconciliation rules are introduced into the respective specification where applicable. The reconciliation rules which cannot be incorporated into existing specifications are implemented in separate modules.

The complete technical specification of DM2 related CDSMs are provided in Appendix I. Technical specifications of RF, HF and DP related CDSMs are near completion subject to final review by the consortium.

Blood Pressure Management Module for Diabetes Patients

The Blood Pressure (BP) Management Module for Diabetes patients encodes the decision support logic presented in D7.1 flowchart 5.2.3 (Blood pressure management). That flowchart is adapted to an implementable one with executable conditions and CDS hooks information and suggestion cards (Figure 2, Figure 3). The details of the decision points of the flowchart are explained in Table 4. The ICD, LOINC and ATC codes in the table are used as example codes to define the conditions. The codes will be reassessed and mapped to local codes when necessary during the implementation phase. The flowcharts in Figure 2 and Figure 3 are not an exact match of D7.1 flowchart 5.2.3. In the flowchart 5.2.3, the blood pressure was immediately checked whether it is below the set thresholds after recommending a new drug. However, in practice it will be checked at the next control visit after the patient has used these drugs. After checking the NICE guideline, a recommendation of scheduling a control visit after 1-2 months is introduced, and the blood pressure measurements are checked at the control visit when the CDSM is invoked a second time. Figure 2 and Figure 3 show the changed control flow.

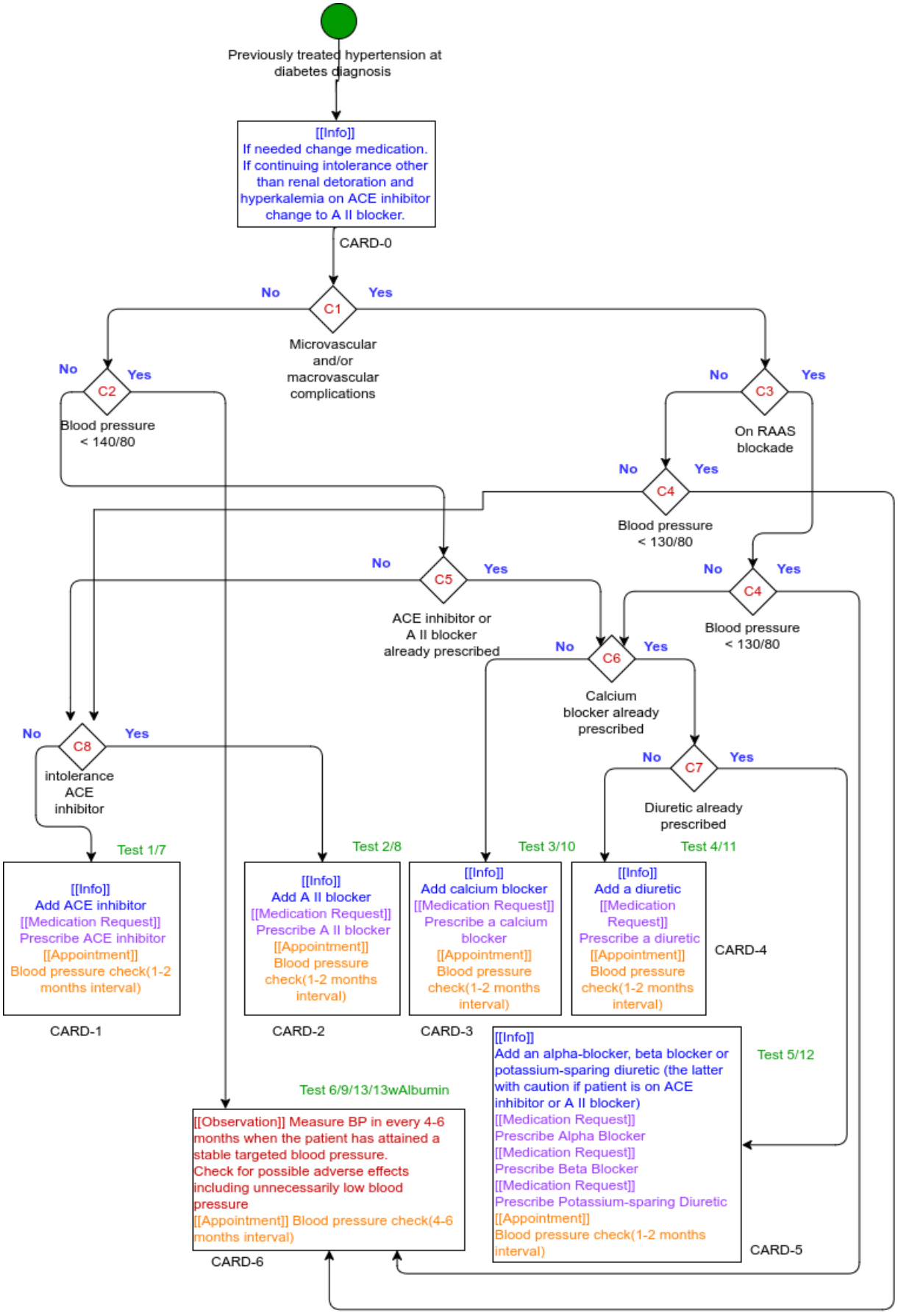

Figure 2: First half of the BP management flowchart

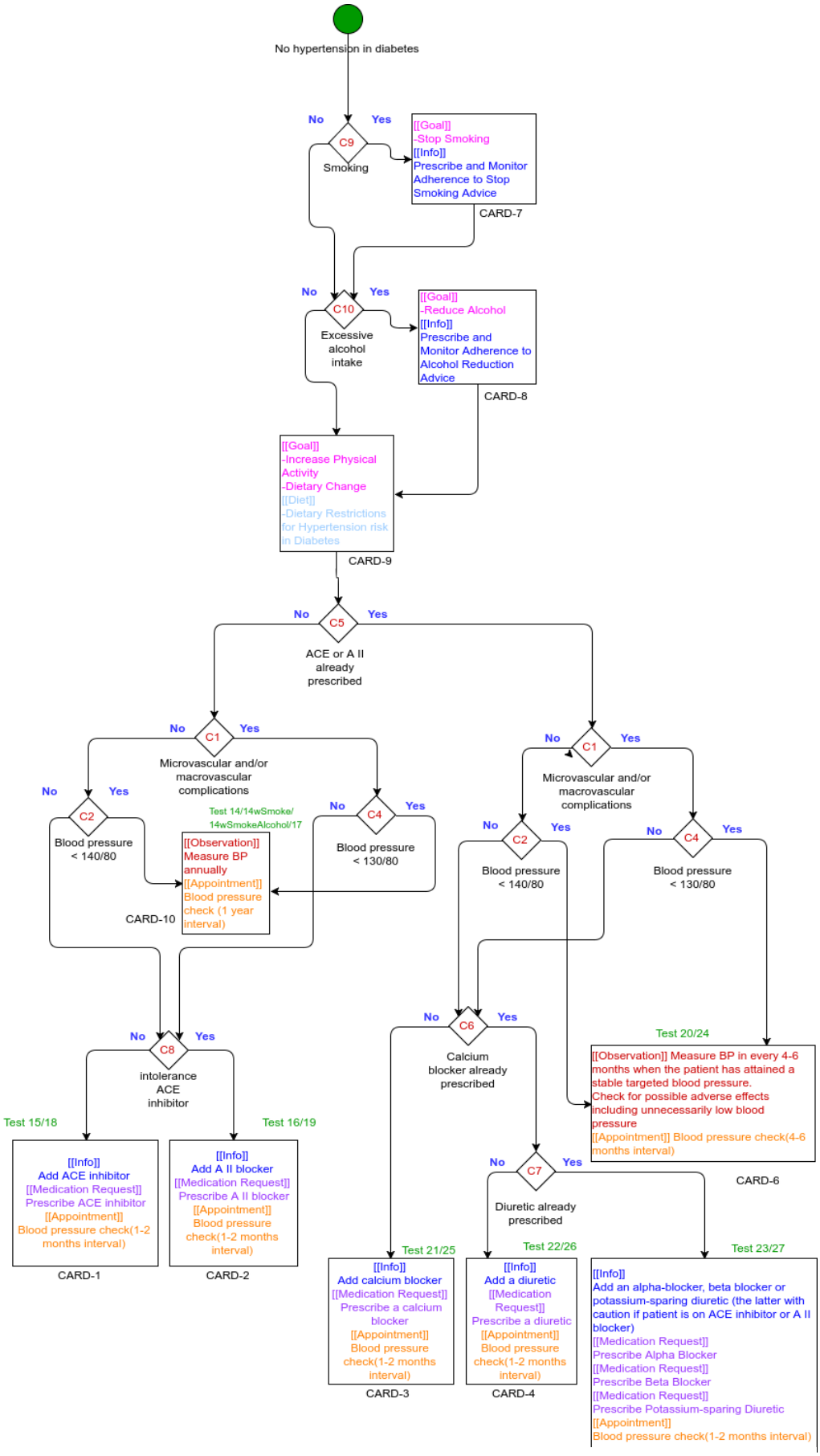

Figure 3: Second half of the BP management flowchart

Table 4: BP management module condition table

Condition No	Condition Clause
C1	If one of the following conditions exists: ICD[E11.2A, E11.2B, E11.4B, E11.4C, E11.4D, G63.2] OR If albumin secretion in urine is ≥ 30 mg/l OR ≥20 µg/min OR ≥30 mg/24h (depending how it is presented)
C2	If systolic blood pressure (LOINC[8480-6]) < 140 and diastolic blood pressure (LOINC[8462-4]) < 80 (Both from 55284-4)
C3	If medication ATC[C09] exists
C4	If systolic blood pressure (LOINC[8480-6]) < 130 and diastolic blood pressure (LOINC[8462-4]) < 80 (Both from 55284-4)
C5	If medication ATC[C09AA or C09CA] exists
C6	If medication ATC[C08] exists
C7	If medication ATC[C03] exists
C8	If condition ICD[T46.4X5A] or allergy ATC[C09AA] exists
C9	If observation LOINC[64234-8] (current smoker) has 373066001(yes)
C10	If observation LOINC[74013-4] (alcoholic drinks per day) > 0

Table 5 – 7 specify the input and output parameters of the module, defining how the module should be implemented as a CDS hooks service. Table 5 lists the clinical concepts processed

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	Hypertension	Input
	Microvascular Conditions	Input
	Macrovascular Conditions	Input
	ACE inhibitor intolerance	Input
Medications	ACE Inhibitors (Angiotensin Converting Enzyme Inhibitor)	Input & Output
	A II Blockers	Input & Output
	Calcium Blocker	Input & Output
	Diuretic	Input & Output
	Alpha Blocker	Output
	Beta Blocker	Output
	Potassium-sparing diuretic	Output
	RAAS Blocker	Input
Vital Signs	Blood Pressure	Input & Output

Social History Observations	Smoking Status	Input
	Alcohol Consumption Status	Input
Allergies or Intolerances	Intolerance to ACE inhibitors	Input

by the blood pressure management service. The concepts will be implemented as FHIR resources and so are grouped into categories corresponding to FHIR resource types. The input/output column indicates whether the concept will be used as input, output, or both.

Table 5: Clinical concepts processed by the BP management service

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	Hypertension	Input
	Microvascular Conditions	Input
	Macrovascular Conditions	Input
	ACE inhibitor intolerance	Input
Medications	ACE Inhibitors (Angiotensin Converting Enzyme Inhibitor)	Input & Output
	A II Blockers	Input & Output
	Calcium Blocker	Input & Output
	Diuretic	Input & Output
	Alpha Blocker	Output
	Beta Blocker	Output
	Potassium-sparing diuretic	Output
	RAAS Blocker	Input
Vital Signs	Blood Pressure	Input & Output
Social History Observations	Smoking Status	Input
	Alcohol Consumption Status	Input
Allergies or Intolerances	Intolerance to ACE inhibitors	Input

In CDS Hooks, the input to a CDS service is a set of FHIR data identified by a prefetch term id. Table 6 describes the mapping from the prefetch term id to related input concepts.

Table 6: BP management service input variables

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	-Type 2 Diabetes diagnosis - Hypertension diagnosis -Microvascular Conditions -Macrovascular Conditions -ACE inhibitor intolerance

medications	All medications used by the patient	-ACE inhibitors -A II Blockers -Calcium Blockers -Diuretic -Alpha Blockers -Beta Blockers -Potassium-sparing diuretic -RAAS Blocker
allergies	Allergies of the patient	ACE Intolerance
bp	Blood pressure	Systolic and diastolic blood pressure
smoking	Smoking Status of the patient	Smoking Status
albumin_level	Albumin level	Albumin level
alcohol	Alcohol consumption status	Alcohol status

CARD 0	
summary	Previous medication can have side effects.
Detailed description	If needed change medication. If continuing intolerance other than renal deterioration and hyperkalemia on ACE inhibitor change to A II blocker.
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127

CARD 1		
summary	ACE inhibitor recommendation	
Detailed description	Add Angiotensin Converting Enzyme Inhibitor, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe ACE inhibitor
	Description	Prescribe ACE inhibitor
	Medication Code	C09AA, Angiotensin Converting Enzyme Inhibitor, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)

	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 2		
summary	A II Blockers recommendation	
Detailed description	Add A II Blockers, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe A II Blockers
	Description	Prescribe A II Blockers
	Medication Code	C09CA, Angiotensin Receptor II, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 3		
summary	Calcium Blocker recommendation	
Detailed description	Add a Calcium blocker, Blood pressure check (1-2 months interval) and Follow-up appointment	

source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Calcium Blocker
	Description	Prescribe Calcium Blocker
	Medication Code	C08, Calcium Blocker, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 4		
summary	Diuretic recommendation	
Detailed description	Add a diuretic, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Diuretic
	Description	Prescribe Diuretic
	Medication Code	C03, Diuretics, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)

	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 5		
Summary	Alpha-blocker, beta blocker or potassium-sparing diuretic recommendation	
Detailed description	Add an alpha-blocker, beta blocker or potassium-sparing diuretic (the latter with caution if patient is on ACE inhibitor or A II blocker), Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Alpha-blocker
	Description	Prescribe Alpha-blocker
	Medication Code	C012CA, Alpha-adrenoreceptor antagonists, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Beta-blocker
	Description	Prescribe Beta-blocker
	Medication Code	C07, Beta blocking agents, ATC

	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Potassium-sparing diuretic
	Description	Prescribe Potassium-sparing diuretic
	Medication Code	C03D, Potassium-sparing agents, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 6		
summary	Measurement of BP in every 4-6 months	
Detailed description	Measure BP in every 4-6 months when the patient has attained a stable targeted blood pressure with a goal.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	

Suggestion 1		
Goal	Category	Safety, http://hl7.org/fhir/goal-category
	Description Code	135840009, Blood Pressure monitoring (regime/therapy)
	Description Text	Keep the blood pressure under 140/80 mmHg.
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Appointment	Title	Treatment Follow-up Appointment
	Description	6 monthly Blood Pressure Management Appointment
	Status	proposed
	start	(Date + 6 months)
	specialty	-

CARD 7	
summary	Life advice about tobacco smoking
Detailed description	Prescribe and Monitor Adherence to Stop Smoking Advice
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127

Suggestion 1		
Goal:	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to stop smoking
Appointment	Title	Stop Smoking Follow-up Appointment
	Description	Follow up to check the patient's smoking status
	Status	Proposed
	start	-
	specialty	-

CARD 8	
summary	Life advice about alcohol consumption
Detailed description	Prescribe and Monitor Adherence to Alcohol Reduction Advice
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127

Suggestion 1		
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to reduce alcohol intake
Appointment	Title	Reduce Alcohol Consumption Follow-up Appointment
	Description	Follow up to check the patient's alcohol consumption status
	Status	Proposed
	start	-
	specialty	-
CARD 9		
summary	General Life Advice	
Detailed description	Recommend increasing physical activity and dietary change if necessary	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to increase physical activity
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to dietary change
CARD 10		
summary	Measurement of BP annually	
Detailed description	Measure BP annually when the patient has attained a stable targeted blood pressure.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC

	performer	PATIENT
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 1 year)
	Specialty	-

Table 7 describes the information or suggestion cards which will be produced by the blood pressure management module. A card without a suggestion subsection is an information card. A suggestion card has a suggestion subsection which describes the care plan goals and the FHIR resources to be created as care plan activities.

Table 7: BP management service output cards

CARD 0		
summary	Previous medication can have side effects.	
Detailed description	If needed change medication. If continuing intolerance other than renal deterioration and hyperkalemia on ACE inhibitor change to A II blocker.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
CARD 1		
summary	ACE inhibitor recommendation	
Detailed description	Add Angiotensin Converting Enzyme Inhibitor, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe ACE inhibitor
	Description	Prescribe ACE inhibitor
	Medication Code	C09AA, Angiotensin Converting Enzyme Inhibitor, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation

	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 2		
summary	A II Blockers recommendation	
Detailed description	Add A II Blockers, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe A II Blockers
	Description	Prescribe A II Blockers
	Medication Code	C09CA, Angiotensin Receptor II, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 3		
summary	Calcium Blocker recommendation	
Detailed description	Add a Calcium blocker, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		

Medication Request	Title	Prescribe Calcium Blocker
	Description	Prescribe Calcium Blocker
	Medication Code	C08, Calcium Blocker, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 4		
summary	Diuretic recommendation	
Detailed description	Add a diuretic, Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Diuretic
	Description	Prescribe Diuretic
	Medication Code	C03, Diuretics, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation

	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 5		
Summary	Alpha-blocker, beta blocker or potassium-sparing diuretic recommendation	
Detailed description	Add an alpha-blocker, beta blocker or potassium-sparing diuretic (the latter with caution if patient is on ACE inhibitor or A II blocker), Blood pressure check (1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Alpha-blocker
	Description	Prescribe Alpha-blocker
	Medication Code	C012CA, Alpha-adrenoreceptor antagonists, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Beta-blocker
	Description	Prescribe Beta-blocker
	Medication Code	C07, Beta blocking agents, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment

	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Potassium-sparing diuretic
	Description	Prescribe Potassium-sparing diuretic
	Medication Code	C03D, Potassium-sparing agents, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 6		
summary	Measurement of BP in every 4-6 months	
Detailed description	Measure BP in every 4-6 months when the patient has attained a stable targeted blood pressure with a goal.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Safety, http://hl7.org/fhir/goal-category

	Description Code	135840009, Blood Pressure monitoring (regime/therapy)
	Description Text	Keep the blood pressure under 140/80 mmHg.
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Appointment	Title	Treatment Follow-up Appointment
	Description	6 monthly Blood Pressure Management Appointment
	Status	proposed
	start	(Date + 6 months)
	specialty	-
CARD 7		
summary	Life advice about tobacco smoking	
Detailed description	Prescribe and Monitor Adherence to Stop Smoking Advice	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal:	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to stop smoking
Appointment	Title	Stop Smoking Follow-up Appointment
	Description	Follow up to check the patient's smoking status
	Status	Proposed
	start	-
	specialty	-
CARD 8		
summary	Life advice about alcohol consumption	
Detailed description	Prescribe and Monitor Adherence to Alcohol Reduction Advice	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Dietary, http://hl7.org/fhir/goal-category

	Description Code	-
	Description Text	Set a goal to reduce alcohol intake
Appointment	Title	Reduce Alcohol Consumption Follow-up Appointment
	Description	Follow up to check the patient's alcohol consumption status
	Status	Proposed
	start	-
	specialty	-
CARD 9		
summary	General Life Advice	
Detailed description	Recommend increasing physical activity and dietary change if necessary	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to increase physical activity
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to dietary change
CARD 10		
summary	Measurement of BP annually	
Detailed description	Measure BP annually when the patient has attained a stable targeted blood pressure.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Appointment	Title	Treatment Follow-up Appointment

	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 1 year)
	Specialty	-

4.2. CDS rule implementation in GDL2

The Guideline Definition Language is a formal language used to express clinical rules and guidelines in a machine-readable format. The language was created to enable development of highly portable computerized Clinical Decision Support logic and modules by leveraging semantically interoperable EHR standards. It is the language of choice for the GDL Editor software, developed by Cambio Healthcare Systems, that utilizes openEHR archetypes to model clinical practice guidelines for computerized CDS. Due to the interoperable nature of openEHR archetypes, the resulting GDL files – referred to as guides or guidelines – are platform independent and agnostic to both natural languages and reference terminologies. The current version of GDL is version 1, the design specification of which is published and maintained by the openEHR foundation.

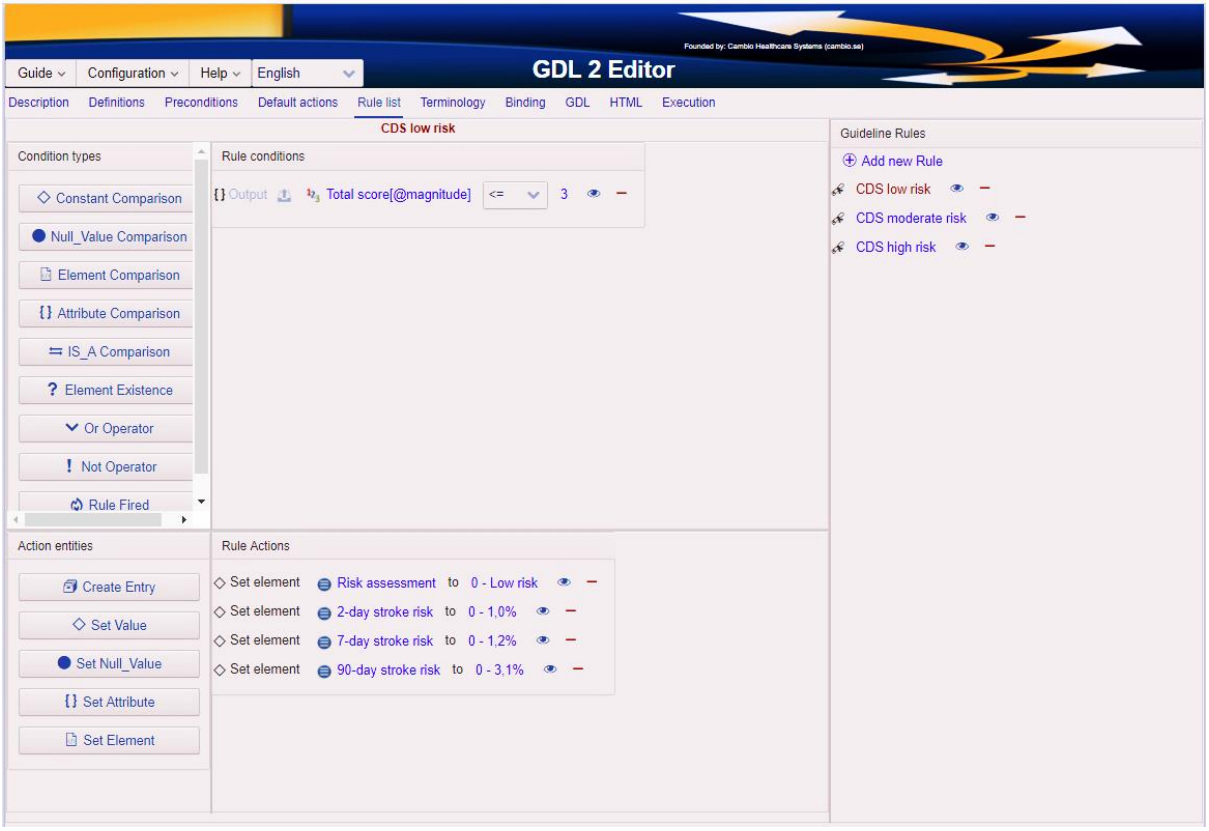

Figure 4 GDLv2 editor screenshot

The version 2 of GDL is a major improvement of version 1. GDL version 2 introduces many unique features specific to this release, including:

- A web-based GDLv2 editor
  The editor is currently under development and will be operational in the beginning of 2018. (See Figure 4 for a screenshot)

- HL7 FHIR resource support
  Besides openEHR archetypes, HL7 FHIR resources are supported in the data binding definitions of the guidelines.

- CDS Hooks support

Several CDS Hooks concepts are directly supported now in GDLv2 as first class building blocks. The Cards, Suggestions and Actions can be used in a nested and hierarchical way directly in the rule statements in GDLv2.

- Output template
  Complex object structure can be created based on a pre-defined template and called upon in the rule statements to simplify the task of creating different output with deeply nested structures.

- Individual referential information
  Referential information in the guideline metadata can now be called upon individually in different rule statements to support communication or consumption by user interfaces.

C3-Cloud uses GDL version 2 to implement CDS rules, because of its added support for FHIR data model and CDS Hooks API. The flowcharts in the CDSM technical specification are modeled as decision trees when they are implemented in GDL2. The GDL decision tree of the blood pressure management module is shown in

Figure 5. Figure 6 – 10 show the GDL2 implementation of the decision tree. Figure 6 shows the data bindings to the input FHIR resources. Figure 7 shows the outptut templates for FHIR resources generation. Figure 8 shows the rules that produce CDS hooks suggestion cards given the data input. Figure 9 shows the ontology term defintions being used inside the GDL2 file. Figure 10 shows the bindings from the local ontology terms to standard coding schemes.

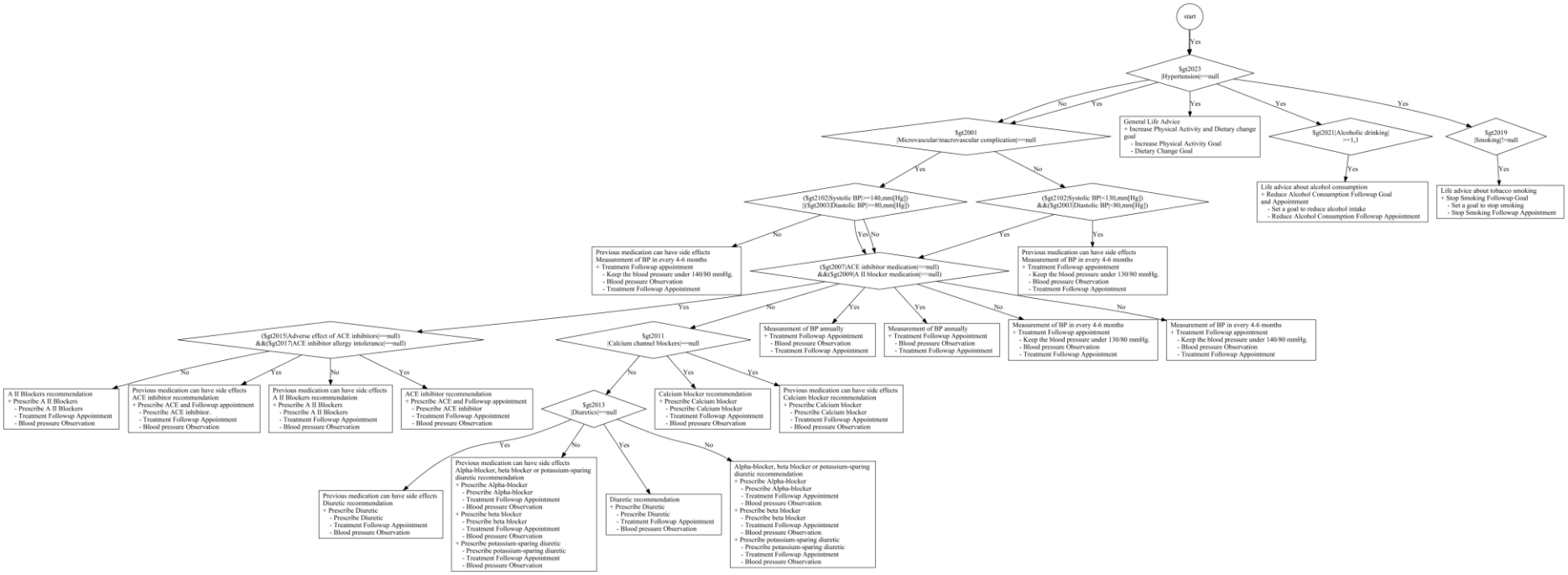

Figure 5: BP management GDLv2 decision tree

```
{
  "gdl_version": "2.0",
  "id": "Diabetes_blood_pressure_management.v0.1",
  "concept": "gt0001",
  "language": {
    "original_language": "ISO_639-1::en"
  },
  "description": {
    "original_author": {
      "name": "Author",
      "organisation": "Cambio Healthcare Systems",
      "email": ""
    },
    "details": {
      "en": {
        "id": "en",
        "purpose": "Sample fhir-based cds-rules for demonstration purpose",
        "keywords": [
          "Diabetes"
        ]
      }
    },
    "other_details": {
      "references": "NICE guideline - Managing blood pressure in adults with type 2 diabetes."
    },
    "references": [
      {
        "id": "1",
        "label": "NICE guideline Hypertension in adults: diagnosis and management",
        "url": "https://www.nice.org.uk/guidance/cg17"
      }
    ]
  },
  "definition": {
    "data_bindings": {
      "gt2000": {
        "id": "gt2000",
        "model_id": "org.hl7.fhir.dstu3.model.Condition",
        "type": "INPUT",
        "elements": {
          "gt2001": {
            "id": "gt2001",
            "path": "/code/coding[0]"
          }
        },
        "predicates": [
          "/code/coding[0] is_a local::gt3000|Microvascular/macrovascular complication|"
        ]
      },
      "gt2002": {
        "id": "gt2002",
        "model_id": "org.hl7.fhir.dstu3.model.Observation",
        "type": "INPUT",
        "elements": {
          "gt2102": {
            "id": "gt2102",
            "path": "/component[0]/valueQuantity"
          },
          "gt2003": {
            "id": "gt2003",
            "path": "/component[1]/valueQuantity"
          }
        },
        "predicates": [
          "/code/coding[0] is_a local::gt3001|Blood pressure measurement|"
        ]
      },
```

Figure 6: BP management GDL2 data bindings

```
},
"templates": {
  "gt1000": {
    "id": "gt1000",
    "model_id": "org.hl7.fhir.dstu3.model.MedicationRequest",
    "object": {
      "resourceType": "MedicationRequest",
      "status": "draft",
      "intent": "proposal",
      "authoredOn": "{$gt4000}",
      "medicationCodeableConcept": {
        "coding": [
          {
            "system": "http://www.whocc.no/atc",
            "code": "{$gt4001}",
            "display": "{$gt4002}"
          }
        ]
      }
    }
  },
  "gt1002": {
    "id": "gt1002",
    "model_id": "org.hl7.fhir.dstu3.model.Appointment",
    "object": {
      "resourceType": "Appointment",
      "id": "appointment-offer",
      "status": "proposed",
      "appointmentType": {
        "coding": [
          {
            "system": "http://hl7.org/fhir/v2/0276",
            "code": "FOLLOWUP",
            "display": "FOLLOWUP"
          }
        ]
      },
      "description": "{$gt4201}",
      "start": "{$gt4200}"
    }
  },
  "gt1003": {
    "id": "gt1003",
    "model_id": "org.hl7.fhir.dstu3.model.Goal",
    "object": {
      "resourceType": "Goal",
      "status": "proposed",
      "category": [
        {
          "coding": [
            {
              "system": "http://hl7.org/fhir/goal-category",
              "code": "safety"
            }
          ]
        }
```


Figure 7: BP management GDL2 output templates

```
},
"rules": {
  "gt5000": {
    "id": "gt5000",
    "priority": 1,
    "when": [
      "$gt2023|Hypertension|!=null",
      "$gt2001|Microvascular/macrovascular complication|==null",
      "($gt2102|Systolic BP|>=140,mm[Hg])||($gt2003|Diastolic BP|>=80,mm[Hg])",
      "($gt2007|ACE inhibitor medication|==null)&&($gt2009|A II blocker medication|==null)",
      "($gt2015|Adverse effect of ACE inhibitors|==null)&&($gt2017|ACE inhibitor allergy intolerance|==null)"
    ],
    "cards": [
      {
        "summary": "Previous medication can have side effects",
        "detail": "If needed change medication. If continuing intolerance other than renal deterioration and
        hyperkalemia on ACE inhibitor change to A II blocker.",
        "source": {
          "label_reference": "$ref[1].label",
          "url_reference": "$ref[1].url"
        },
        "suggestions": [],
        "indicator": "info"
      },
      {
        "summary": "ACE inhibitor recommendation",
        "detail": "Add Angiotensin Converting Enzyme Inhibitor, Blood pressure check(1-2 months interval) and
        Followup appointment",
        "indicator": "info",
        "source": {
          "label_reference": "$ref[1].label",
          "url_reference": "$ref[1].url"
        },
        "suggestions": [
          {
            "label": "Prescribe ACE and Followup appointment",
            "uuid": "20c0d237-1718-4012-94d0-f6b3e6d5953a",
            "actions": [
              {
                "type": "create",
                "description": "Prescribe ACE inhibitor.",
                "resource_template": {
                  "template_id": "gt1000",
                  "assignments": [
                    "$gt4000=$currentDateTime.string",
                    "$gt4001='C09AA'",
                    "$gt4002='Angiotensin Converting Enzyme Inhibitor'"
                  ]
                }
              },
              {
                "type": "create",
                "description": "Treatment Followup Appointment",
                "resource_template": {
                  "template_id": "gt1002",
                  "assignments": [
                    "$gt4200=($currentDateTime.value+2,mo)",
                    "$gt4201='Follow up to check the results of the treatment'"
                  ]
                }
              },
              {
                "type": "create",
                "description": "Blood pressure Observation",
                "resource_template": {
                  "template_id": "gt1004",
                  "assignments": [
                    "$gt4203='85354-9'",
                    "$gt4204='Blood Pressure'",
                    "$gt4205='Have Blood pressure systolic and diastolic test before the control visit'"
                  ]
                }
```

Figure 8: BP management GDL2 rules

```
},
"ontology": {
  "term_definitions": {
    "en": {
      "id": "en",
      "terms": {
        "gt2001": {
          "id": "gt2001",
          "text": "Condition of microvascular/macrovascular complication"
        },
        "gt2002": {
          "id": "gt2002",
          "text": "Systolic BP"
        },
        "gt2003": {
          "id": "gt2003",
          "text": "Diastolic BP"
        },
        "gt2005": {
          "id": "gt2005",
          "text": "RAAS inhibitor medication"
        },
        "gt2007": {
          "id": "gt2007",
          "text": "ACE inhibitor medication"
        },
        "gt2009": {
          "id": "gt2009",
          "text": "ANGIOTENSIN II ANTAGONISTS medication"
        },
        "gt2011": {
          "id": "gt2011",
          "text": "Calcium channel blockers medication"
        },
        "gt2013": {
          "id": "gt2013",
          "text": "Diuretics medication"
        },
        "gt2015": {
          "id": "gt2015",
          "text": "Condition of adverse effect of angiotensin-converting-enzyme inhibitors"
        },
        "gt2017": {
          "id": "gt2017",
          "text": "Allergy intolerance of ACE inhibitor"
        },
        "gt2019": {
          "id": "gt2019",
          "text": "Smoking observation"
        },
        "gt2021": {
          "id": "gt2021",
          "text": "Alcoholic drinking observation"
        },
```


Figure 9 BP management GDL2 ontology term definitions

```
},
"term_bindings": {
  "ICD-10": {
    "id": "ICD-10",
    "bindings": {
      "gt3000": {
        "codes": [
          "ICD-10::E11.2A",
          "ICD-10::E11.2B",
          "ICD-10::E11.4B",
          "ICD-10::E11.4C",
          "ICD-10::E11.4D",
          "ICD-10::G63.2"
        ]
      },
      "gt3007": {
        "codes": [
          "ICD-10::T46.4X5A"
        ]
      },
      "gt3011": {
        "codes": [
          "ICD-10::I10",
          "ICD-10::I11",
          "ICD-10::I12",
          "ICD-10::I13",
          "ICD-10::I15"
        ]
      }
    }
  },
  "LOINC": {
    "id": "LOINC",
    "bindings": {
      "gt3001": {
        "codes": [
          "LOINC::85354-9"
        ]
      },
      "gt3008": {
        "codes": [
          "LOINC::64234-8"
        ]
      },
      "gt3009": {
        "codes": [
          "LOINC::74013-4"
        ]
      }
    }
  },
  "ATC": {
    "id": "ATC",
    "bindings": {
      "gt3002": {
        "codes": [
          "ATC::C09"
        ]
      },
      "gt3003": {
        "codes": [
          "ATC::C09AA"
        ]
      },
      "gt3004": {
```


Figure 10: BP management GDL2 ontology term bindings

4.3. CDS Hooks service

CDS Hooks describes a "hook"-based pattern for invoking decision support from within a clinician's EHR workflow. The API supports:

- Synchronous, workflow-triggered CDS calls returning information and suggestions
- Launching a user-facing SMART app when CDS requires additional interaction

User activity inside the EHR triggers CDS hooks in real-time. Example hooks include:

- *patient-view*: when opening a new patient record;
- *medication-prescribe*: when authoring a new prescription;
- *order-review*: when viewing pending orders for approval).

When a triggering activity occurs, the EHR notifies each CDS service registered for the activity. These services must then provide near-real-time feedback about the triggering event. Each service gets basic details about the EHR context plus whatever service-specific data are required.

Each CDS service will return any number of cards in response to the hook. Cards convey some combination of text (information card), alternative suggestions (suggestion card), and links to apps or reference materials (app link card). A user sees these cards — one or more of each type — embedded in the EHR, and can interact with them as follows:

- *Information card*: provides text for the user to read.
- *Suggestion card*: provides a specific suggestion for which the EHR renders a button that the user can click to accept. Clicking automatically populates the suggested change into the EHR's UI.
- *App link card*: provides a link to an app (often a SMART app) where the user can supply details, step through a flowchart, or do anything else required to help reach an informed decision.

C3-Cloud implements every CDSM as a RESTful service following the CDS Hooks specification. The service accepts FHIR data input as JSON payload of HTTP POST request and returns information or suggestion cards as JSON payload of HTTP 200 response. Figure 11 – 14 show an example message request to the blood pressure management service. This request is triggered by C3DP when a care plan is being created (the hook “careplan-create”) and carries requested patient medical data in the format of FHIR resources, including conditions, medications, and blood pressure observation. Figure 15 – 16 show an example response from the blood pressure management service. The response returns a suggestion card on Calcium blocker recommendation (the CARD 3 in the technical specification of the BP management module Table 7**Error! Reference source not found.**).

```
{
    "hook": "careplan-create",
    "hookInstance": "353530b2-8cea-49e5-bd54-7cc0b381a4d8",
    "fhirServer": "http://fhirtest.uhn.ca/baseDstu3",
    "redirect": "http://demo.cds-hooks.org/service-done.html",
    "user": "Practitioner/example",
    "patient": "29119",
    "prefetch": {
        "patient": {
            "response": {
                "status": "200 OK"
            },
            "resource":{
                "resourceType": "Patient",
                "id": "29119",
                "meta": {
                    "versionId": "94699",
                    "lastUpdated": "2015-09-16T18:12:59.795-05:00"
                },
                "text": {
                    "status": "generated",
                    "div": "<div  xmlns=\"http://www.w3.org/1999/xhtml\">\n        \n
                    <p>Daniel Adams</p>\n      \n          </div>"
                },
                "active": true,
                "name": [
                    {
                        "use": "official",
                        "family": "Adams",
                        "given": [
                            "Daniel",
                            "X."
                        ]
                    }
                ],
                "telecom": [
                    {
                        "system": "email",
                        "value": "daniel.adams@example.com"
                    }
                ],
                "gender": "male",
                "birthDate": "1955-12-23",
                "address": [
                    {
                        "use": "home",
                        "line": [
                            "1 Hill AveApt 14"
                        ],
                        "city": "Tulsa",
                        "state": "OK",
                        "postalCode": "74117",
                        "country": "USA"
                    }
                ]
            }
```


Figure 11: BP management service example request part 1

```
"conditions": {
    "response": {
        "status": "200 OK"
    },
    "resource": {
        "resourceType": "Bundle",
        "type": "searchset",
        "total": 3,
        "link": [
            {
                "relation": "self",
                "url": "http://fhirtest.uhn.ca/baseDstu3/Condition?patient=29119"
            }
        ],
        "entry": [
            {
                "fullUrl": "http://fhirtest.uhn.ca/baseDstu3/Condition/29424",
                "resource": {
                    "resourceType": "Condition",
                    "id": "29424",
                    "meta": {
                        "versionId": "1",
                        "lastUpdated": "2017-02-22T06:05:26.762-05:00"
                    },
                    "clinicalStatus": "active",
                    "code": {
                        "coding": [
                            {
                                "system": "http://hl7.org/fhir/sid/icd-10",
                                "code": "I13.9",
                                "display": "Hypertension"
                            }
                        ],
                        "text": "Essential (primary) hypertension"
                    },
                    "subject": {
                        "reference": "Patient/29119"
                    },
                    "onsetDateTime": "2016-02-08"
                },
                "search": {
                    "mode": "match"
                }
            },
        {
            "fullUrl": "http://fhirtest.uhn.ca/baseDstu3/Condition/29125",
            "resource": {
                "resourceType": "Condition",
                "id": "29125",
                "meta": {
                    "versionId": "1",
                    "lastUpdated": "2017-02-20T09:04:26.474-05:00"
                },
                "subject": {
                    "reference": "Patient/29119"
                },
                "code": {
                    "coding": [
                        {
                            "system": "http://hl7.org/fhir/sid/icd-10",
                            "code": "E11",
                            "display": "Type 2 Diabetes"
                        }
                    ],
                    "text": "Type 2 Diabetes"
                },
                "clinicalStatus": "active",
                "onsetDateTime": "2005-05-22"
            },
            "search": {
                "mode": "match"
```


Figure 12: BP management service example request part 2

```
"medications": {
    "response": {
        "status": "200 OK"
    },
    "resource": {
        "resourceType": "Bundle",
        "id": "25690280-6f53-45d7-a263-a5ea40df7143",
        "meta": {
            "lastUpdated": "2017-02-21T07:19:47.493-05:00"
        },
        "type": "searchset",
        "total": 1,
        "link": [
            {
                "relation": "self",
                "url": "
                http://fhirtest.uhn.ca/baseDstu3/MedicationStatement?_pretty=true&subject=29119"
            }
        ],
        "entry": [
            {
              "fullUrl": "http://fhirtest.uhn.ca/baseDstu3/MedicationStatement/29159",
              "resource": {
                "taken" :  "y",
                "resourceType": "MedicationStatement",
                "id": "29159",
                "meta": {
                  "versionId": "1",
                  "lastUpdated": "2017-02-21T07:19:13.243-05:00"
                },
                "status": "active",
                "medicationCodeableConcept": {
                  "coding": [
                    {
                      "system": "http://www.whocc.no/atc",
                      "code": "C09AA",
                      "display": "ACE inhibitor"
                    }
                  ],
                  "text": "ACE inhibitor"
                },
                "subject": {
                  "reference": "Patient/29119"
                }
              },
              "search": {
                "mode": "match"
              }
            }
        ]
    }
},
"bp": {
    "response": {
        "status": "200 OK"
    },
    "resource": {
        "resourceType": "Bundle",
        "id": "5ecd8b9c-9eae-405c-b277-0c20362f6dad",
        "meta": {
            "lastUpdated": "2017-02-21T01:53:51.206-05:00"
        },
        "type": "searchset",
        "total": 1,
        "link": [
            {
                "relation": "self",
                "url": "
                http://fhirtest.uhn.ca/baseDstu3/Observation?_pretty=true&code=55284-4&patient=29
                119"
            }
        ],
```


Figure 13: BP management service example request part 3

```
            "entry": [
                {
                    "fullUrl": "http://fhirtest.uhn.ca/baseDstu3/Observation/29128",
                    "resource": {
                        "resourceType": "Observation",
                        "id": "29128",
                        "meta": {
                            "versionId": "1",
                            "lastUpdated": "2017-02-20T10:03:05.394-05:00"
                        },
                        "status": "final",
                        "code": {
                            "coding": [
                                {
                                    "system": "http://loinc.org",
                                    "code": "85354-9",
                                    "display": "Blood Pressure"
                                }
                            ]
                        },
                        "subject": {
                            "reference": "Patient/29119"
                        },
                        "effectiveDateTime": "2015-07-20T02:30:43-04:00",
                        "component": [
                            {
                                "code": {
                                    "coding": [
                                        {
                                            "system": "http://loinc.org",
                                            "code": "8480-6",
                                            "display": "Systolic Blood Pressure"
                                        }
                                    ]
                                },
                                "valueQuantity": {
                                    "value": 140,
                                    "unit": "mmHg",
                                    "system": "http://unitsofmeasure.org/",
                                    "code": "mmHg"
                                }
                            },
                            {
                                "code": {
                                    "coding": [
                                        {
                                            "system": "http://loinc.org",
                                            "code": "8462-4",
                                            "display": "Diastolic Blood Pressure"
                                        }
                                    ]
                                },
                                "valueQuantity": {
                                    "value": 90,
                                    "unit": "mmHg",
                                    "system": "http://unitsofmeasure.org/",
                                    "code": "mmHg"
                                }
                            }
                        ]
                    },
                    "search": {
                        "mode": "match"
                    }
                }
            ]
        },
        "smoking": {},
        "alcohol": {},
        "albumin_level": {},
        "allergies": {}
    },
    "context": []
}
```


Figure 14: BP management service example request part 4

```
{
    "cards": [
        {
            "summary": "Previous medication can have side effects",
            "detail": "If needed change medication. If continuing intolerance other than renal
            detoriation and hyperkalemia on ACE inhibitor change to A II blocker.",
            "source": {
                "label": "NICE guideline Hypertension in adults: diagnosis and management",
                "url": "https://www.nice.org.uk/guidance/cg17"
            },
            "suggestions": [],
            "indicator": "info"
        },
        {
            "summary": "Calcium blocker recommendation",
            "detail": "Add a Calcium blocker, Blood pressure check(1-2 months interval) and Followup
            appointment",
            "source": {
                "label": "NICE guideline Hypertension in adults: diagnosis and management",
                "url": "https://www.nice.org.uk/guidance/cg17"
            },
            "suggestions": [
                {
                    "label": "Prescribe Calcium blocker",
                    "uuid": "9f9405b4-cff8-494e-99cb-f8311e30af07",
                    "actions": [
                        {
                            "type": "create",
                            "description": "Prescribe Calcium blocker",
                            "resource": {
                                "resourceType": "MedicationRequest",
                                "subject": {
                                    "reference": "Patient/29119"
                                },
                                "status": "draft",
                                "intent": "plan",
                                "medicationCodeableConcept": {
                                    "coding": [
                                        {
                                            "system": "http://www.whocc.no/atc",
                                            "code": "C08",
                                            "display": "Calcium blocker"
                                        }
                                    ]
                                },
                                "authoredOn": "2017-10-06T07:16:51.296Z"
                            }
                        },
                        {
                            "type": "create",
                            "description": "Treatment Followup Appointment",
                            "resource": {
                                "resourceType": "Appointment",
                                "id": "appointment-offer",
                                "status": "proposed",
                                "appointmentType": {
                                    "coding": [
                                        {
                                            "system": "http://hl7.org/fhir/v2/0276",
                                            "code": "FOLLOWUP",
                                            "display": "FOLLOWUP"
                                        }
                                    ]
                                },
                                "description": "Follow up to check the results of the treatment",
                                "start": "2017-11-20T07:16:51.296Z"
                            }
                        },
```


Figure 15: BP management service example response part 1

```
            {
                "type": "create",
                "description": "Blood pressure Observation",
                "resource": {
                    "resourceType": "ProcedureRequest",
                    "status": "draft",
                    "intent": "proposal",
                    "extension": [
                        {
                            "url": "
                            http://www.c3-cloud.eu/fhir/StructureDefinition/description",
                            "valueString": "Have Blood pressure systolic and diastolic test
                            before the control visit"
                        }
                    ],
                    "category": [
                        {
                            "coding": [
                                {
                                    "system": "
                                    http://hl7.org/fhir/care-plan-activity-category",
                                    "code": "observation",
                                    "display": "Observation"
                                }
                            ]
                        }
                    ],
                    "code": {
                        "coding": [
                            {
                                "system": "http://loinc.org",
                                "code": "85354-9",
                                "display": "Blood Pressure"
                            }
                        ]
                    },
                    "performer": [
                        {
                            "display": "PATIENT"
                        }
                    ]
                }
            }
        ]
    }
]
```


Figure 16: BP management service example response part 2

5. SOFTWARE DEMO

The blood pressure management service described in section 4 is published online for demonstration. The service is a RESTful web service. The service endpoint address is:

https://cds-services.cambiocds.com/c3cloud-cdsm/blood-pressure-management

The service can be tested using a command console tool like cURL or GUI tool like Postman using the provided test cases.

Three test cases are published in the following URL to help interact with the service:

https://documenter.getpostman.com/view/3273168/collection/7LjBPaN

Postman can be installed either as a native application or as a Chrome extension. The following steps describe how to install Postman as a Chrome extension:

1. In Chrome, go to https://chrome.google.com/webstore/detail/postman/fhbjgbiflinjbdggehcddcbncdddomop?hl=en
2. Click the button "ADD TO CHROME" to add the extension (Figure 17)
3. When the app is added, in Chrome go to chrome://apps/
4. Click the "Postman" icon to launch the app

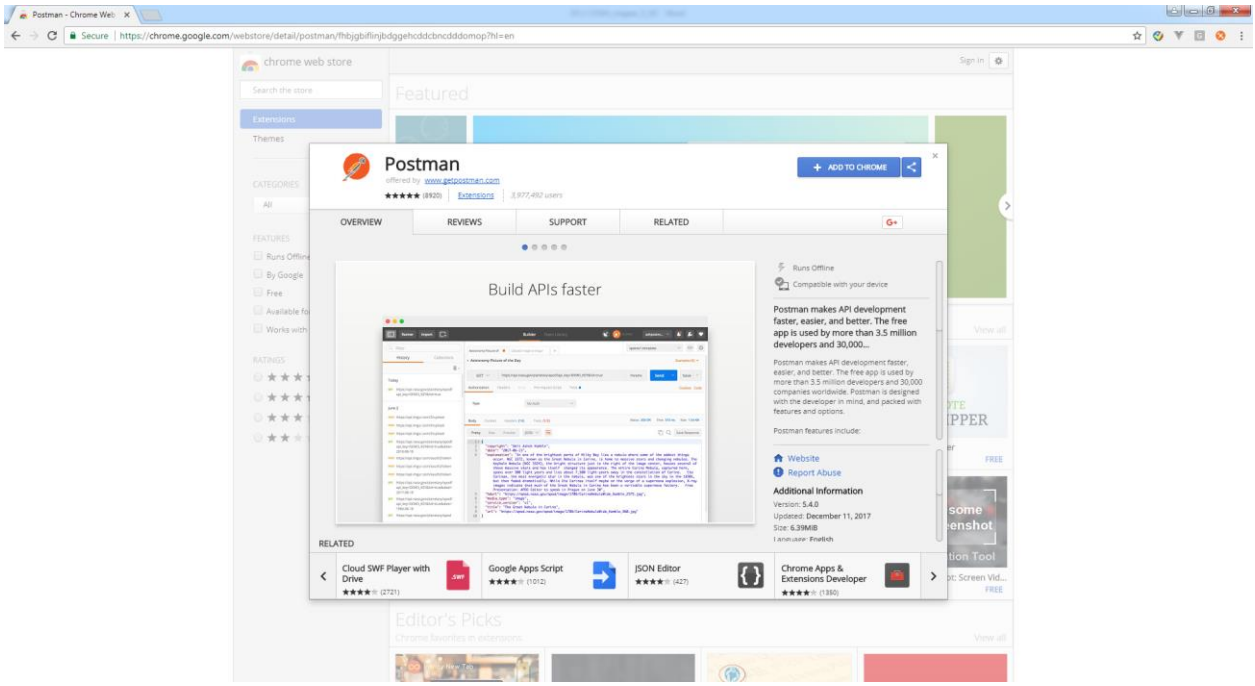

Figure 17: Postman chrome extension

The steps of using Postman and provided test cases to test the CDSM service is described below:

1. Enter the BP management service endpoint to the URL field, and select POST from the list
2. In the `Headers` tab, enter "Content-Type" as Key and "application/json" as Value (Figure 18)
3. In the `Body` tab select "raw", then copy the JSON data from a test case `BODY` into the text area of the `Body` tab (Figure 19)
4. Click "Send" button to submit the HTTP POST request
5. If the CDS service returns the result correctly, the CDS hooks cards should appear in the body of the HTTP 200 response as structured JSON content (Figure 20).

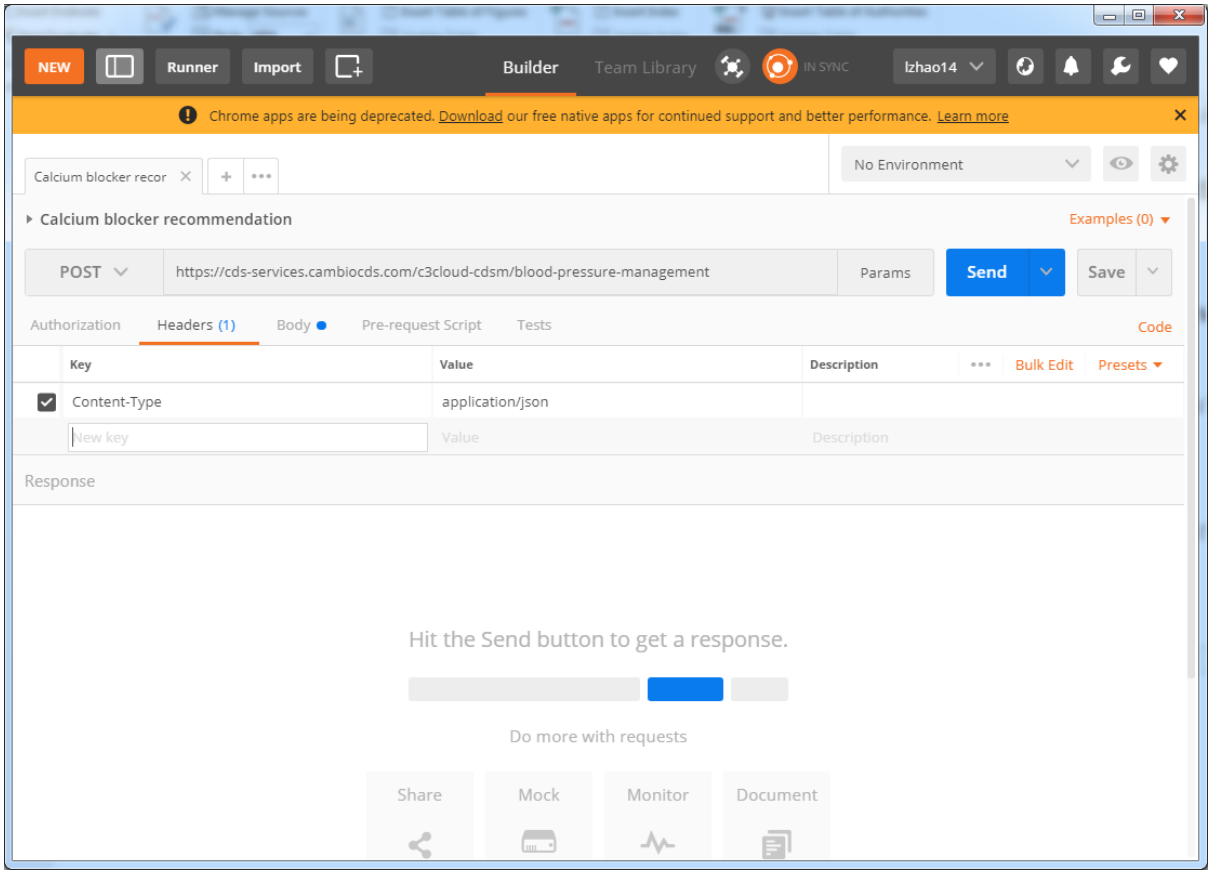

Figure 18: Set Content-Type in Postman

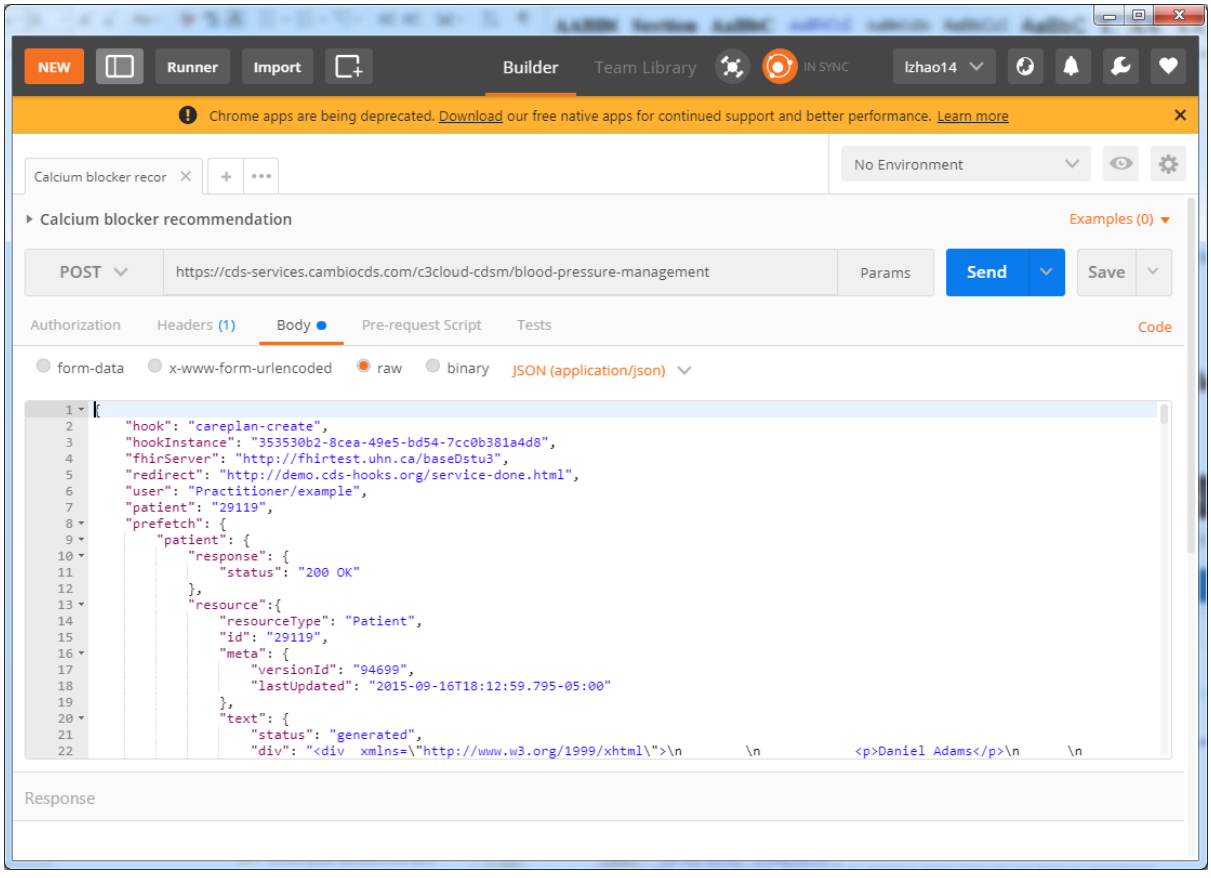

Figure 19: Set request body in Postman

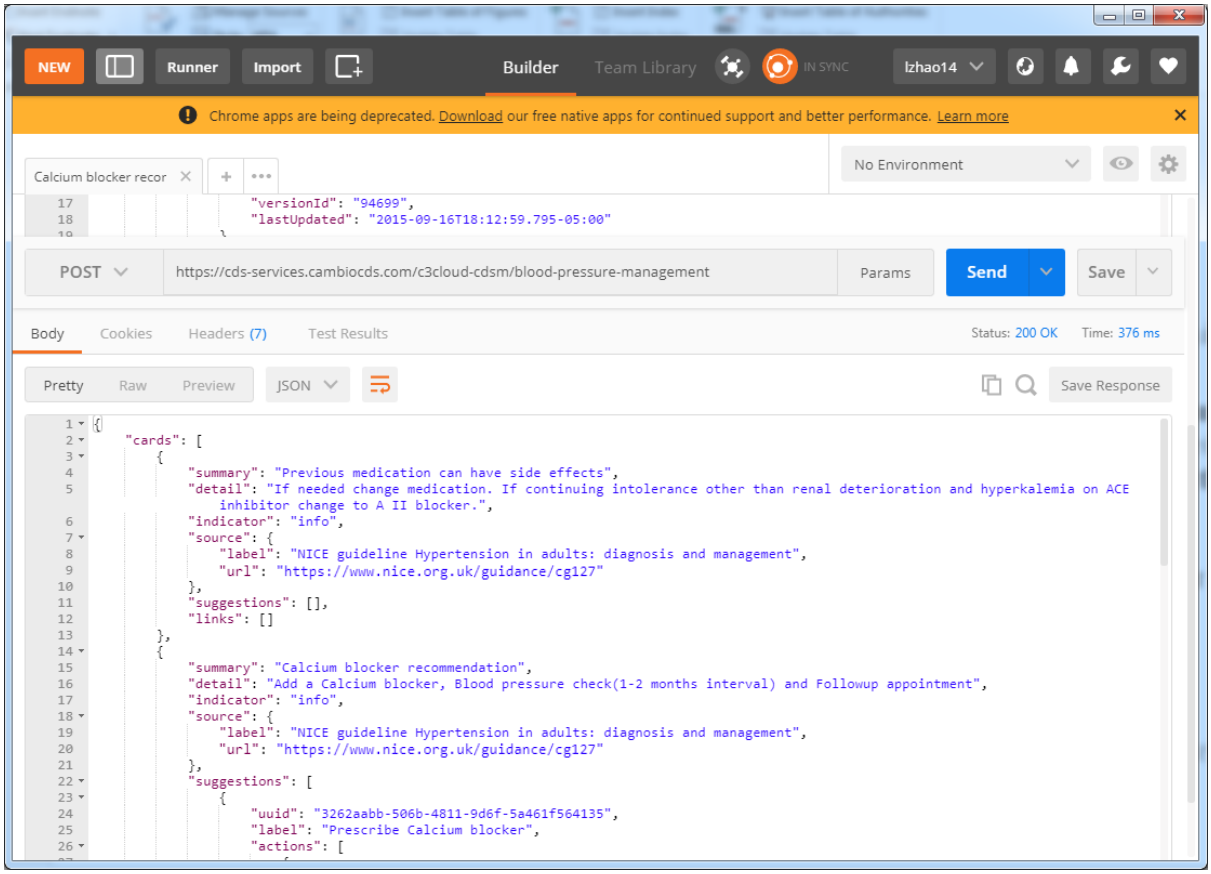

Figure 20: Cards returned as http response body in Postman

The BP management service has been integrated with C3DP. Figure 21**Error! Reference source not found.** shows a screenshot that C3DP invokes the BP management service and receives suggestions from it.

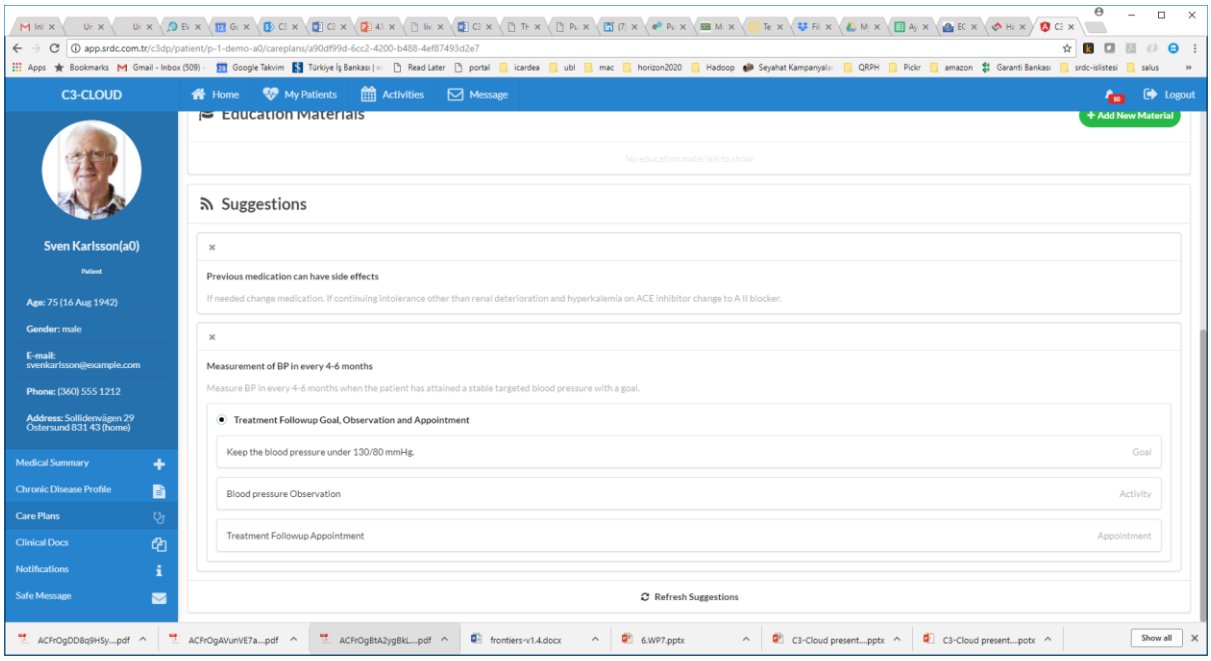

Figure 21: C3DP receives BP management suggestion from CDS

6. FUTURE PLANS

Task 7.2 ends at the end of December 2017 (Month 20). During the period of this work task, we have developed guideline reconciliation rules and technical specifications of CDS modules for the target diseases. Modules are implemented in GDL version 2 following CDS Hooks standard. The future development of CDS will focus on integration with other C3-Cloud components and external resources for drug interaction and polypharmacy management. The future work includes:

- *Integration with C3DP*. Several modules have been integrated with C3DP and demonstrated at the project review on the 8th December 2017. Other modules will be tested and integrated within the scope of Task 7.4.
- *Code mapping and FHIR data*. CDSM relies on proper encoding of patient data as FHIR resources. While CDSM does not have direct integration with the Semantic Interoperability Suite (SIS), Task 6.2 will provide code mappings for the clinical concepts involved in each CDSM and ensure the required patient data being encoded in proper FHIR format. The code mapping will be included as part of GDL2 definition for each CDSM.
- *Language translation*. So far, the medical terms and decision support messages are available in English only. C3-Cloud pilot studies require information being displayed in native languages. The C3-Cloud system needs be translated into Spanish and Swedish for OSAKI and RJH pilots, including all CDS information and suggestions.
- *Integration with external drug-drug interaction databases*. C3-Cloud will reuse existing reliable drug-drug and drug-disease interaction databases to enhance guideline reconciliation and polypharmacy management. The consortium is in discussion with Pharmaceutical Information Centre Ltd (Lääketietokeskus Oy) who is a drug information provider and willing to share their knowledge bases with C3-Cloud after signing an NDA. The database is based on summary product characteristics (SPC) files. ATC is used to code drug ingredients, and ICD-10 is used to code diseases.
- *Integration with existing polypharmacy services*. OSAKIDETZA has an implementation of START/STOPP criteria and is willing to allow other pilot sites to reuse the service. The project will work closely with the OSAKIDETZA team to integrate the polypharmacy service into the C3-Cloud system.

7. REFERENCES

[1] C3-Cloud Deliverable 7.1 – Evidence Based Clinical Guideline Definitions and Flowcharts for Individual Chronic Conditions

[2] C3-Cloud Deliverable 3.2 - Requirements Specification of the C3-Cloud Architecture

[3] C3-Cloud Deliverable 3.3 – Conceptual Design of the C3-Cloud Architecture

[4] CDS Hooks, http://cds-hooks.org/

[5] HL7 Version 3 Standard: Decision Support Service Release 2, DSTU Release 1, 2014. http://www.hl7.org/implement/standards/product_brief.cfm?product_id=12

[6] Timbie JW, Damberg CL, Schneider EC, Bell DS. A conceptual framework and protocol for defining clinical decision support objectives applicable to medical specialties. BMC Med Inform Decis Mak. 3 de septiembre de 2012;12:93.

[7] Wright A, Sittig DF, Ash JS, Feblowitz J, Meltzer S, McMullen C, et al. Development and evaluation of a comprehensive clinical decision support taxonomy: comparison of front-end tools in commercial and internally developed electronic health record systems. J Am Med Inform Assoc JAMIA. 1 de mayo de 2011;18(3):232-42.

[8] Buffel du Vaure C, Ravaud P, Baron G, Barnes C, Gilberg S, Boutron I. Potential workload in applying clinical practice guidelines for patients with chronic conditions and multimorbidity: a systematic analysis. BMJ Open. 2016;6(3):e010119.

[9] Marengoni A, Onder G. Guidelines, polypharmacy, and drug-drug interactions in patients with multimorbidity. BMJ. 11 de marzo de 2015;350:h1059.

[10] Hughes LD, McMurdo MET, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing. enero de 2013;42(1):62-9.

[11] Muth C, Kirchner H, van den Akker M, Scherer M, Glasziou PP. Current guidelines poorly address multimorbidity: pilot of the interaction matrix method. J Clin Epidemiol. noviembre de 2014;67(11):1242-50.

[12] Dumbreck S, Flynn A, Nairn M, Wilson M, Treweek S, Mercer SW, et al. Drug-disease and drug-drug interactions: systematic examination of recommendations in 12 UK national clinical guidelines. BMJ [Internet]. 2015;350. Avalable at: http://www.bmj.com/bmj/350/bmj.h949.full.pdf

[13] Sources of information: PubMed (example: CHF -drug interaction: Page, R. L., O'Bryant, C. L., Cheng, D., Dow, T. J., Ky, B., Stein, C. M., ... & Lindenfeld, J. (2016). Drugs That May Cause or Exacerbate Heart Failure. Circulation, 134(6), e32-e69). Local Guidelines (examples are http://www.fisterra.com/guias-clinicas/ or http://portal.guiasalud.es/). DUOODECIM EBMeDS. The Lexicom databases.

[14] Muth C, Kirchner H, van den Akker M, Scherer M, Glasziou PP. Current guidelines poorly address multimorbidity: pilot of the interaction matrix method. J Clin Epidemiol. noviembre de 2014;67(11):1242-50.

[15] Guideline Definition Language (GDL), https://gdl-lang.org/

[16] Lääketietokeskus, https://www.laaketietokeskus.fi/en

APPENDIX I TECHNICAL SPECIFICATION OF DM2 CDSMS

In Table AI. 1, the list of diabetes related CDS features to be implemented are listed, indicating the source of the clinical information (either D7.1 Flowcharts or Reconciliation Rules), and whether it will be implemented as an external CDS service, or as a part of Care Plan Templates within C3DP. Later in the following sections the specifications of these services are provided.

Table AI. 1: List of CDS features to be implemented as external CDS Services and as a part of Care Plan Template

Source	CDS Features to be implemented	External / Local (i.e. as a part of Care Plan Template by C3DP)
D7.1. Flowchart 5.2.3 – Blood Pressure Management	Blood Pressure Management Service	External
D7.1. Flowchart 5.2.4 & 5.2.5 – Lipid Management	Lipid Management Service	External
D7.1. Flowchart 5.2.6 - HbA1C Targets	HbA1CTarget Service	External
D7.1. Flowchart 5.2.8, 5.2.9, 5.2.10 & 5.2.11 – Drug Treatment for Blood Glucose Management	Blood Glucose Management Service	External
D7.1. Flowchart 5.2.15 – Managing Foot Complications	Managing Diabetic Foot Problem	External
D7.1. Flowchart 5.2.2 & 5.4.4	Diet Management	External
Reconciliation rules for Type 2 Diabetes Management and Renal Failure Guidelines	Management of Diabetic Nephropathy	External
D7.1. Flowchart 5.2.1	Diabetes Education	Local
D7.1. Flowchart 5.2.7	Self-monitoring of blood glucose	Local
D7.1. Flowchart 5.2.12	Management of Gastroparesis	Local
D7.1. Flowchart 5.2.13	Management of Neuropathic pain	Local
D7.1. Flowchart 5.2.14	Management of Autonomic neuropathy	Local
D7.1. Flowchart 5.2.18	Management of Erectile dysfunction	Local
D7.1. Flowchart 5.2.19	Management of Eye disease	Local

1. Specifications of Remote CDS Services

1.1. Blood Pressure Management in DM2 (Flowchart 5.2.3)

In Figure A1. 1 and Figure A1. 2, the flowchart 5.2.3 presented in D7.1 has been re-drawn to annotate the information and suggestion cards that needs to be produced by CDS modules. Conditions of the flowchart are explained in Table AI. 2. Please note that the ICD, LOINC, and ATC codes need to be checked and confirmed by

clinical partners. Some of them are provided by Mikael Lilja (RJH), and there can be some Swedish localization of codes.

Please note that the flowchart is not an exact match of the one available in D7.1. In the Flowchart 5.2.3, after recommending a new drug it was immediately checked whether the blood pressure is below the set thresholds, however they need to be checked at the next control visit after the patient uses these drugs. Checking the NICE guidelines a recommendation of arranging a control visit after 1-2 months is added, and the Blood Pressure measurements are checked next time the CDSM is invoked at the control visit. Hence the control flow has changed as you will see in Figure A1. 1 and Figure A1. 2.

Table AI. 2: Condition Table

Condition No	Condition Clause
C1	If one of the following conditions exists: E11.2A, E11.2B, E11.4B, E11.4C, E11.4D, ICD G63.2 OR If albumin secretion in urine is ≥ 30 mg/l OR ≥20 µg/min OR ≥30 mg/24h (depending how it is presented)
C2	If systolic blood pressure (8480-6) < 140 and diastolic blood pressure (8462-4) < 80 (Both from 55284-4)
C3	If medication C09 exists
C4	If systolic blood pressure (8480-6) < 130 and diastolic blood pressure (8462-4) < 80 (Both from 55284-4)
C5	If medication C09AA or C09CA exists
C6	If medication C08 exists
C7	If medication C03 exists
C8	If condition T46.4X5A or allergy C09AA exists
C9	If observation 64234-8(current smoker) has 373066001(yes)
C10	If observation 74013-4(alcoholic drinks per day) > 0

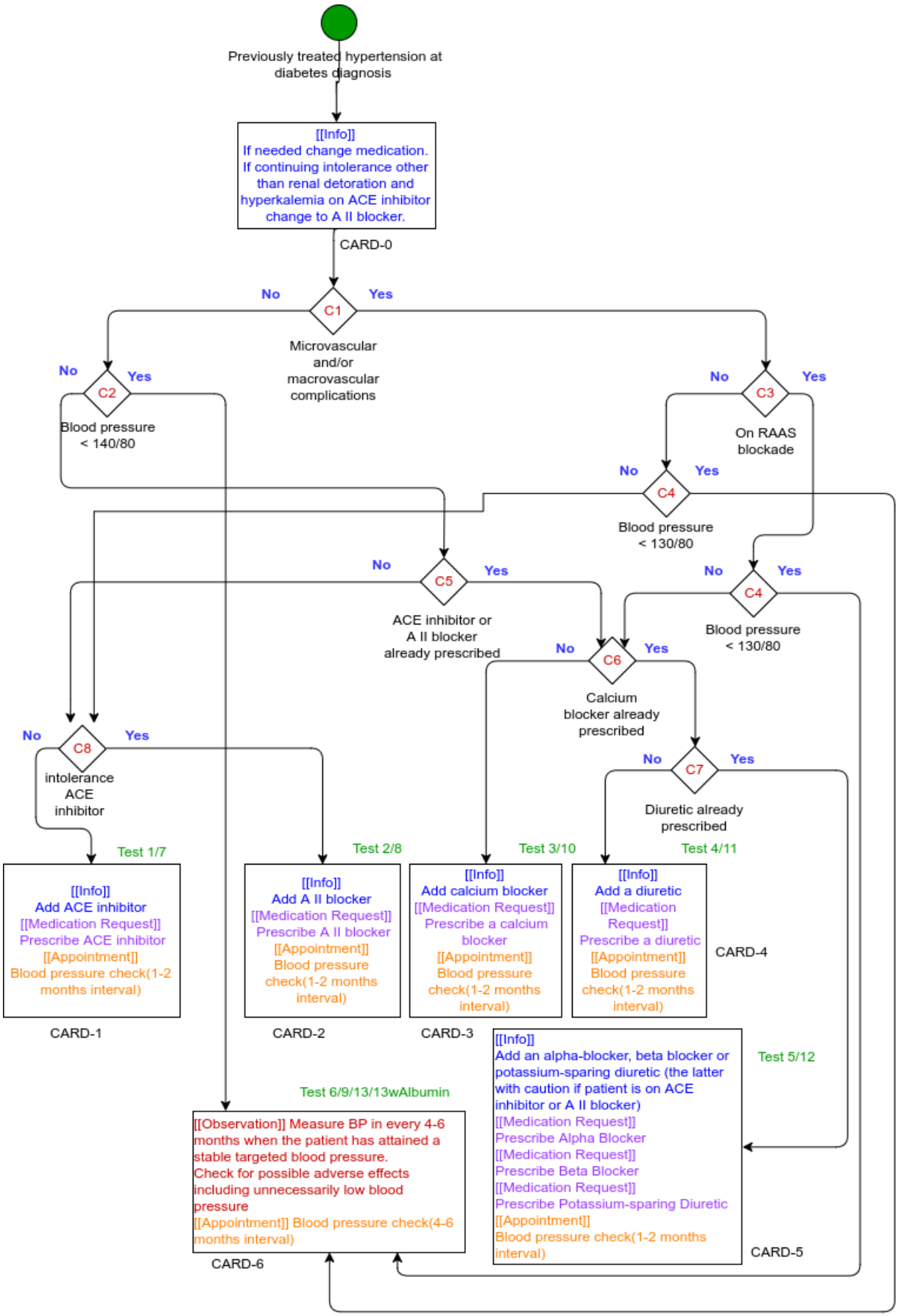

Figure A1. 1: First half of the Blood Pressure Management flowchart

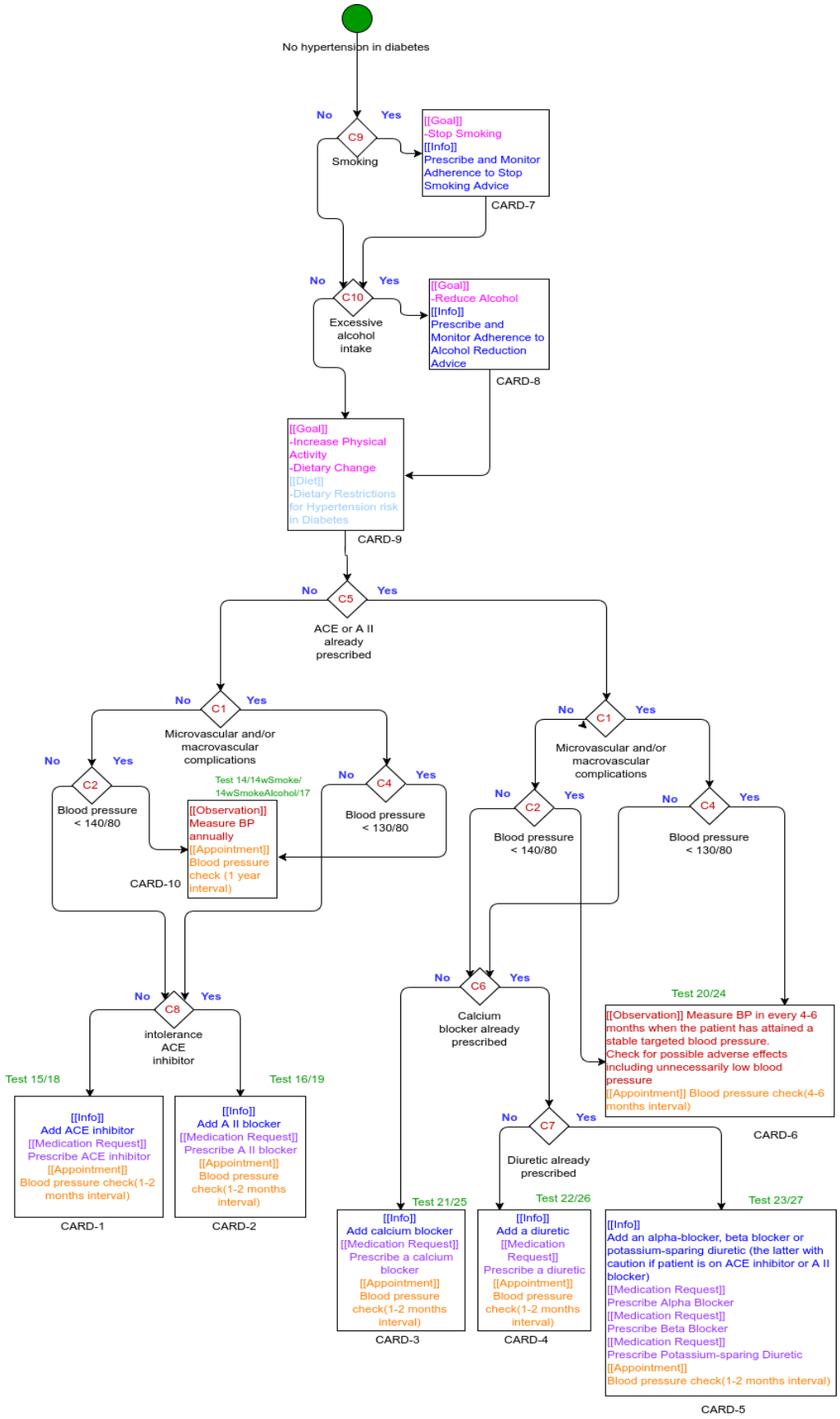

Figure A1. 2: Second half of the Blood Pressure Management flowchart

Table AI. 3: Clinical concepts to be processed by this CDS Service (Blood Pressure Management)

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	Hypertension	Input
	Microvascular Conditions	Input
	Macrovascular Conditions	Input
	ACE inhibitor intolerance	Input
Medications	ACE Inhibitors (Angiotensin Converting Enzyme Inhibitor)	Input & Output
	A II Blockers	Input & Output
	Calcium Blocker	Input & Output
	Diuretic	Input & Output
	Alpha Blocker	Output
	Beta Blocker	Output
	Potassium-sparing diuretic	Output
	RAAS blocker	Input
Vital Signs	Blood Pressure	Input & Output
Social History Observations	Smoking Status	Input
	Alcohol Consumption Status	Input
Allergies	Intolerance to ACE inhibitors	Input

1.1.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDSHooks terminology) presented in Table AI. 4**Error! Reference source not found.**.

Table AI. 4: Prefetch Terms as input to Blood Pressure CDS Service

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	-Type 2 Diabetes diagnosis - Hypertension diagnosis -Microvascular Conditions -Macrovascular Conditions -ACE inhibitor intolerance
medications	All medications used by the patient	-ACE inhibitors -A II Blockers -Calcium Blockers -Diuretic -Alpha Blockers -Beta Blockers -Potassium-sparing diuretic -RAAS Blocker
allergies	Allergies of the patient	ACE Intolerance
bp	Blood pressure	Systolic and diastolic blood pressure
smoking	Smoking Status of the patient	Smoking Status
albumin_level	Albumin level	Albumin level
alcohol	Alcohol consumption status	Alcohol status

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in Figure A1. 1 and Figure A1. 2, to produce the Cards listed in Table AI. 5.

Table AI. 5: Cards to be produced by Blood Pressure CDS Service

CARD 0	
summary	Previous medication can have side effects.
Detailed description	If needed change medication. If continuing intolerance other than renal deterioration and hyperkalemia on ACE inhibitor change to A II blocker.
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127
CARD 1	
summary	ACE inhibitor recommendation

Detailed description	Add Angiotensin Converting Enzyme Inhibitor, Blood pressure check(1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe ACE inhibitor
	Description	Prescribe ACE inhibitor
	Medication Code	C09AA, Angiotensin Converting Enzyme Inhibitor, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 2		
summary	A II Blockers recommendation	
Detailed description	Add II Blockers, Blood pressure check(1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe A II Blockers
	Description	Prescribe A II Blockers
	Medication Code	C09CA, Angiotensin Receptor II, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment

	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 3		
summary	Calcium Blocker recommendation	
Detailed description	Add a Calcium blocker, Blood pressure check(1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Calcium Blocker
	Description	Prescribe Calcium Blocker
	Medication Code	C08, Calcium Blocker, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation

	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 4		
summary	Diuretic recommendation	
Detailed description	Add a diuretic, Blood pressure check(1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Diuretic
	Description	Prescribe Diuretic
	Medication Code	C03, Diuretics , ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 5		
Summary	Alpha-blocker, beta blocker or potassium-sparing diuretic recommendation	
Detailed description	Add an alpha-blocker, beta blocker or potassium-sparing diuretic (the latter with caution if patient is on ACE inhibitor or A II blocker), Blood pressure check(1-2 months interval) and Follow-up appointment	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Medication Request	Title	Prescribe Alpha-blocker

	Description	Prescribe Alpha-blocker
	Medication Code	C012CA, Alpha-adrenoreceptor antagonists, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Beta-blocker
	Description	Prescribe Beta-blocker
	Medication Code	C07, Beta blocking agents, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT

Suggestion 3		
Medication Request	Title	Prescribe Potassium-sparing diuretic
	Description	Prescribe Potassium-sparing diuretic
	Medication Code	C03D, Potassium-sparing agents, ATC
	Dosage Text	-
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment
	Status	proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
CARD 6		
summary	Measurement of BP in every 4-6 months	
Detailed description	Measure BP in every 4-6 months when the patient has attained a stable targeted blood pressure with a goal.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Safety, http://hl7.org/fhir/goal-category
	Description Code	135840009, Blood Pressure monitoring (regime/therapy)
	Description Text	Keep the blood pressure under 140/80 mmHg.
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC

	performer	PATIENT
Appointment	Title	Treatment Follow-up Appointment
	Description	6 monthly Blood Pressure Management Appointment
	Status	proposed
	start	(Date + 6 months)
	specialty	-
CARD 7		
summary	Life advice about tobacco smoking	
Detailed description	Prescribe and Monitor Adherence to Stop Smoking Advice	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal:	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to stop smoking
Appointment	Title	Stop Smoking Follow-up Appointment
	Description	Follow-up to check the patient's smoking status
	Status	Proposed
	start	-
	specialty	-
CARD 8		
summary	Life advice about alcohol consumption	
Detailed description	Prescribe and Monitor Adherence to Alcohol Reduction Advice	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to reduce alcohol intake
Appointment	Title	Reduce Alcohol Consumption Followup Appointment

	Description	Follow-up to check the patient's alcohol consumption status
	Status	Proposed
	start	-
	specialty	-
CARD 9		
summary	General Life Advice	
Detailed description	Recommend increasing physical activity and dietary change if necessary	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to increase physical activity
Goal	Category	Dietary, http://hl7.org/fhir/goal-category
	Description Code	-
	Description Text	Set a goal to dietary change
CARD 10		
summary	Measurement of BP annually	
Detailed description	Measure BP annually when the patient has attained a stable targeted blood pressure.	
source	NICE guideline Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127	
Suggestion 1		
Activity	Title	Blood Pressure Observation
	Description	Have Blood Pressure systolic and diastolic test before the control visit
	Category	Observation
	Code	85354-9, Blood Pressure, LOINC
	performer	PATIENT
Appointment	Title	Treatment Follow-up Appointment
	Description	Follow-up to check the results of the treatment

	Status	proposed
	start	(Date + 1 year)
	specialty	-

1.2.Lipid Management (Flowchart 5.2.4 & 5.2.5)

In Figure A1. 3, the flowcharts 5.2.4 and 5.2.5 presented in D7.1 has been re-drawn to annotate the information and suggestion cards that needs to be produced by CDS modules. Conditions of the flowchart are explained in Table AI. 6. Please note that the ICD, LOINC, and ATC codes need to be checked and confirmed by clinical partners. Some of them are provided by Mikael, and there can be some Swedish localization of codes.

Table AI. 6: Condition Table

Condition No	Condition Clause
C1	Has atorvastatin (C10AA05)?
C2	Has liver transaminases test (AST(1920-8) and ALT(1742-6))
C3	Is liver transaminases bigger 3 times upper limit?
C4	If newly developed muscle pain (M62.838) within 3 months of starting therapy
C5	Has lipid lab tests(hdl(2085-9), ldl(13457-7), cholesterol(2093-3))?
C6	If >=40% reduction in non-HDL cholesterol
C7	If eGFR(33914-3) >= 30ml/min/1.73m2
C8	If there is an indication for secondary cardiovascular prevention (with codes I48, I20-I25, I63, I65, I66, I67.2, I70, K55.1)
C9	Has measured QRISK2(718087004)?
C10	If QRISK2 >= 10% 10 years risk?

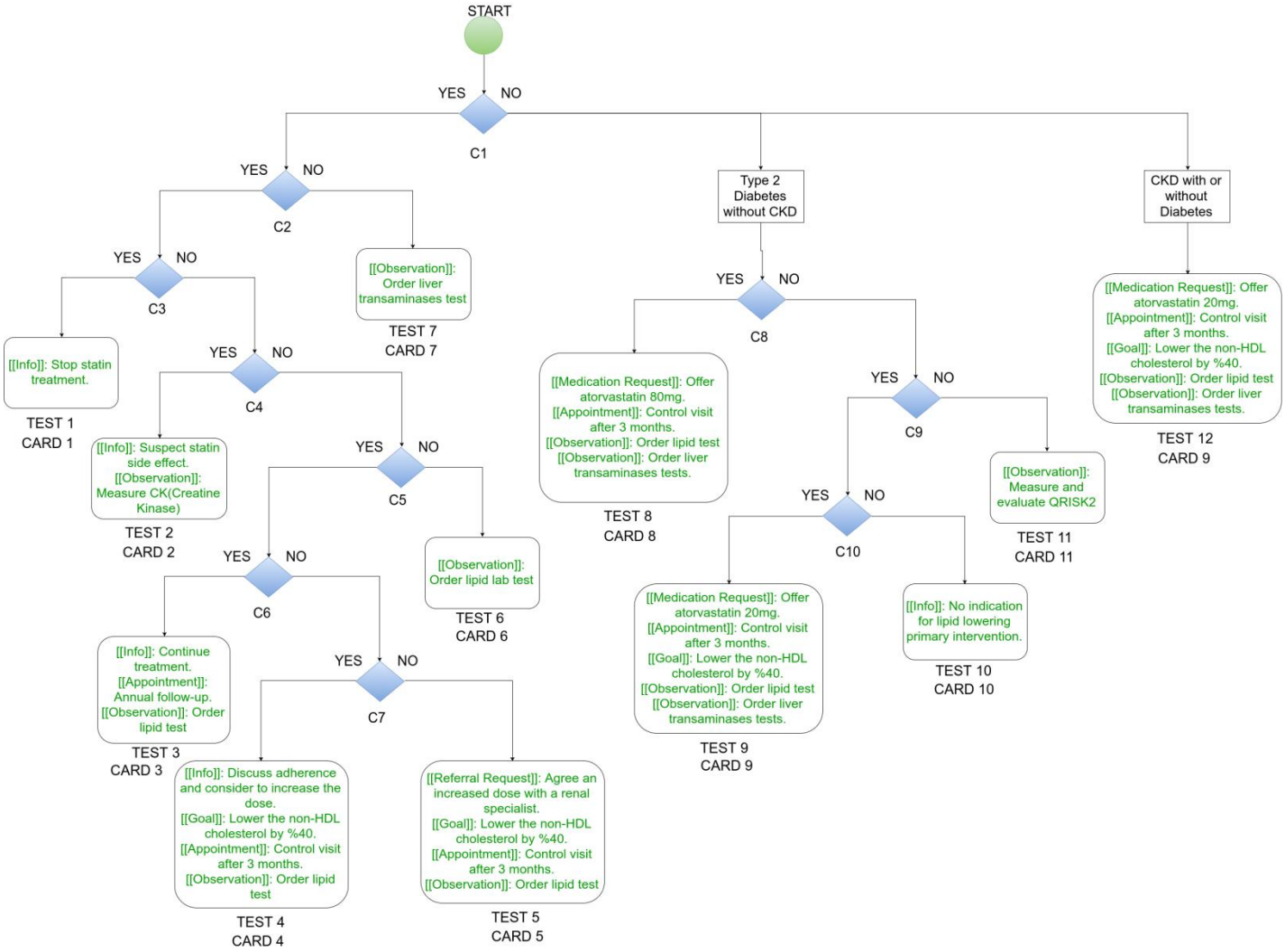

Figure A1. 3: Lipid Management Flowchart (Test Cases)

Table AI. 7: Clinical concepts to be processed by this CDS Service (Lipid Management)

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	CKD	Input
	Macrovascular Conditions	Input
	Muscle pain	Input

Medications	Atorvastatin	Input& Output
Lab Results	LDL	Input & Output
	eGFR	Input
	Aspartate transaminase (AST)	Input & Output
	Alanine transaminase (ALT)	Input & Output
	Lipid Panel Test	Output
	Creatine Kinase	Output
Risk Calculations	Cardiovascular Risk (via QRISK2)	Input & Output

1.2.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDS Hooks terminology) presented in Table AI. 8.

Table AI. 8: Prefetch Terms as input to Lipid Management CDS Service

Prefetch term id	Description	variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	-Type 2 Diabetes diagnosis - CKD -Macrovascular Conditions -Muscle pain
medications	All medications used by the patient	-Atorvastatin
ldl	LDL observation lab result	LDL value
egfr	eGFR observation lab result	eGFR value
ast	AST observation lab result	AST value
alt	ALT observation lab result	ALT value
qrisk	QRISK value coming from QRISK2 service	Qrisk2 value

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in Figure A1. 3, to produce the Cards listed in Table AI. 9.

Table AI. 9: Cards to be produced by Lipid Management CDS Service

CARD 1		
summary	Measure Creatine Kinase (CK)	
Detailed description	Suspect statin side effect and Measure Creatine Kinase (CK)	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
CARD 2		
summary	Measurement of BP annually	
Detailed description	Measure BP annually when the patient has attained a stable targeted blood pressure.	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Activity	Title	Creatine Kinase Observation
	Description	Measure creatine kinase
	Category	Observation
	Code	9643-8, Creatine Kinase, LOINC
	performer	PATIENT
CARD 3		
summary	Continue treatment and offer annual follow-up and lipid test suggestion	
Detailed description	Continue treatment and offer annual follow-up and lipid test suggestion	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26].	

	https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Appointment	Title	Annual follow-up appointment
	Description	Annual follow-up to check the results of Statin Treatment
	Status	proposed
	start	(Date + 1 year)
	specialty	-
Activity	Title	Lipid Panel Test Observation
	Description	Have lipid Panel test before 3 monthly lipid control visit
	Category	Observation
	Code	24331-1, Lipid 1996 panel - Serum or Plasma, LOINC
	performer	PATIENT
CARD 4		
summary	Recommendation for increasing the dose of Statin treatment (atorvastatin 80mg) and suggest lipid test and 3 months control visit	
Detailed description	Increase the dose of atorvastatin to 80 mg. Add a goal to lower the non-HDL Cholesterol by %40. See also NICE guidelines for cardiovascular disease (CG181) and suggest lipid test and 3 months control visit	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Medication Request	Title	Atorvastatin Recommendation
	Description	Atorvastatin Recommendation-80mg
	Medication Code	C10AA05, Atorvastatin, ATC
	Dosage Text	80mg daily
Goal	category	Safety, http://hl7.org/fhir/goal-category"
Goal:	Description code	13457-7, Cholesterol in LDL, LOINC
	Description text	Decrease Non-HDL Cholesterol by %40. Evaluate progress with 3 monthly measurements.
Activity	Title	Lipid Panel Test Observation
	Description	Have lipid Panel test before 3 monthly lipid control visit

	Category	Observation
	Code	24331-1, Lipid 1996 panel - Serum or Plasma, LOINC
	performer	PATIENT
Appointment	Title	Statin Treatment Follow-up Appointment
	Description	Follow-up to check the results of Statin Treatment
	Status	proposed
	start	(Date + 3 months)
	specialty	-
CARD 5		
summary	Referral to a Renal Specialist to agree on an increased statin dose suggest lipid test and 3 months control visit.	
Detailed description	Referral to a Renal Specialist to agree on an increased statin dose suggest lipid test. Add a goal to lower the non-HDL Cholesterol by %40 and 3 months control visit.	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Referral Request	Title	Referral to a Renal Specialist to agree on an increased statin dose
	Description	Referral to a Renal Specialist to agree on an increased statin dose for lipid lowering, Proposed dose 80mg
	status	draft
	specialty	11911009, Nephrologist, SNOMED
Goal	category	Safety, http://hl7.org/fhir/goal-category"
Goal:	Description code	13457-7, Cholesterol in LDL, LOINC
	Description text	Decrease Non-HDL Cholesterol by %40. Evaluate progress with 3 monthly measurements.
Activity	Title	Lipid Panel Test Observation
	Description	Have lipid Panel test before 3 monthly lipid control visit
	Category	Observation
	Code	24331-1, Lipid 1996 panel - Serum or Plasma, LOINC
	performer	PATIENT
Appointment	Title	Statin Treatment Follow-up Appointment
	Description	Follow-up to check the results of Statin Treatment

	Status	Proposed
	start	(Date + 3 months)
	specialty	-
CARD 6		
summary	Order lipid lab tests	
Detailed description	Order lipid lab tests	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Activity	Title	Lipid Panel Test Observation
	Description	Have lipid Panel test before 3 monthly lipid control visit
	Category	Observation
	Code	24331-1, Lipid 1996 panel - Serum or Plasma, LOINC
	performer	PATIENT
CARD 7		
summary	Order liver transaminases test	
Detailed description	Order liver transaminases test (AST and ALT)	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Activity	Title	Aspartate transaminase (AST) test
	Description	Have Aspartate transaminase (AST) test before 3 monthly lipid control visit
	Category	Observation
	Code	1920-8, Aspartate transaminase (AST), LOINC
	performer	PATIENT
Activity	Title	Alanine transaminase (ALT) Test
	Description	Have Alanine transaminase (ALT) test before 3 monthly lipid control visit
	Category	Observation
	Code	1742-6, Alanine transaminase (ALT), LOINC

	performer	PATIENT
CARD 8		
summary	Atorvastatin Recommendation-80mg, lipid and liver transaminases tests	
Detailed description	Offer atorvastatin 80 mg. Appointment for control visit after 3 months. Suggest lipid and liver transaminases tests.	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Medication Request	Title	Atorvastatin Recommendation
	Description	Atorvastatin Recommendation-80mg
	Medication Code	C10AA05, Atorvastatin, ATC
	Dosage Text	80mg daily
Appointment	Title	Statin Treatment Follow-up Appointment
	Description	Follow-up to check the results of Statin Treatment
	Status	proposed
	start	(Date + 3 months)
	specialty	-
Activity	Title	Lipid Panel Test Observation
	Description	Have lipid Panel test before 3 monthly lipid control visit
	Category	Observation
	Code	24331-1, Lipid 1996 panel - Serum or Plasma, LOINC
	performer	PATIENT
Activity	Title	Aspartate transaminase (AST) test
	Description	Have Aspartate transaminase (AST) test before 3 monthly lipid control visit
	Category	Observation
	Code	1920-8, Aspartate transaminase (AST), LOINC
	performer	PATIENT
Activity	Title	Alanine transaminase (ALT) Test
	Description	Have Alanine transaminase (ALT) test before 3 monthly lipid control visit
	Category	Observation

	Code	1742-6, Alanine transaminase (ALT), LOINC
	performer	PATIENT
CARD 9		
summary	Atorvastatin Recommendation-20mg, lipid and liver transaminases tests	
Detailed description	Offer atorvastatin 20 mg. Add a goal to lower the non-HDL Cholestretol by %40. Appointment for control visit after 3 months. Suggest lipid and liver transaminases tests.	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Medication Request	Title	Atorvastatin Recommendation
	Description	Atorvastatin Recommendation-20mg
	Medication Code	C10AA05, Atorvastatin, ATC
	Dosage Text	20mg daily
Goal	category	Safety, http://hl7.org/fhir/goal-category"
	Description code	13457-7, Cholesterol in LDL, LOINC
	Description text	Decrease Non-HDL Cholesterol by %40. Evaluate progress with 3 monthly measurements.
Appointment	Title	Statin Treatment Follow-up Appointment
	Description	Follow-up to check the results of Statin Treatment
	Status	proposed
	start	(Date + 3 months)
	specialty	-
Activity	Title	Lipid Panel Test Observation
	Description	Have lipid Panel test before 3 monthly lipid control visit
	Category	Observation
	Code	24331-1, Lipid 1996 panel - Serum or Plasma, LOINC
	performer	PATIENT
Activity	Title	Aspartate transaminase (AST) test
	Description	Have Aspartate transaminase (AST) test before 3 monthly lipid control visit
	Category	Observation
	Code	1920-8, Aspartate transaminase (AST), LOINC

	performer	PATIENT
Activity	Title	Alanine transaminase (ALT) Test
	Description	Have Alanine transaminase (ALT) test before 3 monthly lipid control visit
	Category	Observation
	Code	1742-6, Alanine transaminase (ALT), LOINC
	performer	PATIENT
CARD 10		
summary	Measure and evaluate QRISK2	
Detailed description	Measure and evaluate QRISK2	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
CARD 11		
summary	Measure and evaluate QRISK2	
Detailed description	Measure and evaluate QRISK2	
source	NICE guideline Cardiovascular disease: risk assessment and reduction, including lipid modification, Chapter 1.3.20-1.3.51 [49, pp. 20-26]. https://www.nice.org.uk/guidance/CG181	
Suggestion 1		
Activity	Title	Measure and evaluate QRISK2
	Description	Measure and evaluate QRISK2
	Category	Observation
	Code	718087004, QRISK2, SNOMED
	performer	PATIENT

1.3.HbA1c Targets (Flowchart 5.2.6)

In Figure A1. 4, the flowchart 5.2.6 presented in D7.1 has been re-drawn to annotate the information and suggestion cards that needs to be produced by CDS modules. Conditions of the flowchart are explained in Table AI. 10.

Please note that in the flowchart 5.2.6 presented in D7.1, not only targets but also some guidance about the frequency of control visits is also presented based on the condition that HbA1c targets are met. Also some notifications to be presented to the doctor are given in the case of HbA1c targets are below the target. These suggestions are moved to the next CDSM, i.e. Initial Drug Treatment & First and Second Intensification of Drug Treatment, because logically this check (i.e. whether HbA1c target is below the set target) needs to be carried out after a drug is prescribed and the effects are seen.

Table AI. 10: Conditions to be checked

Condition No	Condition Clause
C1	If the patient is frail or has reduced life expectancy (these will be asked to the clinician via the Chronic Disease Profile GUI, and the CDSM will receive it in a coded way from the C3DP)
C2	Treatment risk of hypoglycemia ((the patient has the following diagnosis (Hypoglycemia due to type 2 diabetes mellitus (disorder)) OR (Coma associated with diabetes mellitus (disorder)) OR the patient has one of the medication used for the treatment with risk of hypoglycemia: A10A, A10BB, A10BC01, A10BD01, A10BD02, A10BD04, A10BD06, A10BX02, A10BX03) OR eGFR<45 OR The patient has chronic renal failure diagnosis (CKD Stage 4, CKD Stage 5)
C3	If the patient has short expected survival rate or on terminal care

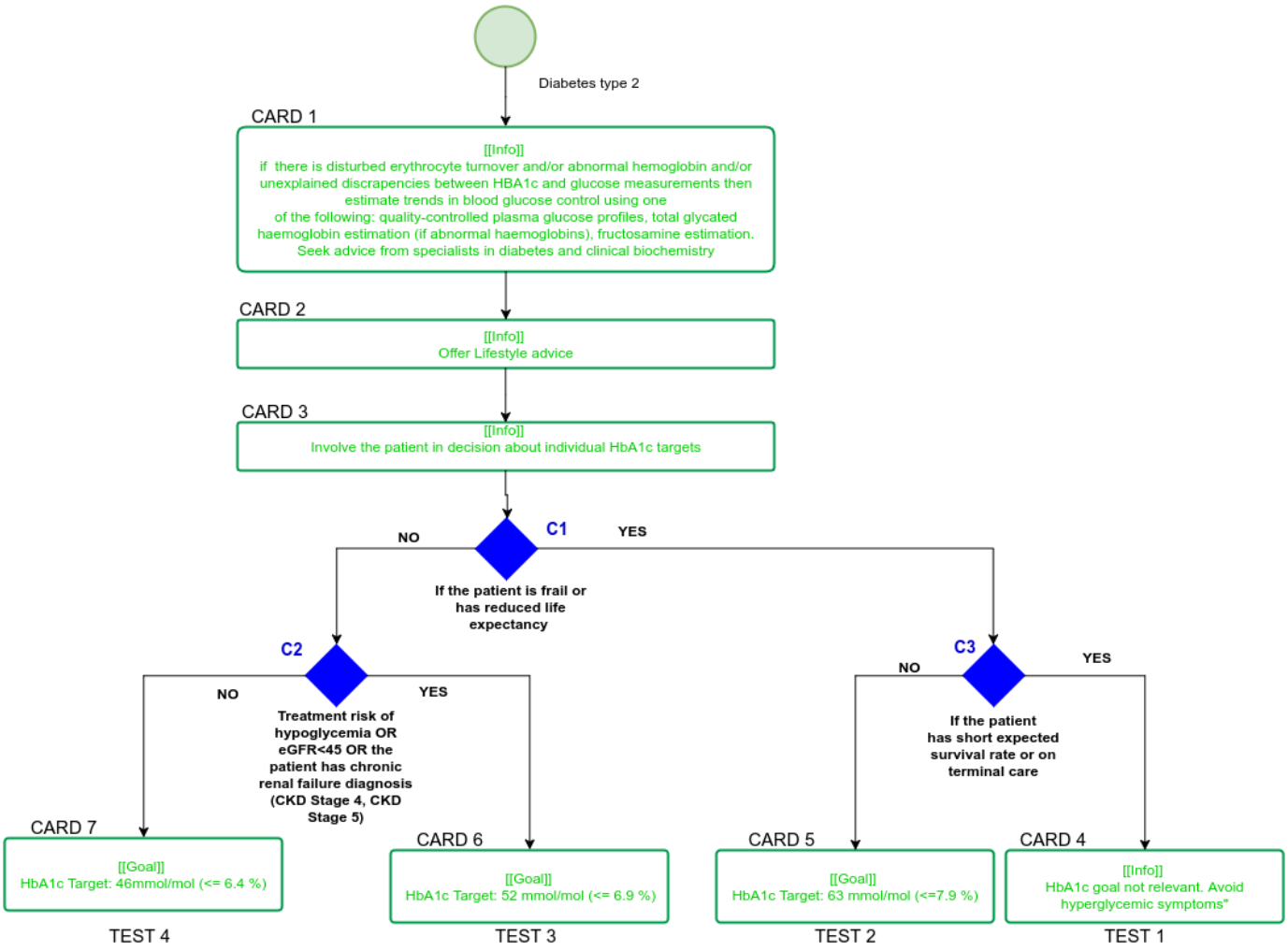

Figure A1. 4: HbA1c Measurements and Targets Flowchart (Test cases)

Table AI. 11: Clinical concepts to be processed by this CDS Service (HbA1C Target)

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	Reduced Life Expectancy	Input
	Treatment risk of hypoglycemia	Input
	Terminal care	Input
Medications	Medication with codes: (A10A, A10BB, A10BC01, A10BD01, A10BD02, A10BD04, A10BD06, A10BX02, A10BX03)	Input

Lab Results	eGFR	Input
Observations	Frailty Score	Input

1.3.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDSHooks terminology) presented in Table AI. 12.

Table AI. 12: Prefetch Terms as input to HbA1C Target CDS Service

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	-Type 2 Diabetes diagnosis - CKD -Macrovascular Conditions -Muscle pain
medications	All medications used by the patient. (With codes)	(A10A, A10BB, A10BC01, A10BD01, A10BD02, A10BD04, A10BD06, A10BX02, A10BX03)
egfr	eGFR observation lab result	eGFR value
frailty	Frailty score of the patient	Frailty score

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in Figure A1. 4, to produce the Cards listed in Table AI. 13**Error! Reference source not found.**.

Table AI. 14: Cards to be produced by HbA1C Target CDS Service

CARD 1	
summary	Estimate trends in glucose control
Detailed description	If disturbed erythrocyte turnover and/or abnormal hemoglobin and/or unexplained discrapencies between HBA1c and glucose measurements then estimate trends in blood glucose control using one of the following: quality-controlled plasma glucose profiles, total glycylated hemoglobin estimation (if abnormal hemoglobins), fructosamine estimation. Seek advice from specialists in diabetes and clinical biochemistry
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18]. https://www.nice.org.uk/guidance/ng28

CARD 2		
summary	Life style advice	
Detailed description	Offer life style advice	
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18]. https://www.nice.org.uk/guidance/ng28	
CARD 3		
summary	Decision about individual HbA1c targets	
Detailed description	Involve the patient in decision about individual HbA1c targets	
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18]. https://www.nice.org.uk/guidance/ng28	
CARD 4		
summary	HbA1c goal not relevant. Avoid hyperglycemic symptoms.	
Detailed description	HbA1c goal not relevant. Avoid hyperglycemic symptoms.	
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18]. https://www.nice.org.uk/guidance/ng28	
CARD 5		
summary	Suggestion for HbA1c target	
Detailed description	Treatment target is supposed to be 63 mmol/mol (<= 7.9%). Patient is frail or has reduced life expectancy. Consider relaxing HbA1c target.	
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Goal	category	Safety, http://hl7.org/fhir/goal-category"
	Description code	51798006, Decreased glucose level (finding), SNOMED
	Description text	Keep HbA1C level below 63 mmol/mol (<= 7.9%)
	Target Measure code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	Target range (coded)	High: 63 mmol/mol (7.9%)
CARD 6		
summary	Suggestion for HbA1c target	
Detailed description	Treatment target is supposed to be 52 mmol/mol (<= 6.9%). Treatment risk of hypoglycemia or eGFR<45 or patient has chronic failure diagnosis. Consider relaxing HbA1c target.	
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18].	

	https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Goal	category	Safety, http://hl7.org/fhir/goal-category"
	Description code	51798006, Decreased glucose level (finding), SNOMED
	Description text	Keep HbA1C level below 52 mmol/mol (<= 6.9%)
	Target Measure code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	Target range (coded)	High: 52 mmol/mol (6.9%)
CARD 7		
summary	Suggestion for HbA1c target	
Detailed description	Treatment target is supposed to be 46 mmol/mol (<= 6.4%). Consider relaxing HbA1c target.	
source	NICE diabetes guideline, Chapter 1.6.1-1.6.11 [48, pp. 16-18]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Goal	category	Safety, http://hl7.org/fhir/goal-category"
	Description code	51798006, Decreased glucose level (finding), SNOMED
	Description text	Keep HbA1C level below 46 mmol/mol (<= 6.4%)
	Target Measure code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	Target range (coded)	High: 46 mmol/mol (6.4%)

1.4.Blood Glucose Management Service (Flowchart 5.2.8 & 5.2.9)

In Figure A1. 5 and Figure A1. 6, the flowchart 5.2.8 and 5.2.9 presented in D7.1 has been re-drawn to annotate the information and suggestion cards that need to be produced by CDS modules. Conditions of the flowchart are explained in Table AI. 15.

Please check that the flowchart is not an exact match of the one available in D7.1. In the Flowchart 5.2.8 and 5.2.9, after recommending a new drug it was immediately checked whether the HbA1c is below the set thresholds, however they need to be checked at the next control visit after the patient uses these drugs. Checking the NICE guidelines a recommendation of arranging a control visit is added, and the HbA1c measurements are checked next time the CDSM is invoked at the control visit. Hence the control flow has changed as you will see in Figure A1. 5 and Figure A1. 6. Also please review that 5.2.8 and 5.2.9 are in fact linked although it is not clearly expressed in D7.1. If metformin is contraindicated, right branch of Flowchart 5.2.9 needs to be implemented. And if Metformin is continued as suggested in Flowchart 5.2.8, after the control visit it has to be checked whether the drug is working properly to reduce HbA1c below the threshold, and if not the left part of the flowchart 5.2.9 needs to be executed. These have been realized in Figure A1. 5 and Figure A1. 6.

In addition to this, the recommendations about the frequency of control visits, and also notifications about possible cause of low HbA1C from Flowchart 5.2.6 are integrated here.

Finally, please note that, in the current flowchart:

- if one of the SGLT2 Inhibitors is currently in use as a part of Dual therapy and eGFR<45, then it is recommended to stop the respective drug (i.e. the one in use, say empagliflozin). Then the flowchart is re-directed to condition C6. If the conditions hold, the recommendation can be BOX 9, which includes the recommendation of 'Prescribing Metformin and SGLT2 inhibitor'. Although it is not implicitly indicated in the flowchart, here the CDSM will recommend one of the other SGLT-2 inhibitors (in our example canagliflozin or dapagliflozin), not the one that has been recently stopped (i.e. empagliflozin).
- These was mentioned in cards CARD 9_1, CARD 9_2 and CARD 9_3. Same concept is used for test17_frombranch and test18_frombranch (testing that stopping one of SGLT2 inhibitors), but not showed in the flowchart. As instance, CARD 9_1, CARD 9_2 and CARD 9_3 are leading the same situation, (after stopping the used SGLT2 inhibitor, recommending other two).
- There is a similar case in Triple Therapy as well.

Some other assumptions:

For the sudden weight loss condition, difference between last two measurements is checked. After calculating the difference between second last and last measurements, if there is a loss of more than 5 kg's, then it is assumed to be sudden.

For eGFR condition, results less than or equal to 45 are accepted to be as the sign of deteriorating or deteriorated kidney function. An annual change in eGFR (ml/min/1.73m2) exceeding 5% is another option to use indicating deteriorating kidney function.

These need to be checked and confirmed by the clinical specialists.

Please note that, in the final implementation Flowchart 5.2.10 and 5.2.11 (Related with Insulin based treatment) needs to be integrated with this one. Please check that there are Information cards as "start Insulin based treatment', ideally at these points the CDSMs implementing Flowcharts 5.2.10 and 5.2.11 needs to be called.

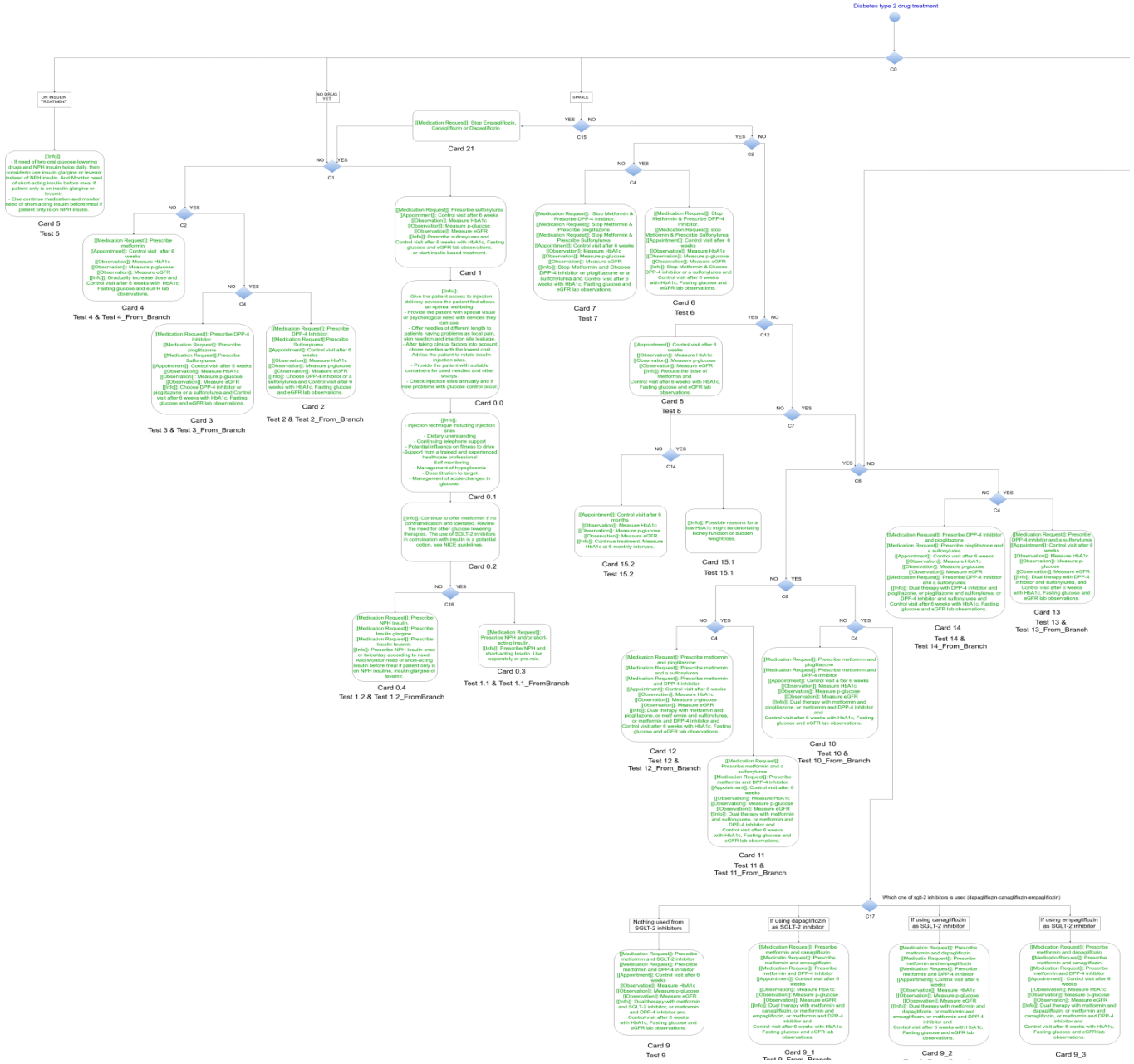

Figure A1. 5: First part of the Initial Drug treatment & First and second intensification of drug treatment flowchart.

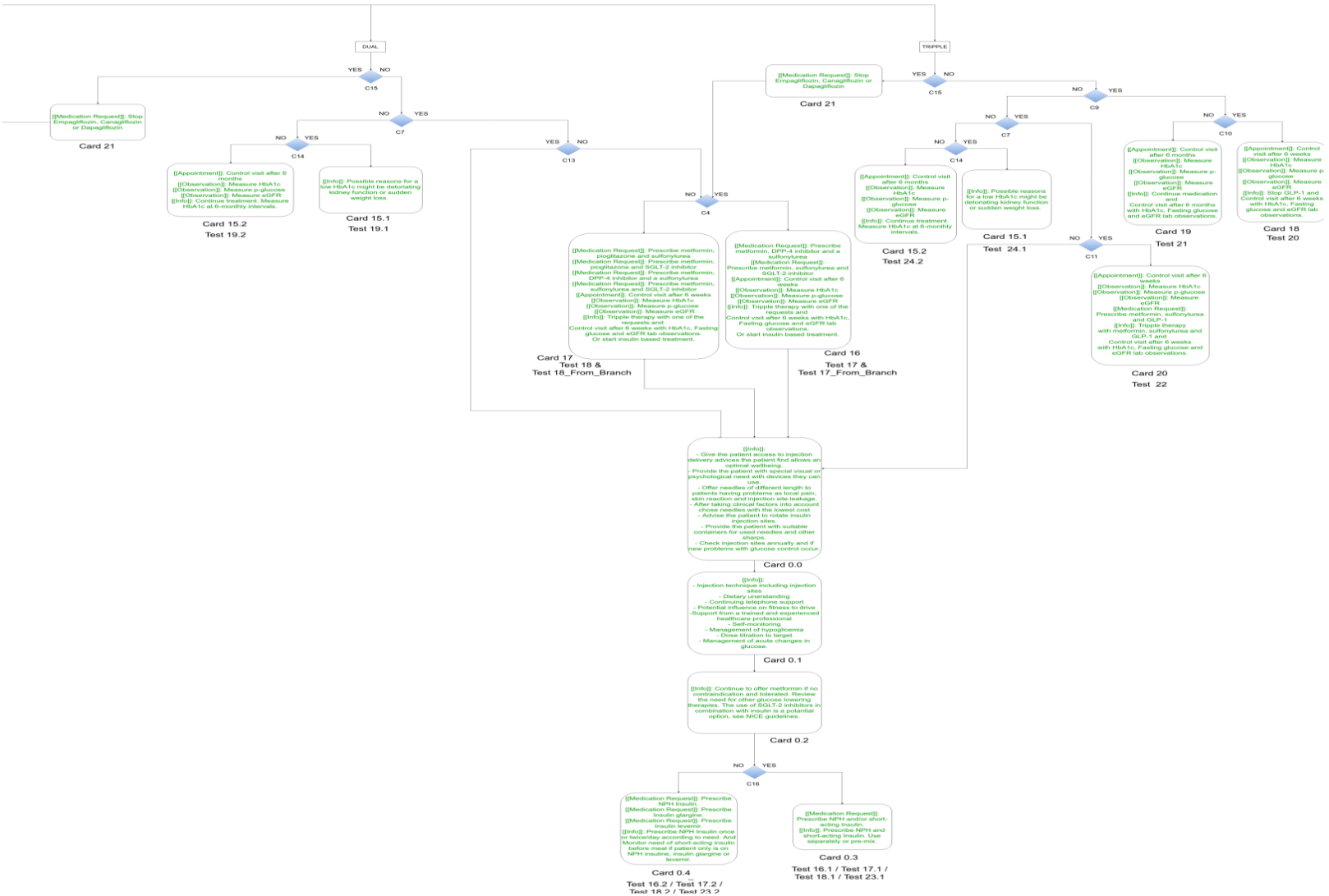

Figure A1. 6: Second part of the Initial Drug treatment & First and second intensification of drug treatment flowchart

Table AI. 15: Condition Table

Condition No	Condition Clause
C0	Which therapy does the patient follow? **A) Single** (Only one of the following metformin, DPP-4 inhibitor or piodlitazone or Sulfonylurea, or Empagliflozin, Canagliflozin or Dapagliflozin) **B) Dual** (metformin AND pioglitazone) OR (metformin AND sulfonylurea) OR (metformin AND DPP4) OR (metformin AND SGLT2) OR (DPP4 AND pioglitazone) OR (DPP4 AND sulfonylurea) OR (pioglitazone AND sulfonylurea) OR (metformin AND Empagliflozin) OR (metformin AND Canagliflozin) OR (metformin AND Dapagliflozin) OR (DPP4 AND Empagliflozin) OR (DPP4 AND Canagliflozin) OR (DPP4 AND Dapagliflozin) OR (pioglitazone AND Empagliflozin) OR (pioglitazone AND Canagliflozin) OR (pioglitazone AND Dapagliflozin) OR (sulfonylurea AND Empagliflozin) OR (sulfonylurea AND Canagliflozin) OR (sulfonylurea AND Dapagliflozin) OR (GLP1 AND Empagliflozin) OR (GLP1 AND Canagliflozin) OR (GLP1 AND Dapagliflozin) OR (Insulin AND Empagliflozin) OR (Insulin AND Canagliflozin) OR (Insulin AND Dapagliflozin) (Metformin AND Insulin) OR (Metformin AND GLP1) OR (pioglitazone AND SGLT2) OR (pioglitazone AND GLP1) OR (pioglitazone AND Insulin) OR (sulfonylurea AND SGLT2) OR (sulfonylurea AND GLP1) OR (sulfonylurea AND Insulin) OR (DPP4 AND SGLT2) OR (GLP1 AND SGLT2) OR (GLP1 AND Insulin) OR (Insulin AND SGLT2) OR (Insulin AND DPP4) **C) Tripple** (metformin AND pioglitazone AND sulfonylurea) OR (metformin AND pioglitazone AND SGLT2) OR (metformin AND DPP4 AND sulfonylurea) OR (metformin AND sulfonylurea AND SGLT2) OR (metformin AND sulfonylurea AND GLP1) (metformin AND pioglitazone AND Empagliflozin) OR (metformin AND pioglitazone AND Canagliflozin) OR (metformin AND pioglitazone AND Dapagliflozin) OR (metformin AND DPP4 AND Empagliflozin) OR (metformin AND DPP4 AND Canagliflozin) OR (metformin AND DPP4 AND Dapagliflozin) OR

	(metformin AND sulfonylurea AND Empagliflozin) OR (metformin AND sulfonylurea AND Canagliflozin) OR (metformin AND sulfonylurea AND Dapagliflozin) OR (DPP4 AND pioglitazone AND Empagliflozin) OR (DPP4 AND pioglitazone AND Canagliflozin) OR (DPP4 AND pioglitazone AND Dapagliflozin) OR (DPP4 AND sulfonylurea AND Empagliflozin) OR (DPP4 AND sulfonylurea AND Canagliflozin) OR (DPP4 AND sulfonylurea AND Dapagliflozin) OR (pioglitazone AND sulfonylurea AND Empagliflozin) OR (pioglitazone AND sulfonylurea AND Canagliflozin) OR (pioglitazone AND sulfonylurea AND Dapagliflozin) OR (Metformin AND Insulin AND Empagliflozin) OR (Metformin AND Insulin AND Canagliflozin) OR (Metformin AND Insulin AND Dapagliflozin) OR (Metformin AND GLP1 AND Empagliflozin) OR (Metformin AND GLP1 AND Canagliflozin) OR (Metformin AND GLP1 AND Dapagliflozin) OR (pioglitazone AND GLP1 AND Empagliflozin) OR (pioglitazone AND GLP1 AND Canagliflozin) OR (pioglitazone AND GLP1 AND Dapagliflozin) OR (pioglitazone AND Insulin AND Empagliflozin) OR (pioglitazone AND Insulin AND Canagliflozin) OR (pioglitazone AND Insulin AND Dapagliflozin) OR (sulfonylurea AND GLP1 AND Empagliflozin) OR (sulfonylurea AND GLP1 AND Canagliflozin) OR (sulfonylurea AND GLP1 AND Dapagliflozin) OR (sulfonylurea AND Insulin AND Empagliflozin) OR (sulfonylurea AND Insulin AND Canagliflozin) OR (sulfonylurea AND Insulin AND Dapagliflozin) OR (GLP1 AND Insulin AND Empagliflozin) OR (GLP1 AND Insulin AND Canagliflozin) OR (GLP1 AND Insulin AND Dapagliflozin) OR (Insulin AND DPP4 AND Empagliflozin) OR (Insulin AND DPP4 AND Canagliflozin) OR (Insulin AND DPP4 AND Dapagliflozin)
C1	Check symptomatic hyperglicemia diagnosis (Ketoacidotic coma in type II diabetes mellitus (disorder) OR Hyperosmolar non-ketotic state in type 2 diabetes mellitus (disorder)) (Most patients are not hospitalized and thus questions to doctor and patient are needed)

C2	Check if metformin is contraindicated. If one of the following conditions exists, metformin is unsuitable. -Allergy to metformin (A10BA02), -eGFR <30 ml/min/1.73m2 , -Severe cardiac failure (already a contraindication for C3-Cloud), -Alcoholism with complications (Alcoholic liver damage (disorder), Alcohol induced disorder co-occurrent and due to alcohol dependence (disorder))
C3	If the patient uses two of the following medications -DPP-4 -Pioglitazone -Sulfonylurea
C4	Check if one of the following conditions exists; -Cardiac Failure -Hepatic Impairment -Diabetic Ketocodosis -Bladder cancer -Uninvestigated macroscopic hematuria
C5	Check eGFR>45 (33914-3 (LOINC))
C6	Is the patient on metformin ?
C7	Check HbA1c>HbA1C Target (4548-4 (LOINC))
C8	Sulfonylurea contraindicated or not tolerated if the patient has one of the followings; -Drug: C02KX01. -Drug allergy (Sulfonylureas (A10BB)) -eGFR < 30 (33914-3 (LOINC)) -Malnutrition -Liver insufficiency (Hepatic coma due to alcoholic liver failure (disorder) OR Hepatic failure (disorder)) -Underweight with a BMI < 18.5. Or significant risk of hypoglycemia if the patient has a diagnosis (Hypoglycemia due to type 2 diabetes mellitus (disorder) OR Coma associated with diabetes mellitus (disorder)).
C9	If the patient uses the following medications -Metformin (A10BA02) -Sulfonylureas (Start with A10BB) -GLP-1 (Start with A10BJ)
C10	If there is a reduction of >=11mmol/mol and/or a weight reduction of >=3% in 6 months
C11	Check if one of the following conditions exists: - BMI>35 - Arthrosis in hip - Arthrosis in knee - Schizophrenia and other psychosis

C12	If patient using metformin have 30<=eGFR<=45 (33914-3 (LOINC))
C13	If the patient uses the following medications [Metformin (A10BA02) & SGLT-2 inhibitor (Start with A10BK)] OR [DPP-4 Inhibitor and pioglitazone] OR [Pioglitazone and sulfonylurea] OR [DPP-4 inhibitor and Sulfonylurea]
C14	If the Patient has a sudden weight loss or (has an eGFR result less than or equal to 45 or an annual chance in eGFR (ml/min/1.73m2) exceeding 5%)
C15	If the patient is using one of the following medications (Empagliflozin, Canagliflozin or Dapagliflozin) AND eGFR<45
C16	Check HbA1c >= 75 mmol/mol (4548-4 (LOINC))
C17	Is one of the SGLT-2 inhibitors used? If used, which one of them? (Dapagliflozin, Canagliflozin or Empagliflozin)

Table AI. 16: Clinical concepts to be processed by this CDS Service (Blood Glucose Management)

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 diabetes	Input
	Symptomatic hyperglycemia	Input
	Alcoholism	Input
	Cardiac Failure	Input
	Hepatic Impairment	Input
	Liver Insufficiency	Input
	Diabetic Ketocodosis	Input
	Bladder cancer	Input
	Uninvestigated macroscopic hematuria	Input
	Malnutrition	Input
	Arthrosis in hip	Input
	Arthrosis in knee	Input
	Schizophrenia and other psychosis	Input
	Significant risk of hypoglycemia	Input
Medications	Metformin	Input & Output
	Pioglitazone	Input & Output
	Sulfonylureas	Input & Output
	DPP4 inhibitor	Input & Output
	GLP-1	Input & Output
	SGLT-2 inhibitor	Input & Output
	Dapagliflozin	Input & Output
	Canagliflozin	Input & Output

	Empagliflozin	Input & Output
	Insulin	Input & Output
Lab Results	eGFR	Input & Output
	HbA1C	Input & Output
	Fasting Glucose	Output
Observations	Weight	Input
	BMI	Input

1.4.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDSHooks terminology) presented in Table AI. 17.

Table AI. 17: Prefetch Terms as input to Blood Glucose Management CDS Service

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	- Type 2 diabetes - Symptomatic hyperglycemia - Alcoholism - Cardiac Failure - Hepatic Impairment - Liver Insufficiency - Diabetic Ketocodosis - Bladder cancer - Uninvestigated macroscopic hematuria - Malnutrition - Arthrosis in hip - Arthrosis in knee - Schizophrenia and other psychosis - Significant risk of hypoglycemia
medications	All medications used by the patient	- Metformin - Pioglitazone - Sulfonylureas - DPP4 inhibitor - GLP-1 - SGLT-2 inhibitor - Dapagliflozin - Canagliflozin - Empagliflozin - Insulin
allergies	Allergies of the patient	- Metformin - Sulfonylureas
egfr	eGFR observation lab result	eGFR value
hba1c	HbA1c observation lab result	HbA1c value
bmi	BMI observation	BMI measurement result

weight	weight observation	Weight
hba1c_target	HbA1c target for goals	HbA1c target value

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in Figure A1. 5 and Figure A1. 6, to produce the Cards listed in Table AI. 18.

Table AI. 18: Cards to be produced by Blood Glucose Management CDS Service

CARD 0.0	
summary	- Give the patient access to injection delivery advices the patient find allows an optimal wellbeing. - Provide the patient with special visual or psychological need with devices they can use. - Offer needles of different length to patients having problems as local pain, skin reaction and injection site leakage. - After taking clinical factors into account chose needles with the lowest cost. - Advise the patient to rotate insulin injection sites. - Provide the patient with suitable containers for used needles and other sharps. - Check injection sites annually and if new problems with glucose control occur.
Detailed description	- Give the patient access to injection delivery advices the patient find allows an optimal wellbeing. - Provide the patient with special visual or psychological need with devices they can use. - Offer needles of different length to patients having problems as local pain, skin reaction and injection site leakage. - After taking clinical factors into account chose needles with the lowest cost. - Advise the patient to rotate insulin injection sites. - Provide the patient with suitable containers for used needles and other sharps. - Check injection sites annually and if new problems with glucose control occur.
source	NICE diabetes guideline Chapter 1.6.38 [48, pp. 26] https://www.nice.org.uk/guidance/ng28
CARD 0.1	
summary	- Injection technique including injection sites. - Dietary unerstanding. - Continuing telephone support. - Potential influence on fitness to drive. - Support from a trained and experienced healthcare professional. - Self. - monitoring. - Management of hypoglicemia. - Dose titration to target. - Management of acute changes in glucose.
Detailed description	- Injection technique including injection sites. - Dietary unerstanding. - Continuing telephone support. - Potential influence on fitness to drive. - Support from a trained and experienced healthcare professional. - Self. - monitoring. - Management of hypoglicemia. - Dose titration to target. - Management of acute changes in glucose.
source	NICE diabetes guideline, Chapter 1.6.32-1.6.37 [48, pp. 24-26]

	https://www.nice.org.uk/guidance/ng28	
CARD 0.2		
summary	Continue to offer metformin if no contraindication and tolerated. Review the need for other glucose lowering therapies. The use of SGLT-2 inhibitors in combination with insulin is a potantial option, see NICE guidelines.	
Detailed description	Continue to offer metformin if no contraindication and tolerated. Review the need for other glucose lowering therapies. The use of SGLT-2 inhibitors in combination with insulin is a potantial option, see NICE guidelines.	
source	NICE diabetes guideline, Chapter 1.6.32-1.6.37 [48, pp. 24-26] https://www.nice.org.uk/guidance/ng28	
CARD 0.3		
summary	Consider starting with NPH and short-acting insulin (separately or pre-mix), Because HbA1c>=75.	
Detailed description	Consider starting with NPH and short-acting insulin (separately or pre-mix), Because HbA1c>=75.	
source	NICE diabetes guideline, Chapter 1.6.32-1.6.37 [48, pp. 24-26] https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe NPH insulin
	Description	Prescribe NPH insulin
	Medication Code	A10AC01, NPH intermediate-acting insulin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe short-acting insulin
	Description	Prescribe short-acting insulin
	Medication Code	A10AB01, short-acting insulin, ATC
	Dosage Text	-
CARD 0.4		
summary	Prescribe NPH Insulin once or twice/day according to need or prescribe insulin glargine or insulin detemir. And Monitor need of short-acting insulin before meal if patient only is on NPH insuline, insulin glargine or detemir(levemir).	
Detailed description	Prescribe NPH Insulin once or twice/day according to need or prescribe insulin glargine or insulin detemir. And Monitor need of short-acting insulin before meal if patient only is on NPH insuline, insulin glargine or detemir(levemir).	
source	NICE diabetes guideline, Chapter 1.6.32-1.6.37 [48, pp. 24-26]	

	https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe NPH insulin
	Description	Prescribe NPH insulin
	Medication Code	A10AC01, NPH intermediate-acting insulin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe insulin glargine
	Description	Prescribe insulin glargine
	Medication Code	A10AE04, insulin glargine, ATC
	Dosage Text	-
Medication Request	Title	Prescribe insulin detemir
	Description	Prescribe insulin detemir
	Medication Code	A10AE05, insulin detemir, ATC
	Dosage Text	-
CARD 1		
summary	Prescribe sulfonylurea with observations and an appointment or start insulin based treatment.	
Detailed description	Prescribe sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations. Or start insulin based treatment.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation

	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 2		
summary	Single therapy with DPP4 inhibitor or sulfonylurea.	
Detailed description	Prescribe DPP4 inhibitor or sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-

Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC

	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 3		
summary	Single therapy with DPP4 inhibitor or pioglitazone or sulfonylurea.	
Detailed description	Prescribe DPP4 inhibitor or pioglitazone or sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation

	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit

	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit

	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 4		
summary	Single therapy with metformin.	
Detailed description	Prescribe metformin 500mg twice a day. Gradually increase the dose to reach this dose (1000mg). Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Metformin recommendation
	Description	Prescribe metformin 500mg twice a day
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	Metformin 500mg twice a day
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT

Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 5		
summary	- If need of two oral glucose-lowering drugs and NPH insulin twice daily, then consider to use insulin glargine or levemir instead of NPH insulin. And Monitor need of short-acting insulin before meal if patient only is on insulin glargine or levemir. - Else continue medication and monitor need of short-acting insulin before meal if patient only is on NPH insulin.	
Detailed description	- If need of two oral glucose-lowering drugs and NPH insulin twice daily, then consider to use insulin glargine or levemir instead of NPH insulin. And Monitor need of short-acting insulin before meal if patient only is on insulin glargine or levemir. - Else continue medication and monitor need of short-acting insulin before meal if patient only is on NPH insulin.	
source	NICE diabetes guideline Chapter 1.6.38 [48, pp. 26]. https://www.nice.org.uk/guidance/ng28	
CARD 6		
summary	Stop Metformin. Single therapy with DPP4 inhibitor or sulfonylurea.	
Detailed description	Stop Metformin and prescribe DPP4 inhibitor or sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Stop Metformin
	Description	Stop Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).

	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Stop Metformin
	Description	Stop Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).

	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 7		
summary	Stop Metformin and Single therapy with DPP4 inhibitor or pioglitazone or sulfonylurea.	
Detailed description	Stop Metformin and Prescribe DPP4 inhibitor or pioglitazone or sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Stop Metformin
	Description	Stop Metformin
	Medication Code	A10BA02, Metformin, ATC

	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Stop Metformin
	Description	Stop Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-

Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC

	performer	PATIENT
Suggestion 3		
Medication Request	Title	Stop Metformin
	Description	Stop Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT

CARD 8		
summary	Reduce the dose of metformin.	
Detailed description	Reduce the dose of metformin. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Reduce the dose of Metformin
	Description	Reduce the dose of Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC

	performer	PATIENT
CARD 9		
summary	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and SGLT-2.	
Detailed description	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and SGLT-2. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC

	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe SGLT-2 inhibitor
	Description	Prescribe SGLT-2 inhibitor
	Medication Code	A10BK, SGLT-2 inhibitors, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT

Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 10		
summary	Dual therapy with Metformin and pioglitazone or Metformin and DPP-4 inhibitor.	
Detailed description	Dual therapy with Metformin and pioglitazone or Metformin and DPP-4 inhibitor. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC

	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT

Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 11		
summary	Dual therapy with Metformin and sulfonylurea or Metformin and DPP-4 inhibitor.	
Detailed description	Dual therapy with Metformin and sulfonylurea or Metformin and DPP-4 inhibitor. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)

	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-

Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 12		
summary	Dual therapy with Metformin and pioglitazone or Metformin and sulfonylurea or Metformin and DPP-4 inhibitor.	
Detailed description	Dual therapy with Metformin and pioglitazone or Metformin and sulfonylurea or Metformin and DPP-4 inhibitor. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-

Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin

	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC

	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 13		
summary	Dual therapy with DPP-4 inhibitor and Sulfonylurea.	
Detailed description	Dual therapy with DPP-4 inhibitor and Sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24].	

	https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT

CARD 14		
summary	Dual therapy with DPP-4 inhibitor and pioglitazone or pioglitazone and sulfonylurea or DPP-4 inhibitor and sulfonylurea.	
Detailed description	Dual therapy with DPP-4 inhibitor and pioglitazone or pioglitazone and sulfonylurea or DPP-4 inhibitor and sulfonylurea. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT

Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation

	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 15.1		
summary	Possible reasons for a low HbA1c might be detoriating kidney function or sudden weight loss.	
Detailed description	Possible reasons for a low HbA1c might be detoriating kidney function or sudden weight loss.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
CARD 15.2		
summary	Continue treatment.	
Detailed description	Continue treatment. Measure HbA1c at 6-monthly intervals.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 months).
	Description	Control visit after these initial treatments (After 6 months).
	Status	Proposed
	start	(Date + 6 months)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation

	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 16		
summary	Tripple therapy with Metformin-DPP4-sulfonylurea or Metformin-sulfonylurea-SGLT2. Or Start insulin based treatment.	
Detailed description	Tripple therapy with Metformin-DPP4-sulfonylurea or Metformin-sulfonylurea-SGLT2. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations. Or Start insulin based treatment.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed

	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Medication Request	Title	Prescribe SGLT-2 inhibitor
	Description	Prescribe SGLT-2 inhibitor
	Medication Code	A10BK, SGLT-2 inhibitors, ATC
	Dosage Text	-

Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 17		
summary	Tripple therapy with Metformin-pioglitazone-sulfonylurea or Metformin-pioglitazone-SGLT2 or Metformin-DPP4-sulfonylurea or Metformin-sulfonylurea-SGLT2. Or Start insulin based treatment	
Detailed description	Tripple therapy with Metformin-pioglitazone-sulfonylurea or Metformin-pioglitazone-SGLT2 or Metformin-DPP4-sulfonylurea or Metformin-sulfonylurea-SGLT2. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations. Or Start insulin based treatment.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		

Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation

	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe pioglitazone
	Description	Prescribe pioglitazone
	Medication Code	A10BG03, Pioglitazone, ATC
	Dosage Text	-
Medication Request	Title	Prescribe SGLT-2 inhibitor
	Description	Prescribe SGLT-2 inhibitor
	Medication Code	A10BK, SGLT-2 inhibitors, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT

Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit

	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 4		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Medication Request	Title	Prescribe SGLT-2 inhibitor
	Description	Prescribe SGLT-2 inhibitor
	Medication Code	A10BK, SGLT-2 inhibitors, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC

	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 18		
summary	Stop GLP-1	
Detailed description	Stop GLP-1 and Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Stop GLP-1 Mimetic
	Description	Stop GLP-1 Mimetic
	Medication Code	A10BJ, Glucagon-like peptide-1 (GLP-1) analogues, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation

	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 19		
summary	Continue medication	
Detailed description	Continue medication and Control visit after 6 months with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 months).
	Description	Control visit after these initial treatments (After 6 months).
	Status	Proposed
	start	(Date + 6 months)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT

Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 20		
summary	Tripple therapy with Metformin-sulfonylurea-GLP1.	
Detailed description	Tripple therapy with Metformin-sulfonylurea-GLP1. Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Sulfonylurea
	Description	Prescribe Sulfonylurea
	Medication Code	A10BB, Sulfonylureas, ATC
	Dosage Text	-
Medication Request	Title	Prescribe GLP-1 Mimetic
	Description	Prescribe GLP-1 Mimetic
	Medication Code	A10BJ, Glucagon-like peptide-1 (GLP-1) analogues, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).

	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 21		
summary	Stop Empagliflozin, Canagliflozin or Dapagliflozin	
Detailed description	Stop Empagliflozin, Canagliflozin or Dapagliflozin	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Stop Empagliflozin.
	Description	Stop Empagliflozin.
	Medication Code	A10BK03, empagliflozin, ATC
	Dosage Text	-
Suggestion 2		

Medication Request	Title	Stop Canagliflozin
	Description	Stop Canagliflozin
	Medication Code	A10BK02, canagliflozin , ATC
	Dosage Text	-
Suggestion 3		
Medication Request	Title	Stop Dapagliflozin.
	Description	Stop Dapagliflozin.
	Medication Code	A10BK01, dapagliflozin, ATC
	Dosage Text	-
CARD 9_1		
summary	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and Canagliflozin (as SGLT2 inhibitor) or Metformin and Empagliflozin (as SGLT2 inhibitor)	
Detailed description	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and Canagliflozin (as SGLT2 inhibitor) or Metformin and Empagliflozin (as SGLT2 inhibitor). Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (after 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-

Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Canagliflozin
	Description	Prescribe Canagliflozin
	Medication Code	A10BK02, canagliflozin, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation

	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Empagliflozin
	Description	Prescribe Empagliflozin
	Medication Code	A10BK03, empagliflozin, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit

	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 9_2		
summary	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and Dapagliflozin (as SGLT2 inhibitor) or Metformin and Empagliflozin (as SGLT2 inhibitor)	
Detailed description	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and Dapagliflozin (as SGLT2 inhibitor) or Metformin and Empagliflozin (as SGLT2 inhibitor). Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-

Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Dapagliflozin
	Description	Prescribe Dapagliflozin
	Medication Code	A10BK01, dapagliflozin, ATC
	Dosage Text	-

Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Empagliflozin
	Description	Prescribe Empagliflozin
	Medication Code	A10BK03, empagliflozin, ATC
	Dosage Text	-

Appointment	Title	Control Visit Appointment after these initial treatments (after 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
CARD 9_3		
summary	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and Dapagliflozin (as SGLT2 inhibitor) or Metformin and Canagliflozin (as SGLT2 inhibitor)	
Detailed description	Dual therapy with Metformin and DPP-4 inhibitor or Metformin and Dapagliflozin (as SGLT2 inhibitor) or Metformin and Canagliflozin (as SGLT2 inhibitor). Control visit after 6 weeks with HbA1c, Fasting Glucose and eGFR lab observations.	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		

Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe DPP-4 inhibitor
	Description	Prescribe DPP-4 inhibitor
	Medication Code	A10BH, DPP-4 inhibitor, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (after 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 2		
Medication Request	Title	Prescribe Metformin

	Description	Prescribe Metformin
	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Dapagliflozin
	Description	Prescribe Dapagliflozin
	Medication Code	A10BK01, dapagliflozin, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (After 6 weeks).
	Description	Control visit after these initial treatments (After 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT
Suggestion 3		
Medication Request	Title	Prescribe Metformin
	Description	Prescribe Metformin

	Medication Code	A10BA02, Metformin, ATC
	Dosage Text	-
Medication Request	Title	Prescribe Canagliflozin
	Description	Prescribe Canagliflozin
	Medication Code	A10BK02, canagliflozin, ATC
	Dosage Text	-
Appointment	Title	Control Visit Appointment after these initial treatments (after 6 weeks).
	Description	Control visit after these initial treatments (after 6 weeks).
	Status	Proposed
	start	(Date + 6 weeks)
	specialty	-
Activity	Title	HbA1C Observation
	Description	Have HbA1C test before the control visit
	Category	Observation
	Code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood, LOINC
	performer	PATIENT
Activity	Title	Fasting Glucose Observation
	Description	Have Fasting Glucose test before the control visit
	Category	Observation
	Code	1558-6, Fasting Glucose, LOINC
	performer	PATIENT
Activity	Title	eGFR Observation
	Description	Have eGFR test before the control visit
	Category	Observation
	Code	33914-3, Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum or Plasma by Creatinine-based formula, LOINC
	performer	PATIENT

1.5.Diabetic Foot Problem (Flowchart 5.2.15)

This flowchart is based on the NICE diabetes guideline, Chapter 1.7.11 [48, p. 28].

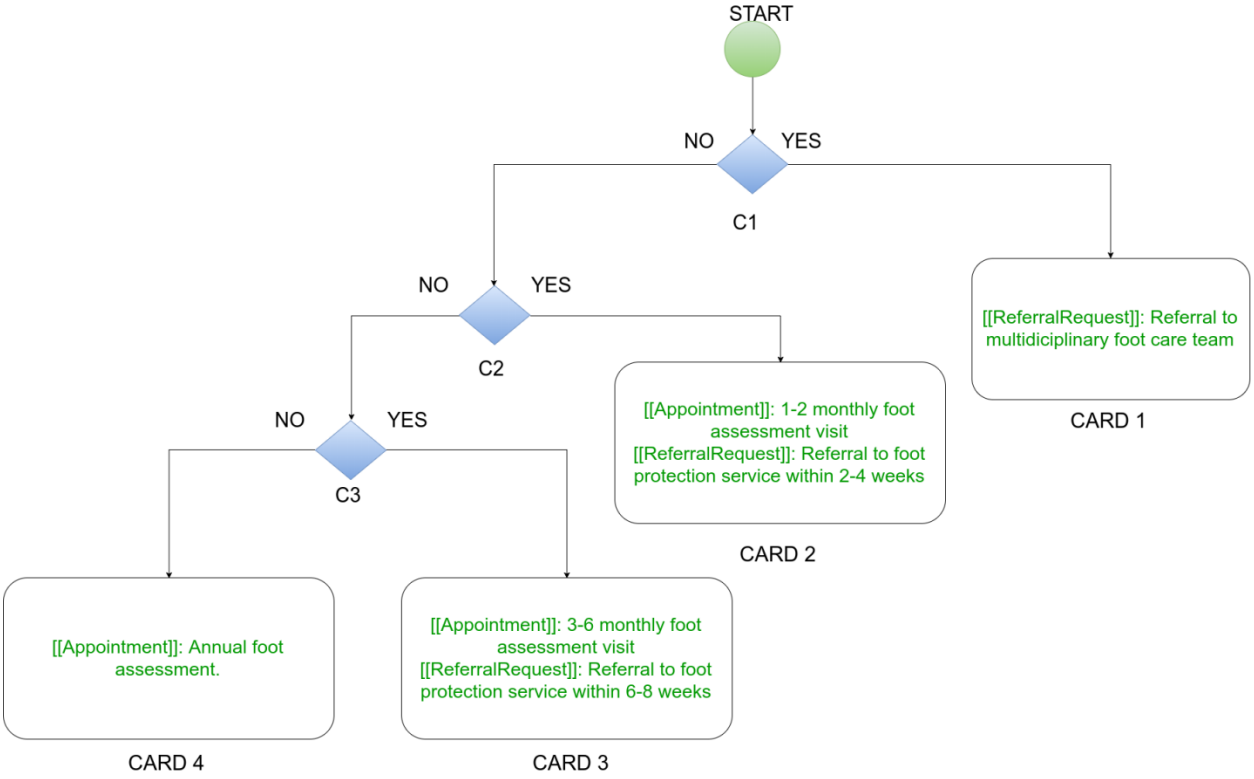

Figure A1. 7: Diabetic Foot Problem flowchart

Table AI. 19: Condition Table

Condition No	Condition Clause
C1	If one of the following conditions exists: Ulceration(L97), spreading infection(-), critical limb ischaemia(-), gangrene(I96), Suspicion of an acute arthropathy(M12)
C2	If one of the following conditions exists: Previous Ulceration therapy(D03), amputation(Z89), renal replacement threapy(714749008), or the combination of neurophaty(G90) and non-critical limb ischaemia(-), or the combination of neurophaty(G90) and callus of limb(L84) and/or deformity of limb(M21) or the combination of non-critical limb ischaemia(-) and callus of limb(L84) and/or deformity of limb(M21).
C3	If one of the following conditions exists: neurophaty(G90), deformity of limb(M21), non-critical limb ischaemia(-).

Table AI. 20: Clinical concepts to be processed by this CDS Service (Foot Problem Management)

Category	*Concept*	*Input / Output (Cards)*
Conditions	Ulceration of limb	Input
	Spreading infection in limbs	Input
	Critical limb ischemia	Input
	Non-critical limb ischemia	Input
	Gangrene	Input
	Suspicion of acute arthropathy	Input
	Neuropathy	Input
	Callus of limb	Input
	Deformity of limbs	Input
	Ulceration therapy	Input
	Renal replacement therapy	Input

1.5.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDS Hooks terminology) presented in Table AI. 21.

Table AI. 21: Prefetch Terms as input to Foot Problem Management CDS Service

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	- Ulceration of limb - Spreading infection in limbs - Critical limb ischemia - Non-critical limb ischemia - Gangrene - Suspicion of acute arthropathy - Neuropathy - Callus of limb

		- Deformity of limbs - Ulceration therapy - Renal replacement therapy

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in Figure AI. 7**Error! Reference source not found.**, to produce the Cards listed in Table AI. 22.

Table AI. 22: Cards to be produced by Foot Problem Management CDS Service

CARD 1		
summary	Referral to a multidisciplinary foot care team	
Detailed description	Referral to a multidisciplinary foot care team	
source	NICE Diabetic foot problems: prevention and management Chapter 1.7.11 [48, p. 28] https://www.nice.org.uk/guidance/ng19	
Suggestion 1		
Referral Request	Title	Referral to a multidisciplinary foot care team
	Description	Referral to a multidisciplinary foot care team
	status	draft
	specialty	408288004, Refer to multidisciplinary foot care team, SNOMED
CARD 2		
summary	Referral to foot protection service within 2-4 weeks and 1 to 2 monthly foot assessment visit	
Detailed description	Referral to foot protection service within 2-4 weeks and 1 to 2 monthly foot assessment visit	
source	NICE Diabetic foot problems: prevention and management Chapter 1.7.11 [48, p. 28] https://www.nice.org.uk/guidance/ng19	
Suggestion 1		
Referral Request	Title	Referral to footcare protection program
	Description	Referral to footcare protection program
	status	draft
	specialty	408286000, Referral to footcare protection program, SNOMED
Appointment	Title	Appointment for 1 to 2 monthly foot assessment visit
	Description	Appointment for 1 to 2 monthly foot assessment visit
	Status	Proposed

	start	(Date + 6 weeks)
	specialty	-
CARD 3		
summary	Referral to foot protection service within 6-8 weeks and 3 to 6 monthly foot assessment visit	
Detailed description	Referral to foot protection service within 6-8 weeks and 3 to 6 monthly foot assessment visit	
source	NICE Diabetic foot problems: prevention and management Chapter 1.7.11 [48, p. 28] https://www.nice.org.uk/guidance/ng19	
Suggestion 1		
Referral Request	Title	Referral to footcare protection program
	Description	Referral to footcare protection program
	status	draft
	specialty	408286000, Referral to footcare protection program, SNOMED
Appointment	Title	Appointment for 3 to 6 monthly foot assessment visit
	Description	Appointment for 3 to 6 monthly foot assessment visit
	Status	Proposed
	start	(Date + 3 months)
	specialty	-
CARD 4		
summary	Appointment for annual control visit	
Detailed description	Appointment for annual control visit	
source	NICE Diabetic foot problems: prevention and management Chapter 1.7.11 [48, p. 28] https://www.nice.org.uk/guidance/ng19	
Suggestion 1		
Appointment	Title	Appointment for annual control visit
	Description	Appointment for annual control visit
	Status	Proposed
	start	(Date + 1 year)
	specialty	-

1.6. Diet Management (Flowchart 5.2.2 & Flowchart 5.4.4)

Previously this was planned to be handled within Care Plan Template as it is a fixed diet for Diabetes patients. However, after the Diabetes & RF Reconciliation rules are reviewed (please see Table AI. 23), we decided that it is needed to implement it as a separate CDSM, as the diet to be suggested is conditional to the diagnosis of the patient.

This flowchart is based on the NICE diabetes guideline, Chapter 1.3 [48, pp. 13–14] and on the NICE CKD guideline CG182, Chapter 1.4.6-1.4.9 [60, pp. 29–30] and Osakidetza Clinical guideline and Renal Failure pathway (as advised by reconciliation rules).

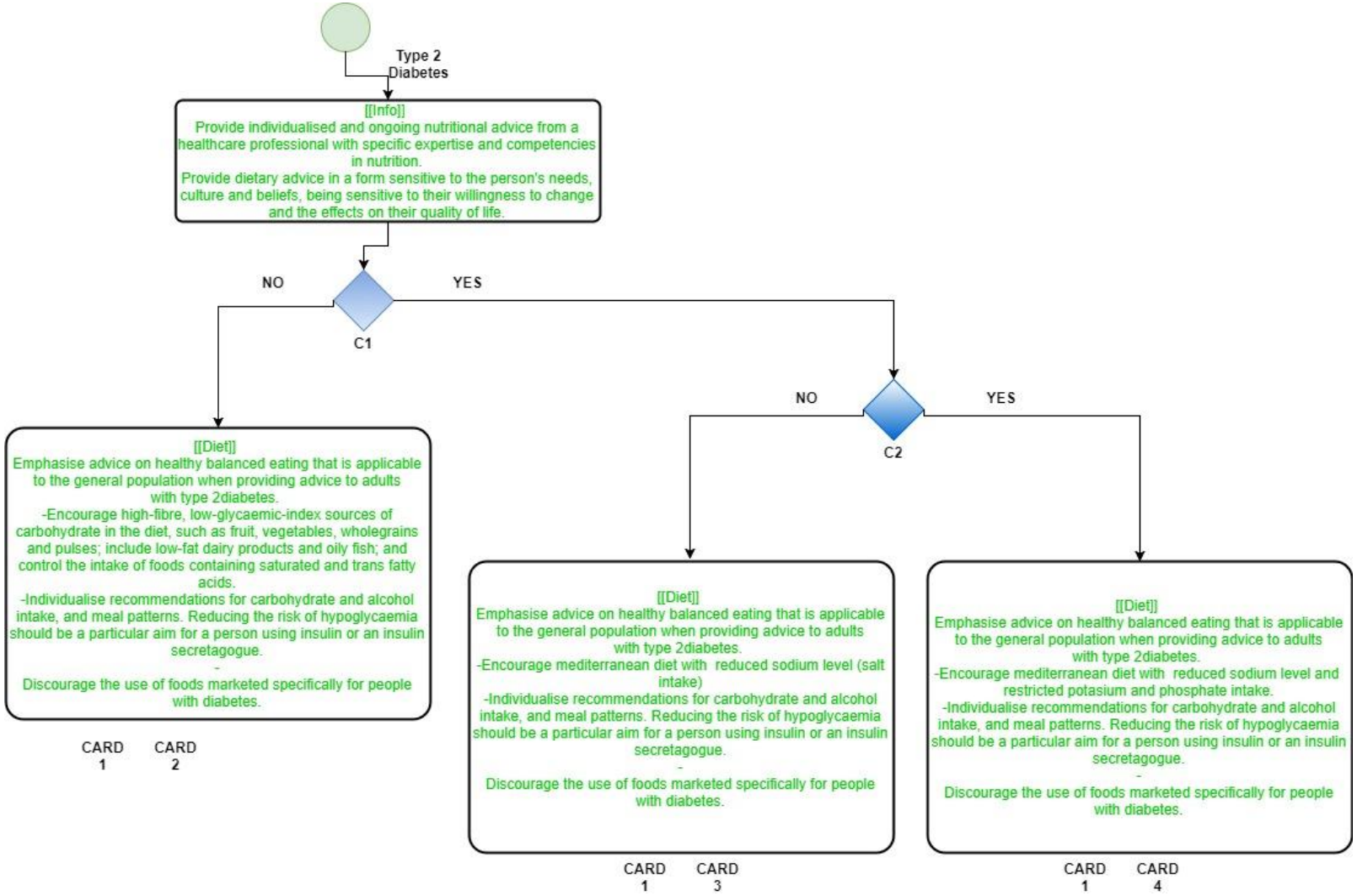

Figure A1. 8: Diet Management Flowchart

Table AI. 23: DM-RF Reconciliation Rules for the "Diet Management"

Rule	Context	Purpose	Description of the purpose	Type of purpose	Clinical condition	Concept / codes	Rule description	Trigger	Input	Output	Reference
Rule3	Reconciling dietary recommendations in comorbidity	Disease-Disease interaction Dietary recommendations in the presence of diabetes and RF	Patients with Diabetes and Renal Failure (stages 2 and 3)	Ac_Diet	RECONCILED RULE DM+RF	ICD-10 Diabetes (RF) eGFR	IF ICD-10 Diabetes AND RF AND eGFR > 30, THEN mediterranean diet with reduced sodium level (salt intake)	Each time eGFR is required	ICD-10 EGFR	Different recommendations between stages 2-3 and 4-5	NICE Guideline DM/RF.- Figure 2 (5.2.2. Diabetes - Dietary advice)- Figure 30 (RF) Osakidetza Clinical guideline and and Renal Failure pathway
Rule 4	Reconciling dietary recommendations in comorbidity	Disease-Disease interaction (diet) Dietary recommendations when diabetes and RF	Patients with DM and RF (stages 4 and 5)	Ac_Diet	RECONCILED RULE DM+RF	ICD-10- Diabetes (RF) eGFR	IF ICD-10 Diabetes AND RF AND eGFR < 30 THEN mediterranean diet with reduced sodium level and restricted potasium and phosphate intake.	Each time eGFR is required	ICD-10 EGFR	Different recommendations between stages 2-3 and 4-5	NICE GuidelineS DM/RF.- Figure 2 (5.2.2. Diabetes - Dietary advice)- Figure 30 (RF) Osakidetza Clinical Guideline and Renal Failure pathway

In Figure A1. 8, the flowchart that can be followed to implement these rules as a CDS service is presented. In Table AI. 24, the clinical concepts that need to be processed within this flowchart are presented. Please see the accompanying Excel Sheet, which maps these clinical concepts to terminology system codes preferred by our pilot sites and CDSM service.

Table AI. 24: Clinical concepts to be processed by this CDS Service (Diet Management)

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	Renal Failure	Input
Lab Results	eGFR	Input

In Table AI. 25, the conditional clauses in the flowchart are clearly described, by referring to the clinical concepts in Table AI. 24.

Table AI. 25: Condition clauses in Diet Management Flowchart

Condition No	Condition Clause
C1	If the patient has Type 2 Diabetes & (Renal Failure diagnosis (Stage 3,4,5) or eGFR<45)
C2	If eGFR<30

1.6.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDSHooks terminology) presented in Table AI. 26.

Table AI. 26: Prefetch Terms as input to Diet Management CDS Service

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	-Type 2 Diabetes diagnosis - Renal Failure diagnosis

eGFR	Latest eGFR test as FHIR Observations	-Value of latest eGFR test

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in figure AI.8 **Error! Reference source not found.**, to produce the Cards listed in Table AI. 27.

Table AI. 27: Cards to be produced by Diet Management CDS Service

CARD 1		
summary	Personalized Diet advice	
Detailed description	-Provide individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition. -Provide dietary advice in a form sensitive to the person's needs, culture and beliefs, being sensitive to their willingness to change and the effects on their quality of life.	
source	NICE diabetes guideline, Chapter 1.3 [48, pp. 13–14]. https://www.nice.org.uk/guidance/ng28	
CARD 2		
summary	Diet Advice to adults with type 2 diabetes	
Detailed description	Diet Advice to adults with type 2 diabetes	
source	NICE diabetes guideline, Chapter 1.3 [48, pp. 13–14]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Goal:	category	Dietary, http://hl7.org/fhir/goal-category"
	Description code	385769008, Encouragement of compliance (regime/therapy), SNOMED International 2017 v1.33.2
	Description text	Comply with the dietary restrictions of type 2 diabetes and diabetes. Evaluate every 6 months.
Activity:	Title	Preparation to correctly follow the prescribed diet
	Description	• Emphasize advice on healthy balanced eating that is applicable to the general population when providing advice to adults with type 2 diabetes. • Encourage high-fibre, low-glycaemic-index sources of carbohydrate in the diet, such as fruit, vegetables, wholegrains and pulses; include low-fat dairy products and oily fish; and control the intake of foods containing saturated and trans fatty acids. • Individualise recommendations for carbohydrate and alcohol intake, and meal patterns. Reducing the risk of hypoglycaemia should be a particular aim for a person using insulin or an insulin secretagogue.

		• Discourage the use of foods marketed specifically for people with diabetes.
	Category	Diet
	Code	5614, Teaching: prescribed diet, Nursing Interventions Classification (NIC)
	performer	HP (Please note that as CDS does not know the identity of individual health professionals, but it indicates whether the activity is targeted for a HP or the PATIENT. Then in PCPDP the necessary assignments are completed by the Care plan editor, i.e. HP).
Activity:	Title	Follow the Diet
	Description	Strictly follow the Diet programme for Type 2 Diabetes patients
	Category	Diet
	Code	385769008, Encouragement of compliance (regime/therapy), SNOMED International 2017 v1.33.2
	performer	PATIENT
CARD 3		
summary	Diet Advice to adults with type 2 diabetes & Renal failure (30<GFR<45)	
Detailed description	Diet Advice to adults with type 2 diabetes: Mediterranean diet with reduced sodium level (salt intake)	
source	NICE Chronic kidney disease in adults: assessment and management CG182, Chapter 1.4.6-1.4.9 [60, pp. 29–30]. https://www.nice.org.uk/guidance/cg182 Osakidetza Clinical guideline and Renal Failure pathway	
Suggestion 1		
Goal:	category	Dietary, http://hl7.org/fhir/goal-category"
	Description code	385769008, Encouragement of compliance (regime/therapy), SNOMED International 2017 v1.33.2
	Description text	Comply with the dietary restrictions mild renal failure and diabetes. Evaluate every 6 months.
Activity:	Title	Preparation to correctly follow the prescribed diet

	Description	• Emphasize advice on healthy balanced eating that is applicable to the general population when providing advice to adults with type 2 diabetes. • Encourage Mediterranean diet with reduced sodium level (salt intake) • Individualise recommendations for carbohydrate and alcohol intake, and meal patterns. Reducing the risk of hypoglycaemia should be a particular aim for a person using insulin or an insulin secretagogue. • Discourage the use of foods marketed specifically for people with diabetes.
	Category	Diet
	Code	5614, Teaching: prescribed diet, Nursing Interventions Classification (NIC)
	performer	HP (Please note that as CDS does not know the identity of individual health professionals, but it indicates whether the activity is targeted for a HP or the PATIENT. Then in PCPDP the necessary assignments are completed by the Care plan editor, i.e. HP).
Activity:	Title	Follow the Diet
	Description	Strictly follow the Diet programme (Mediterranean diet with reduced salt intake)
	Category	Diet
	Code	385769008, Encouragement of compliance (regime/therapy), SNOMED International 2017 v1.33.2
	performer	PATIENT
CARD 4		
summary	Diet Advice to adults with type 2 diabetes & Severe Renal failure (GFR<30)	
Detailed description	Diet Advice to adults with type 2 diabetes: Encourage Mediterranean diet with reduced sodium level and restricted potassium and phosphate intake.	
source	NICE Chronic kidney disease in adults: assessment and management CG182, Chapter 1.4.6-1.4.9 [60, pp. 29–30]. https://www.nice.org.uk/guidance/cg182 Osakidetza Clinical guideline and Renal Failure pathway	
Suggestion 1		
Goal	category	Dietary, http://hl7.org/fhir/goal-category"
	Description code	385769008, Encouragement of compliance (regime/therapy), SNOMED International 2017 v1.33.2
	Description text	Comply with the dietary restrictions of renal failure and diabetes. Evaluate every 6 months.

Activity	Title	Preparation to correctly follow the prescribed diet
	Description	• Emphasize advice on healthy balanced eating that is applicable to the general population when providing advice to adults with type 2 diabetes. • Encourage Mediterranean diet with reduced sodium level and restricted potassium and phosphate intake. • Individualise recommendations for carbohydrate and alcohol intake, and meal patterns. Reducing the risk of hypoglycaemia should be a particular aim for a person using insulin or an insulin secretagogue. • Discourage the use of foods marketed specifically for people with diabetes.
	Category	Diet
	Code	5614, Teaching: prescribed diet, Nursing Interventions Classification (NIC)
	performer	HP (Please note that as CDS does not know the identity of individual health professionals, but it indicates whether the activity is targeted for a HP or the PATIENT. Then in PCPDP the necessary assignments are completed by the Care plan editor, i.e. HP).
Activity	Title	Follow the Diet
	Description	Strictly follow the Diet programme (Mediterranean diet with reduced sodium level and restricted potassium and phosphate intake)
	Category	Diet
	Code	385769008, Encouragement of compliance (regime/therapy), SNOMED International 2017 v1.33.2
	performer	PATIENT

1.7.Management of Diabetic Nephropathy (From DM-RF Reconciliation Rules)

This flowchart is based on the DM-RF Reconciliation Rules prepared by pilot sites which are presented in Table AI. 28:

Table AI. 28: DM-RF Reconciliation Rules for the "Follow up of the patient with diabetic nephropathy"

Rule	Context	Purpose	Description of the purpose	Type of purpose	Clinical condition	Concept / codes	Rule description	Trigger	Input	Output	Reference
Rule 7	Follow up of the patient with diabetic nephropathy	Disease-Disease interaction. Frequency of appointments / encounters with health care professionals	Follow up pattern for a patient with DM2 and nephopathy 1-3a	Ac_Encounter	RECONCILED RULE DM+RF	ICD-10 Diabetes; eGFR	If ICD-10 Diabetes AND eGFR >45 y < 60 THEN schedule one (1) yearly appointment with the GP and three (3) with the Nurse	Each encounter of the patient with the health care professional	eGFR and ICD-10 diabetes	Program one (1) appointment per year with the GP and three (3) appointments with Nurse per year. Appointment with the appropriated healthcare professional	NICE Figure 33 (5.4.7. Frequency of eGFR control-RF)
Rule 8	Follow up of the patient with diabetic nephropathy	Disease-Disease interaction. Frequency of appointments / encounters with health care professionals	Follow up pattern for a patient with DM2 and nephopathy 3b	Ac_Encounter	RECONCILED RULE DM+RF	ICD-10 Diabetes; eGFR	IF ICD-10 Diabetes AND eGFR <30 and <45, THEN schedule two (2) appointments per year with the GP and three (3) with the Nurse	Each encounter of the patient with the health care professional	eGFR and ICD-10 diabetes	Schedule two (2) appointment per year with the GP and three (3) per year with Nurse. Appointment with the appropriated healthcare professional	NICE Figure 33 (5.4.7. Frequency of eGFR control-RF)
Rule 9	Follow up of the patient with diabetic nephropathy	Disease-Disease interaction. Criteria for nephrology referral	Follow up pattern for a patient with DM2 and Nephopathy 3 and 4	Ac_Encounter	RECONCILED RULE DM+RF	ICD-10 Diabetes; eGFR	IF ICD-10 Diabetes AND eGFR <30, THEN referral to Nephrology	Each encounter of the patient with the health care professional	eGFR and ICD-10 diabetes	Referral to Nephrology	NICE Guideline

Rule 11	Follow up of the patient with diabetic nephropathy	Disease-Disease interaction Evaluate progression of the Chronic Kidney Disease and cardiovascular risk of the patient	Laboratory analyses and complementary tests to be performed	Ac_Observation	RECONCILED RULE DM+RF	ICD-10 Diabetes; eGFR	IF ICD-10 Diabetes and eGFR >45 and < 60 THEn schedule albumin-to-creatinin ratio,eGFR (kidney function) and HbA1c every 6 months	Each time eGFR is calculated			
Rule 12	Follow up of the patient with diabetic nephropathy	Disease-Disease interaction. Evaluate progression of Chronic Kidney Disease and Cardiovascular Risk of the patient	Laboratory analyses and complementary tests to be performed	Ac_Observation	RECONCILED RULE DM+RF	ICD-10 Diabetes; eGFR	IF ICD-10 Diabetes and eGFR >30 and < 45 THEN schedule albumin-to-creatinin ratio, eGFR (kidney function) and HbA1c measurements every 3 months	Each time eGFR is calculated	eGFR and ICD-10 diabetes	Type and frequency of lab analyses request	Osakidetza Renal Failure Pathway and Diabetes Clinical guideline
Rule 13	Follow up of the patient with diabetic nephropathy	Disease-Disease interaction. When to involve nephrologist in the follow-up	Criteria for referral to Nephrologist	Ac_Encounter	RECONCILED RULE DM+RF	ICD-10 Diabetes; Hypertension, eGFR	IF ICD-10 Diabetes AND (eGFR > 45 AND albumin-to-creatinin ratio > 300) OR (eGFR decrease ≥ 25% AND change in GFR category) OR (Refractory Hypertension) THEN considering referring to Nephrologist	Each time eGFR is calculated or Refractory Hypertension	eGFR and ICD-10 diabetes, Hypertension	Alert: referral to nephrology	Osakidetza Renal Failure Pathway and Diabetes Clinical guideline

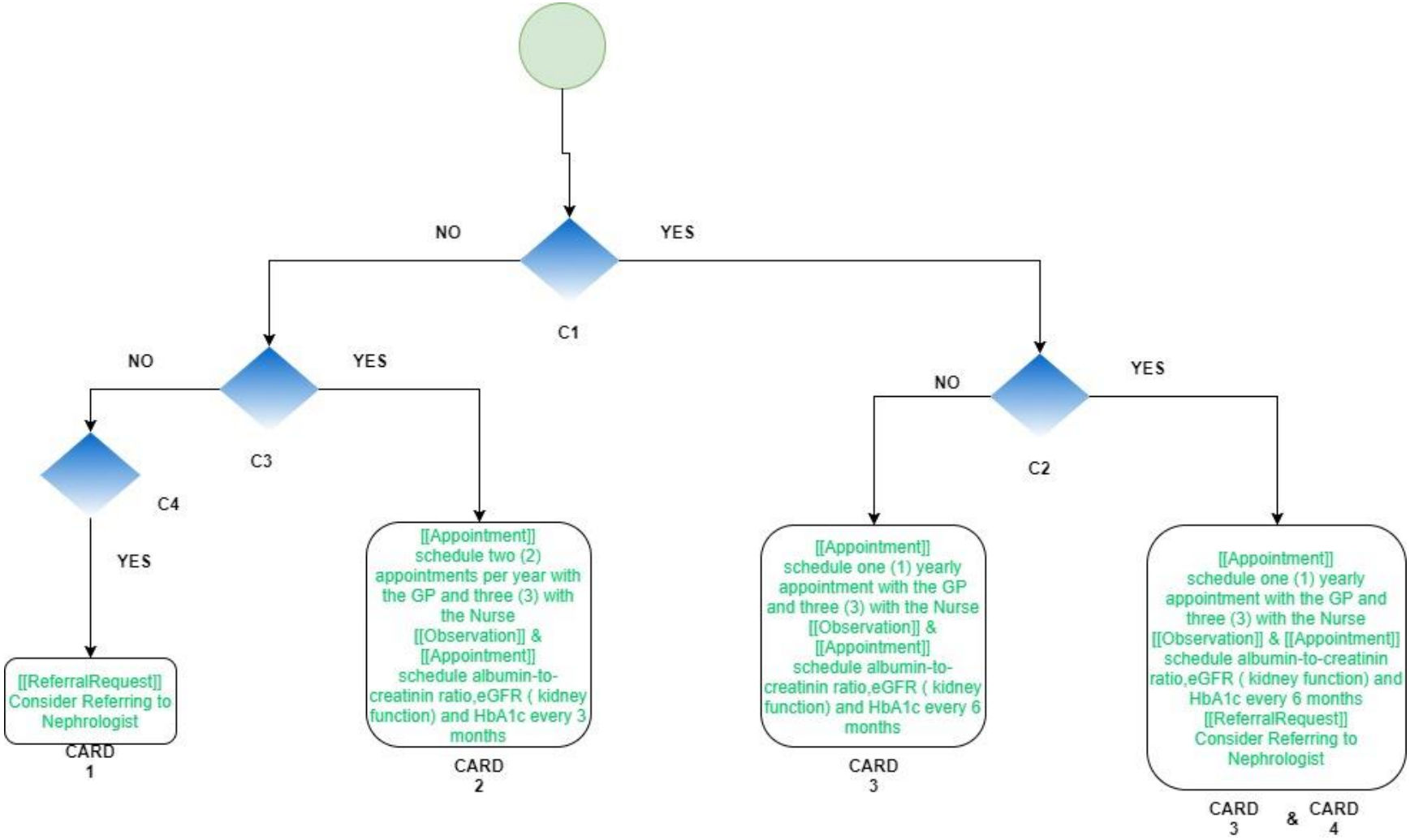

Figure A1. 9: Management of Nephropathy Flowchart

In Figure A1. 9**Error! Reference source not found.**, the flowchart that can be followed to implement these rules as a CDS service is presented. In Table AI. 29, the clinical concepts that need to be processed within this flowchart are presented. Please see the accompanying Excel Sheet, which maps these clinical concepts to terminology system codes preferred by our pilot sites and CDSM service.

Table AI. 29: Clinical concepts to be processed by this CDS Service

Category	*Concept*	*Input / Output (Cards)*
Conditions	Type 2 Diabetes	Input
	Refractory Hypertension	Input
Lab Results	eGFR	Input & Output
	albumin-to-creatinine ratio	Input & Output
	HbA1c	Input & Output
Speciality	Nephrologist	Output
	Nurse	Output
	GP	Output

In Table AI. 30, the conditional clauses in the flowchart are clearly described, by referring to the clinical concepts in Table AI. 29.

Table AI. 30: Condition clauses in Management of Nephropathy Flowchart

<table>
<tr><th>Condition No</th><th>Condition Clause</th></tr>
<tr><td>C1</td><td>If eGFR<60 AND >45</td></tr>
<tr><td>C2</td><td>If (albumin-to-creatinin ratio > 300) OR (eGFR decrease ≥ 25% AND change in GFR category) OR (Refractory Hypertension)
<table>
<tr><th colspan="3">Glomerular filtration rate (GFR) Categories in Chronic Kidney Disease</th></tr>
<tr><th>GFR Category</th><th>GFR (mL/min/1.73m²)</th><th>Description</th></tr>
<tr><td>G1</td><td>>=90</td><td>Normal or High</td></tr>
<tr><td>G2</td><td>60-89</td><td>Mildly decreased*</td></tr>
<tr><td>G3a</td><td>45-59</td><td>Mildly to moderately decreased</td></tr>
<tr><td>G3b</td><td>30-44</td><td>Moderately to severely decreased</td></tr>
<tr><td>G4</td><td>15-29</td><td>Severely decreased</td></tr>
<tr><td>G5</td><td><15</td><td>Kidney failure</td></tr>
</table></td></tr>
<tr><td>C3</td><td>If eGFR>30 AND <45</td></tr>
<tr><td>C4</td><td>If eGFR<30</td></tr>
</table>

1.7.1. Implementation specific details

The CDS Service to be implemented for this flowchart needs to take the following inputs (i.e. prefetch terms in CDSHooks terminology) presented in Table AI. 31.

Table AI. 31: Prefetch Terms as input to Nephropatyh Management CDS Service

Prefetch term id	Description	Variables to be extracted from this prefetch item
conditions	All diagnosis of the patient as FHIR Conditions	-Type 2 Diabetes diagnosis - Refractory Hypertension diagnosis
egfr	Latest 2 eGFR test as FHIR Observations	-Value of latest 2 eGFR tests -Date of latest eGFR test
hba1c	Latest hba1c test as FHIR Observations	-Date of latest hba1c test
albumin/creatinine	Latest albumin/creatinine test as FHIR Observations	-Value of latest albumin/creatinine test -Date of latest albumin/creatinine test
nephropathy-control-visit	Latest Nephropathy-control-visit as FHIR Appointment	-Date of latest Nephropathy-control-visit
next-nephropathy-control-visit	Planned next Nephropathy-control-visit in the current care plan as FHIR Appointment	-Date of next Nephropathy-control-visit in the current care plan

These variables extracted from the listed input parameters will be processed as indicated in the flowchart presented in Figure A1. 9 **Error! Reference source not found.**, to produce the Cards listed in Table AI. 32.

Please note that, in the flowchart presented in Figure A1. 9 **Error! Reference source not found.**, for the sake of simplicity, some detailed checks are not explicitly noted. In the cards (as presented in Table AI. 32), only the next appointment or the lab test in a series of periodic activities is suggested. For example, when this CDS service is run, if the conclusion is to suggest 2 GP appointments, and 3 Nurse appointments yearly for the managing nephropathy, then the CDS produces a card suggesting to add an Appointment with the GP after 6 months, and an Appointment with the Nurse after 4 months. In other words, it does not suggest to add all appointments that will happen in that year at once. Next time this CDS is run (possibly in the next control visit), it will add the next one in the series. As the patient may visit before the planned control visit (maybe spontaneously, or for another planned visit rather than the nephropathy management control visit), the CDS service needs to check the date of the latest nephropathy management control visit, and also the date of the next planned nephropathy management control visit in the care plan, and then, only if necessary an additional appointment visit will be suggested. Similarly, before suggesting a periodic lab result (like HbA1C test in each 3 months), the date of the last HbA1C test, and the dare of the next planned HbA1C test in the care plan will be taken as an input and only if necessary adding a new lab test will be suggested to be added to the care plan.

Table AI. 32: Cards to be produced by Nephropathy Management CDS Service

CARD 1	
summary	Referral for Nephrologist
Detailed description	Referral for Nephrologist (Monitor nephropathy-G4)
source	NICE CKD guideline CG182, Chapter 1.3, Table 2 [60, p. 26].

	https://www.nice.org.uk/guidance/cg182	
Suggestion 1		
ReferralRequest	Title	Referral for Nephrologist
	Description	Referral for Nephrologist (Monitor nephropathy)
	status	proposed
	start	Today
	specialty	Nephrologist
	performer	HP & PATIENT
CARD 2		
summary	Yearly Appointments and Lab tests for management of nephropathy (G3b)	
Detailed description	Schedule two (2) appointment per year with the GP and three (3) per year with Nurse. Schedule albumin-to-creatinin ratio, eGFR (kidney function) and HbA1c measurements every 3 months	
source	NICE CKD guideline CG182, Chapter 1.3, Table 2 [60, p. 26]. https://www.nice.org.uk/guidance/cg182 & Osakidetza Renal Failure Pathway and Diabetes Clinical guideline	
Suggestion 1		
Appointment	Title	GP Appointment for management of nephropathy
	Description	GP Appointment for the six-monthly management of nephropathy
	Status	proposed
	start	(Date+6 months)
	specialty	GP
	performer	HP & PATIENT
Appointment	Title	Nurse Appointment for management of nephropathy
	Description	Nurse Appointment for the quarterly management of nephropathy
	status	proposed
	start	(Date+4 months)
	specialty	NURSE
	performer	HP & PATIENT
Activity	Title	HbA1C Test
	Description	Have HbA1c in every three months
	category	Observation
	code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood,LOINC
	Timing	Date+3 months

	performer	HP & PATIENT
Activity	Title	Albumin/Creatinine Test
	Description	Have Albumin/Creatinine test in every three months
	category	Observation
	code	9318-7, Albumin/Creatinine [Mass Ratio] in Urine,LOINC
	Timing	Date+3 months
	performer	HP & PATIENT
Activity	Title	eGFR Test
	Description	Have eGFR in every three months
	category	Observation
	code	33914-3, eGFR Test, LOINC
	Timing	Date+3 months
	performer	HP & PATIENT
CARD 3		
summary	Yearly Appointments and Lab tests for management of nephropathy (G3a)	
Detailed description	Program one (1) appointment per year with the GP and three (3) appointments with Nurse per year. Schedule albumin-to-creatinin ratio, eGFR (kidney function) and HbA1c measurements every 6 months.	
source	NICE CKD guideline CG182, Chapter 1.3, Table 2 [60, p. 26]. https://www.nice.org.uk/guidance/cg182 & Osakidetza Renal Failure Pathway and Diabetes Clinical guideline	
Suggestion 1		
Appointment	Title	GP Appointment for management of nephropathy
	Description	GP Appointment for the yearly management of nephropathy
	status	proposed
	start	(Date+1 year)
	specialty	GP
	performer	HP & PATIENT
Appointment	Title	Nurse Appointment for management of nephropathy
	Description	Nurse Appointment for the quarterly management of nephropathy
	status	proposed
	start	(Date+4 months)
	specialty	NURSE
	performer	HP & PATIENT

Activity	Title	HbA1C Test
	Description	Have HbA1c in every six months
	category	Observation
	code	4548-4, Hemoglobin A1c/Hemoglobin.total in Blood,LOINC
	Timing	Date+6 months
	performer	HP & PATIENT
Activity	Title	Albumin/Creatinine Test
	Description	Have Albumin/Creatinine test in every six months
	category	Observation
	code	9318-7, Albumin/Creatinine [Mass Ratio] in Urine,LOINC
	Timing	Date+6 months
	performer	HP & PATIENT
Activity	Title	eGFR Test
	Description	Have eGFR in every six months
	category	Observation
	code	33914-3, eGFR Test, LOINC
	Timing	Date+6 months
	performer	HP & PATIENT
CARD 4		
summary	Referral or consulting the nephrologist	
Detailed description	Consider referring or consulting the nephrologist	
source	Osakidetza Renal Failure Pathway and Diabetes Clinical guideline	
Suggestion 1		
ReferralRequest	Title	Referral or consulting the nephrologist
	Description	Consider referring or consulting the nephrologist
	status	proposed
	start	Today
	specialty	Nephrologist
	performer	HP & PATIENT

2. Specifications of Local CDS embedded in Care Plan Templates

The clinical decision support features discussed in the following sections will be taken care of as a part of care plan templates by C3DP, as the suggestions to be provided are static information cards that are not dependent on the detailed clinical context of the patient.

2.1.Diabetes Education

As a part of Diabetes Care Plan Template, the following card will be proposed by C3DP for Diabetes Education:

Table AI. 33: Cards to be proposed for Diabetes Education

CARD		
summary	Diabetes Education	
Detailed description	Provide evidence based structured education to patients and caregivers	
source	NICE diabetes guideline Chapter 1.6.25-1.6.31 [48, pp. 22-24] https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Goal	category	Safety, http://hl7.org/fhir/goal-category
	Description code	311401005, Patient Education, SNOMED International 2017 v1.33.2
	Description text	Offer evidence based structured education to patients and caregivers
Education Material	Title	Recommend Type 2 Diabetes Education
	Description	Type 2 Diabetes Education Material for patients
	Category	Instruction, http://hl7.org/fhir/communication-category
	url	https://patient.info/health/type-2-diabetes
Appointment	Title	Diabetes Education Review
	Description	Diabetes Education Review (at Diagnosis and with annual reinforcement)
	Status	proposed
	start	-
	specialty	DIETITIAN
	performer	HP& PATIENT

In Table AI. 34, the clinical concepts that need to be processed within this CDS feature are presented. Please see the accompanying Excel Sheet, which maps these clinical concepts to terminology system codes preferred by our pilot sites.

Table AI. 34: Clinical concepts to be processed by this CDS Service

Category	*Concept*	*Input / Output (Cards)*
Goal	Patient Education	output
Specialty	Dietetician	output

2.2.Self-monitoring of blood glucose

As a part of Diabetes Care Plan Template, the cards presented in Table AI. 35 will be proposed by C3DP for the management of Gastroparesis. Please note that alternative Suggestions within a Card are implicitly OR'ed.

Table AI. 35: Cards to be proposed for the Self-monitoring of Blood Glucose

CARD 1		
summary	Suggestions on self-monitoring of blood glucose	
Detailed description	-Do not routinely offer self monitoring if there is no risk of hypoglycemia -Consider short term self-monitoring if there is no risk of hypoglycemia only when starting oral or intravenous treatment with corticosteroids	
source	NICE diabetes guideline, Chapter 1.6.12-1.6.16 [48, pp. 18–19] https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Activity	Title	Self-monitoring of Blood Glucose
	Description	Measure your Blood Glucose
	category	Observation
	code	308113006, Self-monitoring of blood glucose (procedure), SNOMED International 2017 v1.33.2
	Timing	-
	performer	PATIENT
CARD 2		
summary	Annual control of patients who are self-monitoring of blood glucose	
Detailed description	-If the patient is self-monitoring blood glucose carry out structured assessment annually of the patients testing skills, knowledge to interpret results and the benefit for the patient	
source	NICE diabetes guideline, Chapter 1.6.12-1.6.16 [48, pp. 18–19].https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Appointment	Title	Appointment for structured assessment of the patients who is self-monitoring blood glucose
	Description	Carry out structured assessment annually of the patients testing skills, knowledge to interpret results and the benefit for the patient
	Status	proposed
	start	(Date+12 months)
	specialty	GP
	performer	HP & PATIENT

2.3.Management of Gastroparesis

As a part of Diabetes Care Plan Template, the cards presented in Table AI. 36 will be proposed by C3DP for the management of Gastroparesis. Please note that alternative Suggestions within a Card are implicitly OR'ed.

Table AI. 36: Cards to be proposed for the management of Gastroparesis

CARD 1		
summary	Diagnosis of Gastroparesis	
Detailed description	Think of gastroparesis as one possible diagnosis if erratic blood glucose control or unexplained gastric bloating or vomiting	
source	NICE diabetes guideline, Chapter 1.7.1-1.7.4 [48, pp. 26–27]. https://www.nice.org.uk/guidance/ng28	
CARD 2		
summary	Treatment of Gastroparesis	
Detailed description	If treatment of vomiting is needed consider alternating use of erythromycin and metoclopramide. Consider domperidone only in exceptional circumstances if it is the only effective treatment.	
source	NICE diabetes guideline, Chapter 1.7.1-1.7.4 [48, pp. 26–27]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Medication Request	Title	Erythromycin Recommendation
	Description	If treatment of vomiting is needed consider alternating use of erythromycin and metoclopramide
	Medication code	J01FA01, Erythromycin, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
Suggestion 2		
Medication Request	Title	Metoclopramide Recommendation
	Description	If treatment of vomiting is needed consider alternating use of erythromycin and metoclopramide
	Medication code	A03FA01, Metoclopramide, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-

Suggestion 3		
Medication Request	Title	Domperidone Recommendation
	Description	Consider domperidone only in exceptional circumstances if it is the only effective treatment
	Medication code	A03FA03, domperidone, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
CARD 3		
summary	Referral for Gastroenterologist	
Detailed description	Consider referral to specialist if in doubt of differential diagnosis or if persistent severe vomiting	
source	NICE Chronic kidney disease in adults: assessment and management CG182, Chapter 1.3, Table 2 [60, p. 26]. https://www.nice.org.uk/guidance/cg182	
Suggestion 1		
ReferralRequest	Title	Referral for Gastroenterologist
	Description	Consider referral to specialist if in doubt of differential diagnosis or if persistent severe vomiting
	status	proposed
	start	Today
	specialty	Gastroenterologist
	performer	HP & PATIENT

In Table AI. 37 the clinical concepts that need to be processed within this CDS feature are presented. Please see the accompanying Excel Sheet, which maps these clinical concepts to terminology system codes preferred by our pilot sites.

Table AI. 37: Clinical concepts to be processed by this CDS Service

Category	*Concept*	*Input / Output (Cards)*
Medication	Erythromycin	output
	Metoclopramide	output
	Domperidone	output
Specialty	Gastroenterologist	output

2.4.Management of Neuropathic pain

As a part of Diabetes Care Plan Template, the cards presented in Table AI. 37 will be proposed by C3DP for the management of Neuropathic pain. Please note that alternative Suggestions within a Card are implicitly OR'ed.

Table AI. 38: Cards to be proposed for the management of Neuropathic pain

CARD 1		
summary	Patient communication in the management of neurotic pain	
Detailed description	Discuss - severity of pain and its impact on lifestyle and daily activity - potential benefits and adverse effects of pharmacologic treatment - the importance of dosage titration - coping strategies for pain - non-pharmacologic treatments and psychological therapies	
source	NICE diabetes guideline, Chapter 1.7.5 [48, p. 27]. NICE guideline on neuropathic pain in adults https://www.nice.org.uk/guidance/ng28 https://www.nice.org.uk/guidance/cg173	
CARD 2		
summary	Treatment of Neuropathic pain	
Detailed description	Use one of the alternative treatment options for neuropathic pain	
source	NICE diabetes guideline, Chapter 1.7.5 [48, p. 27]. NICE guideline on neuropathic pain in adults https://www.nice.org.uk/guidance/ng28 https://www.nice.org.uk/guidance/cg173	
Suggestion 1		
Medication Request	Title	Tramadol Recommendation
	Description	Consider tramadol only if acute rescue medication is needed
	Medication code	N02AX02, Tramadol, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
Suggestion 2		
Medication Request	Title	Capsaicin cream Recommendation
	Description	Consider capsaicin cream for localized pain in patients who wish to avoid or can't tolerate oral treatment
	Medication code	N01BX04, capsaicin, ATC

	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	Topical
Suggestion 3		
Medication Request	Title	Amitriptyline Recommendation
	Description	Offer Amitriptyline, Duloxetine, Gabapentin or Pregabalin
	Medication code	N06AA09, Amitriptyline, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
Suggestion 4		
Medication Request	Title	Amitriptyline Recommendation
	Description	Offer Amitriptyline, Duloxetine, Gabapentin or Pregabalin
	Medication code	N06AX21, Duloxetine, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
Suggestion 5		
Medication Request	Title	Amitriptyline Recommendation
	Description	Offer Amitriptyline, Duloxetine, Gabapentin or Pregabalin
	Medication code	N03AX16, Pregabalin, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
Suggestion 6		
Medication Request	Title	Amitriptyline Recommendation
	Description	Offer Amitriptyline, Duloxetine, Gabapentin or Pregabalin
	Medication code	N03AX12, Gabapentin, ATC

	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-
CARD 3		
summary	Drugs to be avoided for the treatment of Neuropathic pain	
Detailed description	Do not use cannabis sativa extract, capsaicin patch or lacosamide or lamotrigine or levetiracetam or morphine or oxcarbazepine or topiramate or venlafaxine or for long term use tramadol	
source	NICE diabetes guideline, Chapter 1.7.5 [48, p. 27]. NICE guideline on neuropathic pain in adults https://www.nice.org.uk/guidance/ng28 https://www.nice.org.uk/guidance/cg173	
CARD 4		
summary	Follow up of the treatment of Neuropathic pain	
Detailed description	If the treatment is effective and tolerated: - continue medication - carry out regular clinical reviews - if you plan to withdraw medications, taper the withdrawal If the treatment is not effective: - change to one of the other drugs above and if needed switch again - if you plan to withdraw or switch the medication, taper the withdrawal - consider referring patient with severe pain or if the pain significantly limits lifestyle and daily activities	
source	NICE diabetes guideline, Chapter 1.7.5 [48, p. 27]. NICE guideline on neuropathic pain in adults https://www.nice.org.uk/guidance/ng28 https://www.nice.org.uk/guidance/cg173	

In Table AI. 39 the clinical concepts that need to be processed within this CDS feature are presented. Please see the accompanying Excel Sheet, which maps these clinical concepts to terminology system codes preferred by our pilot sites.

Table AI. 39: Clinical concepts to be processed by this CDS Service

Category	*Concept*	*Input / Output (Cards)*
Medication	Tramadol	output
	Capsaicin	output
	Amitriptyline	output
	Gabapentin	output
	Duloxetine	output
	Pregabalin	output

2.5.Management of Autonomic neuropathy

As a part of Diabetes Care Plan Template, the cards presented in Table AI. 40 will be proposed by C3DP for Management of Autonomic neuropathy. Please note that it is very unlikely for the patients having diabetes diagnosis that is more recent than 10 years to suffer autonomic neuropathy.

Table AI. 40: 47 Cards to be proposed for the management of autonomic neuropathy

CARD 1	
summary	Diagnosis of Autonomic Neuropathy
Detailed description	Think about the possibility of autonomic neuropathy in patients: -who lose the warning signs of hypoglycemia -with unexplained diarrhoea, in particular at night -with unexplained bladder emptying problems -with abnormal sweating
source	NICE diabetes guideline, Chapter 1.7.6-1.7.10 [48, p. 27]. https://www.nice.org.uk/guidance/ng28
CARD 2	
summary	Side effects of the Treatments for Autonomic Neuropathy
Detailed description	Be aware of increased likelihood of side effects (e.g. ortostatic hypotension) when using tricyclic or antihypertensive drugs.
source	NICE diabetes guideline, Chapter 1.7.6-1.7.10 [48, p. 27]. https://www.nice.org.uk/guidance/ng28

2.6.Management of Erectile dysfunction

As a part of Diabetes Care Plan Template, the cards presented in Table AI. 41 will be proposed by C3DP for the management of Erectile dysfunction in male patients.

Table AI. 41: Cards to be proposed for the management of Erectile dysfunction

CARD 1	
summary	Patient communication in the management of erectile dysfunction
Detailed description	Offer men with type 2 diabetes the opportunity to discuss erectile dysfunction at their annual review. Educate and support men with erectile dysfunction
source	NICE diabetes guideline, Chapter 1.7.13-1.7.16 [48, p. 28]. https://www.nice.org.uk/guidance/ng28
CARD 2	
summary	Treatment of Erectile Dysfunction
Detailed description	Consider phosphodiesterase-5 inhibitor if no contraindications
source	NICE diabetes guideline, Chapter 1.7.13-1.7.16 [48, p. 28]. https://www.nice.org.uk/guidance/ng28

Suggestion 1		
Medication Request	Title	Phosphodiesterase-5 inhibitor Recommendation
	Description	Consider phosphodiesterase-5 inhibitor if no contraindications
	Medication code	phosphodiesterase-5 inhibitor, ATC
	Dosage instruction (text)	-
	doseQuantity	-
	timing	-
	route	-

CARD 4	
summary	Follow up of the treatment of Phosphodiesterase-5 inhibitor treatment
Detailed description	If the treatment is effective and tolerated: - continue medication If the treatment is not effective: - discuss referral for medical, surgical or psychological management
source	NICE diabetes guideline, Chapter 1.7.13-1.7.16 [48, p. 28]. https://www.nice.org.uk/guidance/ng28

2.7.Management of Eye disease

As a part of Diabetes Care Plan Template, the cards presented in Table AI. 42 will be proposed by C3DP for the management of Diabetic Eye Disease, if the Diabetes is recently diagnosed.

Table AI. 42: Cards to be proposed for the management of Eye Disease in Diabetic patients

CARD		
summary	Monitoring eye disease	
Detailed description	Add a goal for monitoring eye disease and a referral for retinography immediately. Perform first screening no later than after 3 months from referral. Use mydriasis with tropicamide when photographing. Use trained staff and quality assured technology. Perform visual testing as a part of the screening programme.	
source	NICE diabetes guideline Chapter 1.7.17-1.7.25 [48, pp. 28–29]. https://www.nice.org.uk/guidance/ng28	
Suggestion 1		
Goal	category	Safety, http://hl7.org/fhir/goal-category
	Description code	274412005, Eye disorder Screening, SNOMED International 2017 v1.33.2
	Description text	Eye disease screening
ReferralRequest	Title	Initial referral for retinography

	Description	Referral for retinography due to diagnosis of diabetes. Use mydriasis with tropicamide when photographing. Use trained staff and quality assured technology. Perform visual testing as a part of the screening programme.
	status	proposed
	start	Today
	specialty	Ophthalmologist
	performer	HP & PATIENT

In Table AI. 43 the clinical concepts that need to be processed within this CDS feature are presented. Please see the accompanying Excel Sheet, which maps these clinical concepts to terminology system codes preferred by our pilot sites.

Table AI. 43: Clinical concepts to be processed by this CDS Service

Category	*Concept*	*Input / Output (Cards)*
Goal	Eye disorder Screening	output
Specialty	Ophthalmologist	output

In C3DP, the date of the last Ophthalmologist referral will be checked, and a new Referral after 12 months will be added once the referral is completed.

ANNEX 1 RECONCILED RULES TEMPLATE

A spreadsheet template was used for reconciling rules with the following column readings and explanations:

Table Annex1- 1: Reconciliation template headings and descriptions

Header	Description
Rule	Guideline rule reference
Context	Guideline rule description
Purpose	Clinical context of the CDS rules, such as target disease combination, stages in clinical process, relevant clinical activity, decision making point, etc.
Description of the Purpose	Explanation of the problem to be addressed: what, who (responsible actor where (location/setting), when (timeline)…..
Type of Purpose	**Classify as (use FHIR categories for goals and activities, see** Table Annex1- 2): • Goals • Activities • Risk assessment • Pharmacotherapy
Clinical Condition	Clinical conditions to be reconciled
Concept/Codes	Key clinical concepts relevant for the rule execution. The precise meaning of each concept is defined.
Rule Description	Detailed description of the CDS rules/algorithm. Could be if…then…else statement, mathematical formula, or a link to more sophisticated description such as flowchart.
Trigger	Trigger condition of the CDS rules, i.e. when the rules should be triggered.
Input	What input are needed by the rules? E.g. patient age, gender, blood pressure, medication list, etc.
Output	What kind of output should the rules produce? Examples include alert, reminder, medication suggestion, care plan goal/activity suggestion, risk report, or just text information.
Reference	Source of information, i.e. provenance of the rules, such as D7.1, NICE. The more specific, the better, e.g. page or section number
Notes	Any other information that helps implementation
Peer Review Agreement	Description of agreement reached

Table Annex1- 2: Types of purpose

FHIR Category	Type	Definition
G_dietary	Goal	Goals related to the consumption of food and/or beverages.
G_safety	Goal	Goals related to the personal protection of the subject.
G_behavioral	Goal	Goals related to the manner in which the subject acts.
G_nursing	Goal	Goals related to the practice of nursing or established by nurses.
G_physiopherapy	Goal	Goals related to the mobility and motor capability of the subject.
Ac_Diet	Activity	Plan for the patient to consume food of a specified nature
Ac_Drug	Activity	Plan for the patient to consume/receive a drug, vaccine or other product
Ac_Encounter	Activity	Plan to meet or communicate with the patient (in-patient, out-patient, phone call, etc.)
Ac_Observation	Activity	Plan to capture information about a patient (vitals, labs, diagnostic images, etc.)
Ac_Procedure	Activity	Plan to modify the patient in some way (surgery, physiotherapy, education, counseling, etc.)
Ac_Supply	Activity	Plan to provide something to the patient (medication, medical supply, etc.)
Ac_Other	Activity	

ANNEX 2 FINAL RECONCILED RULES FROM TWO DISEASES (DIABETES AND RENAL FAILURE) COMBINATION

15 rules have been reconciled for this disease pair.

Rule	Rule 1	Rule 2
Context	Identify interaction between a medication and co-morbidity.	Identify interaction between a medication and co-morbidity.
Purpose	Identify drug-disease interaction	Identify drug-disease interaction
Description of the purpose	Patient with Type 2 Diabetes in Dapaglifozin therapy. Declining renal function due to diabetic nephropathy. At what point should the Dapaglifozin be stopped?	Patient with Type 2 Diabetes in Canaglifozin or Empaglifozin therapy. Declining renal function due to diabetic nephropathy. At what point should the Canaglifozin or Empaglifozin be stopped?
Type of purpose	Pharmacotherapy	Pharmacotherapy
Clinical condition	DIABETES + RENAL FAILURE	DIABETES + RENAL FAILURE
Concept/codes	eGFR: Dapaglifozin	eGFR: Canaglifozin or Empaglifozin
Rule description	IF estimated glomerular filtratrion rate (measure of renal function (eGFR)) is less than 60 mL/minute/1.73m2 STOP Dapaglifozin therapy	IF estimated glomerular filtratrion rate (measure of renal function (eGFR)) is less than 45 mL/minute/1.73m2 STOP Canaglifozin or Empaglifozin
Trigger	Each time a renal function is inputted for a patient on Dapaglifozin therapy	Each time a renal function is inputted for a patient on Canaglifozin or Empaglifozin therapy
Input	eGFR & Whether a patient is Dapaglifozin -Therapy	eGFR & Whether a patient is Canaglifozin or Empaglifozin -Therapy
Output	Alert to STOP Dapaglifozin if GFR < 60	Alert to STOP Canaglifozin o Empaglifozin if GFR < 45 ml/min
Reference	NICE Guideline INFAC Bulletin (monthly newsletter aimed at updating knowledge in pharmacotherapy of health professionals in the Basque Country. It provides reviews of drug treatments of various diseases, drug reviews, short news about drugs, etc.)	NICE Guideline-Figure 2 (5.2.2. Diabetes - Dietary advice)-Figure 30 (RF) INFAC Bulletin (monthly newsletter aimed at updating knowledge in pharmacotherapy of health professionals in the Basque Country. It provides reviews of drug treatments of various diseases, drug reviews, short news about drugs, etc.)
Notes	The current situation is: These drugs need to be stopped when EGFR reaches <30mls/min/1.73m2. But it could change.	As in the current guidelines, Canagliflozin or Empagliflozin is not directly suggested, this check can be done after such drugs are manually added to the care plan. We can check this in the beginning of "Glucose Management-Drug theraphy" section. Canaglifozin and Empaglifozin need to be stopped when EGFR reaches <30mls/min/1.73m2. This is the current situation but it could change
Peer review agreement	-To be handled by the drug interacion module (external database).	-To be handled by the drug interacion module (external database).

Rule	Rule 3	Rule 4
Context	Reconciling dietary recommendations in comorbidity	Reconciling dietary recommendations in comorbidity

Rule	Rule 3	Rule 4
Purpose	Disease-Disease interaction Dietary recommendations in the presence of diabetes and RF	Disease-Disease interaction (diet) Dietary recommendations when diabetes and RF
Description of the purpose	Patients with Diabetes and Renal Failure (stages 2 and 3)	Patients with DM and RF (stages 4 and 5)
Type of purpose	Ac_Diet	Ac_Diet
Clinical condition	DIABETES + RENAL FAILURE	DIABETES + RENAL FAILURE
Concept/codes	ICD-10 Diabetes (RF) eGFR	ICD-10-Diabetes (RF) eGFR
Rule description	IF ICD-10 Diabetes AND RF AND eGFR > 30, THEN Mediterranean diet with reduced sodium level (salt intake)	IF ICD-10 Diabetes AND RF AND eGFR < 30 THEN Mediterranean diet with reduced sodium level and restricted potassium and phosphate intake.
Trigger	Each time eGFR is required	Each time eGFR is required
Input	ICD-10 EGFR	ICD-10 EGFR
Output	Different recommendations between stages 2-3 and 4-5	Different recommendations between stages 2-3 and 4-5
Reference	NICE Guideline DM/RF.-Figure 2 (5.2.2. Diabetes - Dietary advice)-Figure 30 (RF) Osakidetza Clinical guideline and Renal Failure pathway	NICE GuidelineS DM/RF.-Figure 2 (5.2.2. Diabetes - Dietary advice)-Figure 30 (RF) Osakidetza Clinical Guidelina and Renal Failure pathway
Notes	A link to educational material on diet should be provided. To be invoked in "Dietary Advice" section	
Peer review agreement	Dietary advice is additive so patients need to stick to diet appropriate to diabetes and control sodium intake. The localities of each pilot site have to be applied.	As this rule is out of the scope of the project, clinicians will be informed about it. Thus, the CDSM will add the following sentence: "The information in C3-CLOUD is not validated for a GFR<30. Consider referral to a specialist".

Rule	Rule 5	Rule 6
Context	Need to identify criteria to assess a good metabolic control in diabetes	Need to identify criteria to assess a good metabolic control in diabetes
Purpose	Disease-Disease interaction. Criteria for glycaemic control in diabetic nephropathy	Disease-Disease interaction. Criteria for glycaemic control in diabetic nephropathy
Description of the purpose	Patients with DM and chronic renal failure WITHOUT frailty	Patients with DM and chronic renal failure WITH frailty
Type of purpose	G_Safety	G_Safety
Clinical condition	DIABETES + RENAL FAILURE	DIABETES + RENAL FAILURE
Concept/codes	eGFR,ICD-10 DIABETES	EGFR,ICD-10 DIABETES, Frailty?
Rule description	IF HbA1c >6,4 % THEN Alert: poorly controlled (NICE) IF HbA1c >6,9 % THEN Alert: poorly controlled (Basque Country guidelines) (SWFT - we use mmols of glucose per mol of haemoglobin for HbA1c. We might have to calculate HcA1c as a %)	If HbA1c >7,9 %, THEN alert poorly controlled
Trigger	Each time Hb A1c measure is required	Each time Hb A1c measure is required

Rule	Rule 5	Rule 6
Input	HbA1c+eGFR	HbA1c+eGFR-Frailty
Output	Alert poor control	Alert poor control
Reference	NICE Figure 6 (5.2.6. HbA1c measurements and targets-DM) Osakidetza Clinical Guideline	Osakidetza Clinicla Guideline
Notes	To be invoked in "Dietary Advice" section	Need to define the criteria of frailty
Peer review agreement	Agreed to be a single condition (diabetes) rules. The localities of each pilot site have to be applied (threshold values, units).	It is agreed it is Diabetes (single condition) rule. It is agreed to keep it in pair diseases reconciliation documents also. The "frailty" issue will be tackled in the single disease. Frailty is a non-consensual definition at the international level. The question if the patient is frail or not is going to be added as a specific question. According the reply, the clinicians can loosen the target a bit of not.

Rule	Rule 7	Rule 8
Context	Follow up of the patient with diabetic nephropathy	Follow up of the patient with diabetic nephropathy
Purpose	Disease-Disease interaction. Frequency of appointments/encounters with health care professionals	Disease-Disease interaction. Frequency of appointments/encounters with health care professionals
Description of the purpose	Follow up pattern for a patient with DM2 and nephopathy 1-3a	Follow up pattern for a patient with DM2 and nephopathy 3b
Type of purpose	Ac_Encounter	Ac_Encounter
Clinical condition	DIABETES + RENAL FAILURE	DIABETES + RENAL FAILURE
Concept/codes	ICD-10 Diabetes;eGFR	ICD-10 Diabetes;eGFR
Rule description	If ICD-10 Diabetes AND eGFR >45 y < 60 THEN schedule one (1) yearly appointment with the GP and three (3) with the Nurse	IF ICD-10 Diabetes AND eGFR <30 and <45, THEN schedule two (2) appointments per year with the GP and three (3) with the Nurse
Trigger	Each encounter of the patient with the health care professional	Each encounter of the patient with the health care professional
Input	eGFR and ICD-10 diabetes	eGFR and ICD-10 diabetes
Output	Program one (1) appointment per year with the GP and three (3) appointments with Nurseper year. Appointment with the appropiated healthcare professional	Schedule two (2) appointment per year with the GP and three (3) per year with Nurse . Appointment with the appropiated healthcare professional
Reference	NICE Figure 33 (5.4.7. Frequency of eGFR control-RF)	NICE Figure 33 (5.4.7. Frequency of eGFR control-RF)
Notes		
Peer review agreement	It is agreed to keep per year: 1 GP appointment and 2 nurse appointments. Local frequency of follow up appointments should be followed the NICE guidelines. However they are not always included. In that case, the NICE guidelines	It applies the same as for rule 7

Rule	Rule 7	Rule 8
	recommendations for the follow up appointments will be adapted to the local situations (for single and combined diseases).	

Rule	Rule 9	Rule 10
Context	Follow up of the patient with diabetic nephropathy	Changes using statins in diabetic nephropathy
Purpose	Disease-Disease interaction. Criteria for nephrology referral	Drug-disease interaction
Description of the purpose	Follow up pattern for a patient with DM2 and Nephopathy 3 and 4	Establish the prescription of statins
Type of purpose	Ac_Encounter	Ac_Drug
Clinical condition	DIABETES + RENAL FAILURE	DIABETES + RENAL FAILURE
Concept/codes	ICD-10 Diabetes;eGFR	Risk assessment scale/score (QRISK2, Regicor), EGFR
Rule description	IF ICD-10 Diabetes AND eGFR <30, THEN referral to Nephrology	IF ICD-10 Diabetes and eGFR < 60 THEN offer statins
Trigger	Each encounter of the patient with the health care professional	Each time cardiovascular risk is calculated?
Input	eGFR and ICD-10 diabetes	eGFR and ICD-10 diabetes
Output	Referral to Nephrology	Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD
Reference	NICE Guideline	NICE guideline figure 4 flowchart (5.2.4)
Notes		*Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved and eGFR is 30 ml/min/1.73 m^2 or more.* *Agree the use of higher doses with a renal specialist if eGFR is less than 30 ml/min/1.73 m2*
Peer review agreement	It is a Renal Failure (single disease) rule.	It is a Renal Failure (single disease) rule.

Rule	Rule 11	Rule 12
Context	Follow up of the patient with diabetic nephropathy	Follow up of the patient with diabetic nephropathy
Purpose	Disease-Disease interaction Evaluate progression of the Chronic Kidney Disease and cardiovascular risk of the patient	Disease-Disease interaction. Evaluate progression of Chronic Kidney Disease and Cardiovascular Risk of the patient
Description of the purpose	Laboratory analyses and complementary tests to be performed	Laboratory analyses and complementary tests to be performed
Type of purpose	Ac_Observation	Ac_Observation
Clinical condition	DIABETES + RENAL FAILURE	RECONCILED RULE DIABETES + RENAL FAILURE
Concept/codes	ICD-10 Diabetes;eGFR	ICD-10 Diabetes;eGFR
Rule description	IF ICD-10 Diabetes and eGFR >45 and < 60 THEn schedule albumin-to-creatinin ratio,eGFR (kidney function) and HbA1c every 6 months	IF ICD-10 Diabetes and eGFR >30 and < 45 THEN schedule albumin-to-creatinin ratio, eGFR (kidney function) and HbA1c measurements every 3 months

Rule	Rule 11	Rule 12
Trigger	Each time eGFR is calculated	Each time eGFR is calculated
Input		eGFR and ICD-10 diabetes
Output		Type and frequency of lab analyses request
Reference		Osakidetza Renal Failure Pathway and Diabetes Clinical guideline
Notes	Could be also Purpose:risk assessment	Could be Purpose:risk assesment
Peer review agreement	It is a Diabetes (single disease) rule. It will be updated accordingly in the diabetes rules guideline.	It applies the same as for rule 11.

Rule	Rule 13	Rule 14
Context	Follow up of the patient with diabetic nephropathy	Treatment of Hypertension in patient with diabetic nephropathy
Purpose	Disease-Disease interaction. When to involve nephrologist in the follow-up	Disease-disease interaction.Values of Blood pressure Target
Description of the purpose	Criteria for referral to Nephrologist	Target for Blood pressure values
Type of purpose	Ac_Encounter	G_Safety
Clinical condition	DIABETES + RENAL FAILURE	DIABETES + RENAL FAILURE
Concept/codes	ICD-10 Diabetes; Hypertension, eGFR	ICD-10 Diabetes; ICD-10 Hypertension
Rule description	IF ICD-10 Diabetes AND (eGFR > 45 AND albumin-to-creatinin ratio > 300) OR (eGFR decrease ≥ 25% AND change in GFR category) OR (Refractory Hypertension) THEN considering referring to Nephrologist	IF ICD-10 Diabetes AND ICD-Hypertension THEN target values systolic blood pressure < 130 and diastolic blood pressure <80
Trigger	Each time eGFR is calculated or Refractory Hypertension	First time an ICD 10 Hypertension code appears
Input	eGFR and ICD-10 diabetes, Hypertension	ICD-10 Diabetes and High Blood Pressure
Output	Alert: referral to nephrology	Show target value
Reference	Osakidetza Renal Failure Pathway and Diabetes Clinical guideline	NICE Figure 34 (5.4.8.1. Blood pressure treatment in CKD without diabetes mellitus) and 35 (5.4.8.2. Blood pressure treatment in CKD with Diabetes)
Notes	Resistant hypertension is defined as blood pressure that remains above goal in spite of concurrent use of three antihypertensive agents of different classes. Some patients with resistant hypertension cannot be controlled, even with maximal medical therapy (five or more drugs including chlorthalidone and a mineralocorticoid receptor antagonist) under the care of a hypertension specialist. Such patients are referred to as having refractory hypertension.(https://www.uptodate.com/contents/definition-risk-factors-and-evaluation-of-resistant-hypertensio,n acccessed7August2017)	Values in Osakidetza Guidelines are different (140/80).
Peer review agreement	Rule description has changed: instead of "refer to the nephrologist", "consider referring or consulting the nephrologist"	It is a single disease (diabetes) rule.

Rule	Rule 15
Context	Treatment of Hypertension in patient with diabetic nephropathy
Purpose	Disease-disease interaction. Election of antihypertensive therapy
Description of the purpose	Election antihypertensive therapy
Type of purpose	Ac_Drug
Clinical condition	DIABETES + RENAL FAILURE
Concept/codes	CD-10 Diabetes; ICD-10 Hypertension
Rule description	If ICD-10 Diabetes AND ICD-10 Hypertension THEN Anti-Hipertensive Angiotensin-converting enzyme (ACE) inhibitors OR Angiotension II Receptor Blockers A2RB (if ACEI adverse efects)
Trigger	First time an ICD 10 Hypertension code appears
Input	ICD-10 Diabetes and High Blood Pressure
Output	Indicate ACEI or A2RBs
Reference	NICE Figure 34 (5.4.8.1. Blood pressure treatment in CKD without diabetes mellitus) and 35 (5.4.8.2. Blood pressure treatment in CKD with Diabetes) Osakidetza Clinical Guideline.
Notes	
Peer review agreement	There are local discrepancies in the use of treatment, depending if the patient suffers diabetes or diabetes plus renal failure. In Basque Country the patient with both conditions are treated with IECA, otherwise with diuretic. The NICE guideline recommendations will be adapted to each pilot site. In SWFT, NICE guidelines will be applied and ACE inhibitor will be first choice

ANNEX 3 FINAL RECONCILED RULES FROM TWO DISEASES (DIABETES AND DEPRESSION) COMBINATION

6 rules have been reconciled for this disease pair.

Rule	Rule 1	Rule 2
Context	Interaction between medication & co-morbidity	Interaction between medication & co-morbidity
Purpose	Drug-disease interaction.	Drug-disease interaction.
Description of the purpose	Patient with depression on insulin and/or oral glucose lowering medication might experience an altered glucose control if given SSRI	Patients with diabetic neuropathy might have tramadol as a rescue medication. This is contra-indicated if treated with MAOi for depression
Type of purpose	Ac_Drug	Ac_Drug
Clinical condition	DIABETES + DEPRESSION	DIABETES + DEPRESSION
Concept/codes	ATC codes in combination	ATC codes in combination
Rule description	If ATC insulin/oral glucose lowering medication is given SSRI send warning	No combination of these ATC codes acceptable
Trigger	Each time SSRI is prescribed if already on insulin/glucose lowering oral medication	Each time a combination of ATC codes occur
Input	Prescription (ATC) with SSRI added to insulin /glucose lowering oral drugs	ATC codes
Output	Alert to be aware and arrange extra controls	Warning to stop combination
Reference	**S**SRI product information	MAOi product information
Notes		MAOIs are not commonly used in Primary Care but we should know this interaction when we are prescribing Tramadol
Peer review agreement	To be handled by the drug interaction module (external database).	To be handled by the drug interaction module (external database).

Rule	Rule 3	Rule 4
Context	Interaction between medication & co-morbidity	Interaction between medication & co-morbidity
Purpose	Drug-disease interaction.	Drug-disease interaction.
Description of the purpose	Patient with depression on insulin and/or oral glucose lowering medication might experience an altered glucose control if given mirtazapin	Patient with depression on Bupropion have an increased risk of epileptic seizures if treated with insulin and/or oral glucose lowering medication
Type of purpose	Ac_Drug	Ac_Drug
Clinical condition	DIABETES + DEPRESSION	DIABETES + DEPRESSION
Concept/codes	ATC codes in combination	ATC codes in combination
Rule description	If on ATC insulin/oral glucose lowering medication is given mirtazapin send warning	If on ATC insulin/oral glucose lowering medication is given Bupropion send warning
Trigger	Each time mirtazapin is prescribed if already on insulin/glucose lowering oral medication	Each time a combination of ATC codes occur
Input	Prescription (ATC) with mirtazapin added to insulin /glucose lowering oral drugs	ATC codes

Rule	Rule 3	Rule 4
Output	Alert to be aware and arrange extra controls	Alert to be aware
Reference	mirtazapin product information	Bupropion product information d
Notes		
Peer review agreement	To be handled by the drug interaction module (external database).	To be handled by the drug interaction module (external database).

Rule	Rule 5	Rule 6
Context	Interaction between medication & co-morbidity	Interaction between medication & co-morbidity
Purpose	Drug-disease interaction.	Drug-disease interaction.
Description of the purpose	Patient with depression on insulin and/or oral glucose lowering medication might experience an altered glucose control if given Venlafaxin	Patient with depression on agomelatin experience a risk for hepatic insufficiency. This risk is increased in patients with hepatic steatosis with increased prevalence in obesity and/or diabetes type 2.
Type of purpose	Ac_Drug	Ac_Drug
Clinical condition	DIABETES + DEPRESSION	DIABETES + DEPRESSION
Concept/codes	ATC codes in combination	ATC code + ICD code diabetes type 2 and/or hepatic steatosis and/or BMI >30 in combination
Rule description	If ATC insulin/oral glucose lowering medication is given Venlafaxin send warning	If ATC agomelatin is prescribed in patients with ATC diabetes and/or hepatic steatosis and/or BMI>30 send warning.
Trigger	Each time Venlafaxin is prescribed if already on insulin/glucose lowering oral medication	Agomelatin prescription
Input	Prescription (ATC) with Venlafaxin added to insulin /glucose lowering oral drugs	ATC codes, BMI, ICD
Output	Alert to be aware and arrage extra controls	Alert to be aware
Reference	Venlafaxin product information.	Agomelatin product information. Bupropion is contraindicated in liver disease, regardless of whether or not it has diabetes. It is a generic rule
Notes		The Technical sheet in spanish doesn't mention Diabetes. Bupropion is contraindicated in severe liver diseases and that is beyond the "normal" hepatic steatosis often found in type 2 Diabetes.
Peer review agreement	To be handled by the drug interaction module (external database).	Send warning if the patient has an ICD-10 Code for hepatic steatosis (it is not very common in these patients) and/or if the patient is obese (BM≥30)

ANNEX 4 FINAL RECONCILED RULES FROM TWO DISEASES (DIABETES AND HEART FAILURE) COMBINATION

4 rules have been reconciled for this disease pair.

Rule	Rule 1	Rule 2
Context	Potential interaction in diet advices	Slightly different medication in heart failure with/without hypertension compared to in hypertension in diabetes
Purpose	Disease-disease interaction.	Disease-Disease interaction
Description of the purpose	In diabetes more profound dietary advices are given than in HF though there is nothing contradicting in the two advices	All patients with HF should have ACEi (or an ARB) together with a beta blocker (if no contra-indications). This will thus also be the first step in blood pressure treatment in patients having both DM and HF. Thereafter for DM the subsequent steps in 5.2.3 are followed.
Type of purpose	Ac_Diet	Ac_Drug
Clinical condition	DIABETES + HEART FAILURE	DIABETES + HEART FAILURE
Concept/codes	ICD codes	ICD codes
Rule description	If both ICD codes dietary advices for diabetes should be used	If HF and hypertension always treat with ACI (or ARB) together with BB irrespective of blood pressure if tolerated. If more blood pressure medication is needed use 5.2.3 for the continuation
Trigger	Each time both ICD diagnoses occur	ICD heart failure
Input	ICD	ICD codes
Output	Chose diabetes advices	Follow heart failure recommendations first until patient has both ACEi (ARB) + BB therafter 5.2.3
Reference		
Notes		Unstable HF patients after treatment with ACEi (ARB) ? BB and patients with fluid overload are outside the scope of C3-Cloud
Peer review agreement		

Rule	Rule 3	Rule 4
Context	Pioglitazone contraindicated in HF	Saxagliptin, sitagliptin, can exacerbate HF
Purpose	Drug-disease interaction	Drug-disease interaction
Description of the purpose	Pioglitazone contraindicated in HF	Saxagliptin should be used with caution in patiens wiht HF
Type of purpose	Ac_Drug	Ac_Drug
Clinical condition	DIABETES + HEART FAILURE	DIABETES + HEART FAILURE
Concept/codes	ATC and ICD in combination	ATC and ICD in combination

Rule	Rule 3	Rule 4
Rule description	If HF warn if the patient is on Pioglitazone or if it is prescribed	WARNING: In patients with Diabetes and heart failure, if saxagliptin or sitagliptin is prescribed, it might worsen HF.
Trigger	ATC pioglitazone if ATC HF or could be the other way around also	ATC
Input	ATC and ICD in combination	ATC and ICD in combination
Output	Alert a warning	
Reference	NICE diabetes 1.6.24	Circulation 2016; 134:e-69 Reference document for drugs that worsen heart failure
Notes		
Peer review agreement		Rephrase the rule description as a WARNING It is accepted to use the Circulation 2016; 134 e-69 as reference document together with the NICE guideline

ANNEX 5 FINAL RECONCILED RULES FROM TWO DISEASES (RENAL FAILURE AND HEART FAILURE) COMBINATION

11 rules have been reconciled for this disease pair.

Rule	Rule 1	Rule 2
Context	Clinical Review	Clinical Review
Purpose	Symptom Assessment	Risk Assessment
Description of the purpose	Alert clinician to consider whether cough is due to ACE-i or HF [or ARA II alSo (2% Losartán) in BC]	
Type of purpose	Risk assessment	Pharmacotherapy
Clinical condition	RENAL FAILURE + HEART FAILURE	RENAL FAILURE + HEART FAILURE
Concept/codes	Cough code; ACE-i code **ICD**-10 code ATC code	ACE-i or ARB code; renal failure code
Rule description	IF cough symptom code entered AND patient taking ACE-i THEN consider ACE-i as cause of cough AND consider switching to ARB	IF code for ACE-i or ARB prescription entered AND patient has RF code THEN monitor renal function more closely
Trigger	clinical data entry	ACE-i or ARB code in presence of pre-existing RF code
Input	Cough symptom code IF pre-existing ACE-i code	ACE-i or ARB code and pre-existing RF code
Output	Reminder to clinician to consider ACE-i as possible cause of cough. **BC-** ARA II alSo (2% Losartán)	Reminder to clinician to arrange early monitoring of renal function with continued monitoring as renal function results require
Reference	BNF	NICE HF guideline; BNF
Notes	Is cough included because HF may appear as a cough? But this rule would apply to ACE-i regardless of their indication. It would also be worth for Hypertension… This is a generic ACE-i rule for a HF patient not an HF-RF interaction.	This is a generic ACE-i/ARB rule. You could very well have perfect GFR but a stenosis of the renal artery though the risk increases if you have RF. We need generic rules not to combine ACEi and ARB and generic rules for extra controls (potassium) and precautions when combining ACE-i or ARB with spironolactone or eplerone. This in particular if existing RF, but not only. These issues should be decided by the clinician managing the patient not by the computer system
Peer review agreement	This is a generic rule to be applied in the earlier stages. I t is not a rule for disease combination, it is a rule for ACE-i. It should be applied before reconciliation.	F code for ACE-i or ARB prescription entered AND patient has RF code THEN monitor renal function more closely: 1 week, 1 month and then annually

Rule	Rule 3	Rule 4
Context	Clinical Review	Clinical Review
Purpose	Monitoring	Monitoring

Rule	Rule 3	Rule 4
Description of the purpose	if renal function deteriorates when ACE-i or ARB prescribed consider reducing dose or stopping	if renal function deteriorates when taking spironolactone consider stopping drug
Type of purpose	Pharmacotherapy	Pharmacotherapy
Clinical condition	RENAL FAILURE + HEART FAILURE	RENAL FAILURE + HEART FAILURE
Concept/codes	Renal function blood test result code	Renal function blood test result code
Rule description	IF prescribed an ACE-i or ARB AND eGFR falls below 30 THEN reduce dose or stop drug. "If a fall in GRF of 20% or more is seen as a consequence of ARB/ACEi medication discuss with specialist" "If a fall in GFR after 1 week is seen, but it is less than 25%, repeat the test in 1-2 weeks." "If a fall in GFR of 30% or more is seen, strongly suspect renal artery stenosis, discuss with specialist and discontinue the medication"	IF prescribed spironolactone AND eGFR <30 THEN stop spironolactone. If a fall in GRF of 20% or more is seen as a consequence of ARB/ACEi medication discuss with specialist" "If a fall in GFR after 1 week is seen, but it is less than 25%, repeat the test in 1-2 weeks." "If a fall in GFR of 30% or more is seen, strongly suspect renal artery stenosis, discuss with specialist and discontinue the medication"
Trigger	Renal function result in presence of pre-existing ACE-i or ARB code	Renal function result in presence of pre-existing spironolactone code
Input	eGFR <30; ACE-i or ARB code	eGFR <30; spironolactone code
Output	ALERT responsible clinician to review prescription	ALERT responsible clinician to stop spironolactone
Reference	BNF The Renal Association (May 2006).UK CKD Guidelines and secondary care. NICE 2014. Chronic kidney disease early identification and management of chronic kidney disease in adults in primary and secondary care	BNF The Renal Association (May 2006).UK CKD Guidelines and secondary care. NICE 2014. Chronic kidney disease early identification and management of chronic kidney disease in adults in primary and secondary care
Notes	A GFR of 30 won´t give an alarm, this means that we also have to introduce a Delta value cut-off for the system to react upon. The system also has to react upon a GFR <30 and always inform that the system is not validated any further. This goes for most of the following rules, but has to be a generic response when this situation occurs	A Delta value cut off would be good but a generic response to icotrol potassium should be given for spironolactone and epleron (rule 11). Data base of drugs in Renal Failure (Renbase). According to the necessity of generic rules to monitor potassium.
Peer review agreement	This is a generic rule to be applied in the earlier stages. It should be applied before reconciliation	Agreement on using the delta value cut off. The value of Delta value has been reviewed in the bibliography. Add: "If the EGFR drop is more than 10mls/min then consider stopping or changing the spirolactone"

Rule	Rule 5	Rule 6
Context	Clinical Review	Clinical Review
Purpose	Monitoring	Monitoring
Description of the purpose	if renal function deteriorates when taking bisoprolol reduce dose	if renal function deteriorates when taking ivabradine use with caution or stop

Rule	Rule 5	Rule 6
Type of purpose	Pharmacotherapy	Pharmacotherapy
Clinical condition	RENAL FAILURE + HEART FAILURE	RENAL FAILURE + HEART FAILURE
Concept/codes	Renal function blood test result code	Renal function blood test result code
Rule description	IF prescribed Bisoprolol AND eGFR <20 THEN reduce dose	IF prescribed Ivabradine AND eGFR <15 THEN use with caution/stop
Trigger	Renal function result in presence of pre-existing Bisoprolol code	Renal function result in presence of pre-existing Ivabradine code
Input	eGFR <20; Bisoprolol code	eGFR <15; Ivabradine code
Output	ALERT responsible clinician to reduce dose	ALERT responsible clinician to consider stopping drug
Reference	BNF	BNF
Notes	Outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.	Outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.
Peer review agreement	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"

Rule	Rule 7	Rule 8
Context	Clinical Review	Clinical Review
Purpose	Monitoring	Monitoring
Description of the purpose	if renal function deteriorates when taking hydrallazine reduce dose	if renal function deteriorates when taking digoxin reduce dose and check blood levels regularly
Type of purpose	Pharmacotherapy	Pharmacotherapy
Clinical condition	RENAL FAILURE + HEART FAILURE	RENAL FAILURE + HEART FAILURE
Concept/codes	Renal function blood test result code	Renal function blood test result code
Rule description	IF prescribed Hydrallazine AND eGFR <30 THEN reduce dose	IF prescribed Digoxin AND eGFR <60 THEN monitor digoxin levels and adjust dose if necessary
Trigger	Renal function result in presence of pre-existing Hydrallazine code	Renal function result in presence of pre-existing Digoxin code
Input	eGFR <30; Hydrallazine code	?eGFR<60: Digoxin code
Output	ALERT responsible clinician to reduce dose	ALERT responsible clinician to Monitor digoxin levels
Reference	BNF	BNF
Notes	Outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.	Data base of drugs in Renal Failure (Renbase)
Peer review agreement	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"	

Rule	Rule 9	Rule 10
Context	Clinical Review	Clinical Review
Purpose	Monitoring	Monitoring
Description of the purpose	if renal function deteriorates when taking Entresto reduce dose	if renal function deteriorates when taking Eplerenone then reduce dose if eGFR 30 - 60
Type of purpose	Pharmacotherapy	Pharmacotherapy
Clinical condition	RENAL FAILURE + HEART FAILURE	RENAL FAILURE + HEART FAILURE
Concept/codes	Renal function blood test result code	Renal function blood test result code
Rule description	IF prescribed Entresto AND eGFR <30 THEN reduce dose	IF prescribed Eplerenon AND eGFR 30 - 60 THEN reduce dose to 2mg alternate days and monitor renal function.
Trigger	Renal function result in presence of pre-existing Entresto code	Renal function result in presence of pre-existing Eplerenone code
Input	eGFR <30 code; Entresto code	eGFR 30 - 60 code; Eplerenone code
Output	ALERT responsible clinician to reduce dose	ALERT responsible clinician to reduce dose
Reference	BNF	BNF
Notes	Outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.	Outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.
Peer review agreement	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"

Rule	Rule 11
Context	Clinical Review
Purpose	Monitoring
Description of the purpose	if renal function deteriorates when taking Eplerenone then STOP if eGFR <30
Type of purpose	Pharmacotherapy
Clinical condition	RENAL FAILURE + HEART FAILURE
Concept/codes	Renal function blood test result code
Rule description	IF prescribed Eplerenon AND eGFR <30 THEN Stop drug.
Trigger	Renal function in the presence of pre-existing Eplerenone code
Input	eGFR <30 code; Eplerenone code
Output	ALERT responsible clinician to reduce dose
Reference	BNF
Notes	In case the the potassium rises then we would need to alter the dose. This rules is outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.
Peer review agreement	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision".

ANNEX 6 FINAL RECONCILED RULES FROM TWO DISEASES (DEPRESSION AND RENAL FAILURE) COMBINATION

5 rules have been reconciled for this disease pair.

Rule	Rule 1	Rule 2
Context	Identify Interaction between a medication & co-morbidity	Interaction between disease & disease
Purpose	Drug-disease interaction. Treatment of Depression in patient with renal failure	Disease-Disease interaction
Description of the purpose	Patient with depression on an MAOI caution with hypertension & renal disease. At what point should the MAOI be stopped?	Patient with chronic RF should be reviewed for signs & symptoms of depression
Type of purpose	Ac_Drug	Risk assessment
Clinical condition	RENAL FAILURE + DEPRESSION	RENAL FAILURE + DEPRESSION
Concept/codes	eGFR ICD-10 for Renal failure and Depression	Depression scale - PHQ-9 ICD-10 for Renal failure and Depression
Rule description	If EGFR is <30 - MAOI should be stopped	If depression scale is 5+ treat as/for depression
Trigger	Each time RF is inputted for a patient on MAOI	6 monthly assessment (year 1) then yearly
Input	eGFR & whether patient on MAOI	Depression scale & renal failure
Output	Alert to stop MAOI if EGFR <30	Alert to consider treatment if score sufficient
Reference	NICE BNF Kidney International 2012:Feb;81(3):247-55 - Practical Apporach to treating depression in pts with RF	NICE Kidney International 2012:Feb;81(3):247-55 - Practical Apporach to treating depression in pts with RF
Notes	First a generic warning is needed if GRF falls <30 as we can't say that the decision support rules are validated any longer. In very rare cases of drug intolerance a MAOi could potentially be used but not lithium as I see it. Should only adjust with the MAOIs? Almost all antidepressants require some dose adjustment in Renal Failure.	RF used fro CRF (Chronic renal Falilure) and CKD (Chronic Kidney Diseases)
Peer review agreement	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision". To be handled by the drug interaction module (external database).	The reference document Kidney International is accepted to be used as Reference document together the NICE guideline for renal failure.

Rule	Rule 3	Rule 4
Context	Interaction between a medication & co-morbidity	Interaction between a medication & co-morbidity
Purpose	Drug-disease interaction Treatment of Depression in patient with renal failure	Drug-disease interaction Dose adjustment

Rule	Rule 3	Rule 4
Description of the purpose	If patient has RF and an anti-depressant is prescribed for depression, it can cause arrhythmias	Dose adjustment if anti-depressant used in patients with chronic kidney disease
Type of purpose		Pharmacotherapy
Clinical condition	RENAL FAILURE + DEPRESSION	RENAL FAILURE + DEPRESSION
Concept/codes	Depression scale - PHQ-9 with Pete ICD-10 Depression AND (ICD-10 RF) OR EGFR<60) EGFR ATC-any antidepressant??	eGFR ICD-10 Depression
Rule description	If patient has RF & depression an SSRI should be the anti-depressant of choice	If patient has RF & depression, anti-depressant requires dose adjustment (as per British Columbia Provincial Regions Agency Advice Sheet - broken down by type of anti-depressant and then by individual drug & level of RF) - http://www.bcrenalagency.ca/resource-gallery/Documents/Antidepressant%20Use%20in%20Adults%20with%20Chronic%20Kidney%20Disease.pdf
Trigger	Decision to treat depression *???* *Each time Any Antidepressant is prescribed???* *ATC other than SSRI?? First prescription, prorrogue??* **SWFT -** agree, rule applied each time an anti-depressant is prescribed	Each time RF inputted for patient on anti-depressant
Input	Depression scale & renal failure ATC or substance name	
Output	Alert to suggest SSRIs	
Reference	NICE Kidney International 2012:Feb;81(3):247-55 - Practical Apporach to treating depression in patients with RF	
Notes	Several possible triggers to make "decision to treat" computer readable (understandable): would any of the suggested ones be valid?	Each antidepressant has its own recommendations according to eGFR Inclusion and exclusions criteria can be different for the recruitment and during the trial. Tha patient can worsen during the piloting.
Peer review agreement	The reference document Kidney International is accepted to be used as Reference document together the NICE guideline for renal failure.	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"

Rule	Rule 5
Context	Disease-Disease Interaction
Purpose	Disease-Disease interaction Diagnosis/Risk assessment
Description of the purpose	Tiredness can be due to renal failure rather than depression
Type of purpose	
Clinical condition	RENAL FAILURE + DEPRESSION

Rule	Rule 5
Concept/codes	Symptom code for tiredness/fatigue
Rule description	IF(symptoms code for tiredness OR fatigue present) THEN consider deteriorating renal function AND (Check renal function & Hb)
Trigger	Symptom code for tiredness/fatigue
Input	Symptom code for tiredness/fatigue
Output	Alert responsible clinician to check renal function and Hb
Reference	RF NICE guidance
Notes	
Peer review agreement	

ANNEX 7 FINAL RECONCILED RULES FROM TWO DISEASES (DEPRESSION AND HEART FAILURE) COMBINATION

9 rules have been reconciled for this disease pair.

Rule	Rule 1	Rule 2
Context	Identify interaction between a medication and co-morbidity	Identify interaction between a medication and co-morbidity
Purpose	Treatment of Depression in patient with heart failure	Treatment of Depression in patient with heart failure
Description of the purpose	Avoid risk in patients with uncompensated HF receiving antidepressant treatment	Avoid risk in patients with HF receiving antidepressant treatment
Type of purpose	Pharmacotherapy/ Ac_Drug FHIR Goals catergories=Safety	Pharmacotherapy/ Ac_Drug FHIR Goals catergories=Safety
Clinical condition	DEPRESSION + HEART FAILURE	DEPRESSION + HEART FAILURE
Concept/codes	ICD-10 Depression AND ICD-10 Heart Failure AND (ATC citalopram or escitalopram)	ICD-10 Depression AND ICD-10 Heart Failure AND (ATC tricyclic antidepressant)
Rule description	IF ICD-10 Depression AND ICD-10 Heart Failure AND (ATC citalopram or escitalopram is PRESCRIBED (STARTED OR PRORROGED) THEN ALERT Not recommended in patients with uncompensated HF: Dose-dependent QT prolongation risk ;	IF ICD-10 Depression AND ICD-10 Heart Failure AND (ATC tricyclic antidepressant is PRESCRIBED (STARTED OR PRORROGED) THEN ALERT risk of cardiovascular side effects including postural hypotension and arrhythmias
Trigger	Each time citalopram or escitalopram is prescribed	Each time tricyclic antidepressant is prescribed
Input	ATC or substance name	ATC or substance name
Output	ALERT =Not recommended in patients with uncompensated HF: monitor for cardiac arrhythmia signs	ALERT =risk of cardiovascular side effects including postural hypotension and arrhytmias
Reference	Circulation. 2016; 134:e32-e69 https://crediblemeds.org	Circulation. 2016; 134:e32-e69 NICE guidance/cg90 and cg91 STOPP criteria
Notes	Only includes alerts for drugs QT/TdP Risk Categories= KRT (Known Risk of TdP, torsades de pointes) Outside the scope of C3-Cloud (inclusion criteria), but the patient might develop during the trial.	
Peer review agreement	"Please, take this rule as a suggestion. As it is about out of the scope of the project, further research should be carried out before making a clinical decision"	

Rule	Rule 3	Rule 4
Context	Identify interaction between a medication and co-morbidity	Identify interaction between a medication and co-morbidity
Purpose	Treatment of Depression in patient with heart failure	Treatment of Depression in patient with heart failure
Description of the purpose	Avoid risk in patients with HF receiving antidepressant treatment	Avoid risk in patients with HF receiving antidepressant treatment
Type of purpose	Pharmacotherapy/ Ac_Drug FHIR Goals catergories=Safety	Pharmacotherapy/ Ac_Drug FHIR Goals catergories=Safety

Rule	Rule 3	Rule 4
Clinical condition	DEPRESSION + HEART FAILURE	DEPRESSION + HEART FAILURE
Concept/codes	ICD-10 Depression AND ICD-10 Heart Failure AND (ATC venlafaxine or desvenlafaxine or duloxetine)	ICD-10 Depression AND ICD-10 Heart Failure AND (ATC venlafaxine or desvenlafaxine)
Rule description	IF ICD-10 Depression AND ICD-10 Heart Failure AND (ATC venlafaxine or desvenlafaxine or duloxetine is PRESCRIBED (STARTED OR PRORROGED) THEN ALERT risk of exacerbation of hypertension; monitor blood pressure	IF ICD-10 Depression AND ICD-10 Heart Failure AND (ATC venlafaxine or desvenlafaxine is PRESCRIBED (STARTED OR PRORROGED) THEN ALERT higher doses can exacerbate cardiac arrhythmias
Trigger	Each time venlafaxine or desvenlafaxine or duloxetine is prescribed	Each time venlafaxine or desvenlafaxine is prescribed
Input	ATC or substance name	ATC or substance name
Output	ALERT =risk of exacerbation of hypertension	ALERT =risk of exacerbation of hypertension; monitor blood pressure
Reference	NICE guidance/cg90 and cg91	NICE guidance/cg91
Notes	Desvenlafaxine: although not cited in NICE cg90: same recommendations as for venlafaxine	Desvenlafaxina: although not cited in NICE cg90: same recommendations as for venlafaxine
Peer review agreement		

Rule	Rule 5	Rule 6
Context	Identify interaction between a medication and co-morbidity	Identify disease-disease interaction
Purpose	Treatment of Depression in patient with heart failure	Risk assessment of Dp in HF
Description of the purpose	Avoid risk in patients with HF receiving antidepressant treatment	depression identification in a HF patient
Type of purpose	Pharmacotherapy/ Ac_Drug FHIR Goals categories=Safety	Ac-Procedure
Clinical condition	DEPRESSION + HEART FAILURE High blood pressure	DEPRESSION + HEART FAILURE
Concept/codes	ICD-10 Depression AND ICD-10 Heart Failure AND ATC (venlafaxine or desvenlafaxine)	ICD-10-HF
Rule description	IF ICD-10 Depression AND ICD-10 Heart Failure AND (ATC bupropion is PRESCRIBED (STARTED OR PRORROGED) THEN ALERT "Monitor blood pressure, STOP bupropion if clinically relevant increase in blood pressure occurs"	IF ICD 10 HF THEN consider Dp diagnosis
Trigger	Each time bupropion is prescribed	When HF diagnosis is made (ICD-10 HF)
Input	ATC or substance name	ICD-10 HF
Output	ALERT ="Monitor blood pressure, STOP bupropion if clinically relevant increase in blood pressure occurs"	Consider the diagnosis of Depression
Reference	Technical Note of bupropion **SWFT -** agreed	NICE HF CG108 (D7.1 fig 27)
Notes		

Rule	Rule 5	Rule 6
Peer review agreement		

Rule	Rule 7	Rule 8
Context	Identify disease-disease interaction	Identify disease-disease interaction
Purpose	Depression treatment in HF	Depression treatment in HF
Description of the purpose	Antidepressant psychosocial intervention for depression in HF patients	Indication for pharmacological treatment in a patient with CHFand Dp
Type of purpose	Ac-Procedure	Ac-Pharmacotreatment
Clinical condition	DEPRESSION + HEART FAILURE	DEPRESSION + HEART FAILURE
Concept/codes	ICD-10-Dp;ICD-10-HF	ICD-10-Dp;ICD-10-HF
Rule description	IF ICD-10 Dp AND ICD-10 HF THEN Prescribe low intensity Psychosocial interventions	IF ICD-10 Dp AND ICD-10 HF AND no response to psychosocial treatment THEN Consider antidepressant
Trigger	When diagnosis is made (ICD-10 CODES for Dp and HF)	When diagnosis is made (ICD-10 CODES for Dp and HF)
Input	ICD-10 HF and Dp	ICD-10 HF and Dp
Output	Refer for low intensity antidepressant psychosocial interventions	Consider antidepressant
Reference	NICE Dp CGL (D7.1 fig 40)	NICE HF CG108 (D7.1 fig 27)
Notes	treatment :group exercise, interpersonal treatment ,Cognitive Behavioral Therapy CBT. When HF, option should be "exercise".	
Peer review agreement		

Rule	Rule 9
Context	Identify disease-disease interaction
Purpose	Depression and HF follow up
Description of the purpose	Reconcile follow up schedule in a patient with HF and Dp
Type of purpose	AC-Encounter
Clinical condition	DEPRESSION + HEART FAILURE
Concept/codes	ICD-10-Dp;ICD-10-HF
Rule description	IF ICD-10 Dp AND ICD-10 HF AND stable patient THEN Follow up /3 month
Trigger	Every encounter with HC professional
Input	ICD-10 HF and Dp
Output	FOLLOW UP / 3 MONTH
Reference	NICE HF CG108 (D7.1 fig 26)
Notes	
Peer review agreement	

ANNEX 8 FINAL RECONCILED RULES FROM THREE DISEASES (DIABETES, RENAL FAILURE AND HEART FAILURE) COMBINATION

1 rule has been reconciled for this disease triplet.

Rule	**Rule 1**
Context	Follow up of the patient with diabetic nephropathy and heart failure
Purpose	Disease-Disease interaction. Frequency of appointments/encounters with health care professionals
Description of the purpose	Follow up pattern for a patient with DM2, nephropathy 1-3a and heart failure
Type of purpose	Ac_Encounter
Clinical condition	DIABETES + RENAL FAILURE + HEART FAILURE
Concept/codes	ICD-10 Diabetes; eGFR; ICD-10 heart Failure
Rule description	If the patient has DM, RF AND HF: If ICD-10 Diabetes AND eGFR >45 y < 60 THEN check Egft three times per year
Trigger	Each encounter of the patient with the health care professional
Input	eGFR and ICD-10 diabetes and heart failure
Output	Program one 3 appointments per year with the appropriated healthcare professional
Reference	NICE Figure 33 (5.4.7. Frequency of eGFR control-RF)
Notes	Similar to rule 8 of Diabetes and Renal Failure
Peer review agreement	It is agreed to keep 3 appointments per year with the appropriated health care professional (differences among pilot sites) Local frequency of follow up appointments should be followed the NICE guidelines. However they are not always included. In that case, the NICE guidelines recommendations for the follow up appointments will be adapted to the local situations (for single and combined diseases).

ANNEX 9 FINAL RECONCILED RULES FROM FOUR DISEASES (DIABETES, RENAL FAILURE, HEART FAILURE AND DEPRESSION) COMBINATION

1 rule has been reconciled for this 4-disease combination.

Rule	**Rule 1**
Context	Follow up of the patient with renal failure, heart failure and depression
Purpose	Disease-Disease interaction. Frequency of appointments/encounters with health care professionals
Description of the purpose	Follow up pattern for a patient with DM2, nephropathy 1-3a, heart failure and depression
Type of purpose	Ac_Encounter
Clinical condition	DIABETES + RENAL FAILURE + HEART FAILURE + DEPRESSION
Concept/codes	ICD-10 Diabetes;eGFR; ICD-10 heart Failure; ICD-10 Depression
Rule description	If the patient has DM, RF, HF and Dp: If ICD-10 Diabetes, Heart Failure, Depression AND eGFR >45 y < 60 THEN check Egft three times per year
Trigger	Each encounter of the patient with the health care professional
Input	eGFR and ICD-10 diabetes and heart failure and depression
Output	Program one 3 appointments per year with the appropriated healthcare professional
Reference	NICE Figure 33 (5.4.7. Frequency of eGFR control-RF)
Notes	Similar to rule 8 of Diabetes and Renal Failure
Peer review agreement	It is agreed to keep 3 appointments per year with the appropriated health care professional (differences among pilot sites) Local frequency of follow up appointments should be followed the NICE guidelines. However they are not always included. In that case, the NICE guidelines recommendations for the follow up appointments will be adapted to the local situations (for single and combined diseases).