An Integrated Solution for Sustainable Care for Multimorbid Elderly Patients with Dementia

WP3: Foundation of the Clinical Decision Support Services for the Management of Multimorbid Elderly Patients with Dementia

D3.1: A Computer Interpretable Guidelines Specification of the Complete CAREPATH Decision Support Logic

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Executive Summary

The deliverable 3.1 presents the process that contributes to the “Foundations of the Clinical Decision Support Services for the management of multimorbid elderly patients with dementia” to define the “Patient-oriented Computer Interpretable Clinical guideline modelling”. The main objective of WP3 is to establish the foundations of the Clinical Decision Support tools to be employed in CAREPATH, based on the consolidated guidelines recommended by WP6.

The first release of this deliverable on M8 covered the conceptual methodology for modelling clinical practice guidelines, an overview of the clinical decision support service architecture, and how the clinical decision support services will be specified.

The current release of D3.1 covers the final implemented methodology for rule-based modelling of Computer Interpretable Guidelines (CIG) from the clinical master guideline, as well as the process of transforming consolidated holistic clinical guideline to computer interpretable guidelines which are implementable in clinical decision support module (CDSM) resulting in a patient-centred and customized care. It is based on deliverable 6.2 provided by clinical partners, as a collection of selected guidelines agreed to be used as guidance and actions within the master holistic consensus guideline.

Finally, the developed rules and flowcharts are presented for implementation in Tasks 3.2, 3.4 and 4.5. All guidelines and their rule-based models for mild cognitive impairment (MCI) and mild dementia as well as relevant multimorbidities within the CAREPATH project have been addressed in this document.

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Abbreviations

AICP	Adaptive Integrated Care Platform
CAREPATH	An Integrated Solution for Sustainable Care for Multimorbid Elderly Patients with Dementia
CDS	Clinical Decision Support
CIG	Computer Interpretable Guideline
CPG	Clinical Practice Guideline
CRG	Clinical Reference Group
EHR	Electronic Health Record
FHIR	Role Based Access Control
HTTP	Hyper Text Transfer Protocol
ICD	International Classification of Diseases
M1/M16	Project Month 1 / Month 16
PEP	Patient Empowerment Platform
RBAC	Role Based Access Control
UML	Unified Modelling Language
WP	Work Package
LOINC	Logical Observation Identifiers Names and Codes
ATC	Anatomical Therapeutic Chemical
HF	Heart Failure
CKD	Chronic Kidney Disease

1. Introduction

1.1 Document Scope

The goal of Task 3.1 'Patient-oriented Computer Interpretable Clinical guideline modelling' is to model clinical practice guidelines so they can be executed as computer interpretable guidelines, to guide clinical decision-making based on evidence-based guidelines. Figure 1 shows the overview for Task 3.1 and its dependencies on other work packages in the CAREPATH project.

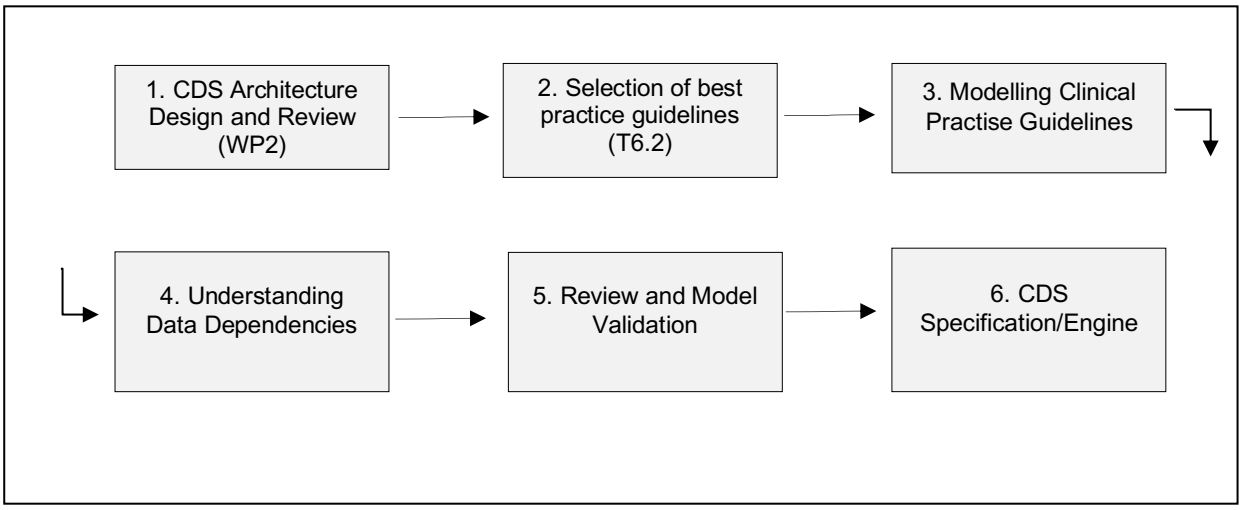

Figure 1: Overview of Task 3.1 and Dependencies

While WP2 focuses on specification of the overall architecture, including the Clinical Decision Support (CDS) module, and how it will interact with the rest of the CAREPATH infrastructure, this work package (WP3) aims to develop patient-oriented computer interoperable clinical guidelines. In the case of computer interpretable guidelines (CIG), this includes how the CIGs will be communicated with the rest of the modules (output), including the API for data that CIG will need (input). This affects the work in T3.1 as the task will annotate the guideline models with elements of these specifications. For example, the modelled guidelines will be annotated using semantic interoperability standards (e.g., ICD-10 codes) to avoid ambiguity on clinical terms. Examples of other such standards include the FHIR resources from which information will be retrieved, and the CDS-hooks cards (1) that will be produced at each step of the guideline algorithm.

Task 6.2 is the task that identifies the best practice guidelines that will be adapted and modelled into the CAREPATH guidelines, from the review of relevant guidelines identified in D6.1. The task integrates relevant guidelines, reconciling potential conflicts, resulting in the CAREPATH integrated guidelines. Task 3.1 then unpacks the decision making in the CAREPATH integrated guidelines and models them as algorithms using flowcharts and activity diagrams. This has explicitly modelled every decision and path a patient may follow during their care. Where the guidelines are not clear, input has been elicited from the CAREPATH Clinical Reference Group (CRG) in WP6. If the pilot sites have identified aspects that need to be implemented differently in their local setting, these will be recorded as localizations. Use of the model-based approaches enable clear and traceable documentation of these variations.

Following specification of the decision-making logic, the task annotates parts of the models with terminological codes for medical concepts, medications, as well as the FHIR resources (2) from which the data will be taken. This allows unambiguous specification of what concepts the guidelines refer to, and which data elements correspond to each decision. This is a key step, as the models created are in a form that is appropriate for review and validation by the CRG. Additionally, by identifying the data elements that are needed from the FHIR repository, the task also

provides early specification of the requirements on pilot sites, with regards to integrating their Electronic Health Records with the CAREPATH FHIR repository, thus de-risking the deployment task (Task 4.8). The guideline models are reviewed and validated by the CRG and clinicians at the pilot sites (according to the integration protocol of each site).

Finally, the annotated CAREPATH guideline models will be used by Tasks 3.2 and 3.4 for definition with CDS Hooks specification and by Task 4.5 for implementation as executables in the CDSS engine. Task 3.1 is crucial to the verification and validation of the CDSS, as the models that will be produced will be the link between the validation offered by the CRG, and the requirements provided to the CDS technical team. All rules, decisions, and algorithms in the models should be fully traceable to the code in the implementation. The model specification can therefore act as the requirements for the CDSS. Hence, the technical teams can verify that their implementation is what was specified in the models to a very high degree of confidence. Furthermore, the models are to be reviewed and approved by the CRG, hence, offering high degree of confidence in its validity. This is enabled by the increased comprehensibility of models, as they break down and visualize information that may be difficult to review as text, which could result in ambiguities.

1.2 Document Structure

The deliverable describes the process of analysing clinical master guideline, developing rule-based models, and review and validation of these developed models through the methodological approach for development of CIGs in detail. Finally, the process and steps for development of CIGs in CAREPATH project is presented. The collection of refined rules for each morbidity is provided as appendices.

For reference, Release 1 of D3.1 is provided in Annex A.

1.3 Clinical Decision Support System (CDSS)

Clinical Decision Support Systems (CDSS) provide decision support aids offering treatment suggestions, carry out risk assessments and provide guidance about polypharmacy management as well as being utilized by the Adaptive Integrated Care Platform (AICP) during the creation and update of care plans. The CDSS also includes an Early Warning System (EWS), utilising algorithms built using machine learning techniques to identify potentially preventable situations.

- **Suggestion for Clinical Guidelines:** In CAREPATH, we will build clinical decision support services to deliver personalized guidance to healthcare professionals about the goals and interventions (treatment actions, patient monitoring activities and lifestyle management activities) that can be put into the active care plan of the patient. These suggestions will be built upon the recommendations of the clinical guidelines to achieve patient-centred and customised care. The exact content of Clinical Decision Support Systems (CDSS) to be implemented in CAREPATH depends on the output of Task 6.2 in which a holistic patient centred CAREPATH best practice guideline will be established. Task 3.1 delivers the rules that will be implemented as clinical decision support services based on the holistic clinical guideline flow. The architectural design of the CDSS for clinical guideline suggestions, from a technical perspective is defined in D2.3 Section 3.3.4.

2. Definition of CAREPATH Guideline

Candidate guidelines have been identified in D6.1, such as guidelines for frailty, which are reviewed and cross referenced against current practice at pilot sites. Additional guidelines have also been considered for example, the guidance using concept of intrinsic capacity. Task 6.2 has assessed the guidelines identified in D6.1 to create a consensus guideline for the project, also taking into account local variations at the sites. The second release of

this deliverable (this document) models these guidelines after these have been defined in deliverable 6.2 (the latest version of the document is dated 25 October 2022 (D6.2 version 1v5) and is reflected in the rules defined in this document).

The review of the formalised guidelines has been undertaken by the CRG, liaising with local clinicians where applicable. Identification of variation in terms of process, clinical decision making, as well as representation and use of semantic interoperability concepts is modelled. The task received the consolidated guidelines from WP6, which represented best practice. Task 3.1 transformed the clinical guidelines into models amenable to ICT software execution. The task employed state of the art Computer Interpretable Guideline practice, to model the flow, information dependencies, as well as decisions that need to be made by the software. The logic of the guidelines also identified the information, which when implemented will result in patient-centred and customised care. The task also enriches the decision-making based on clinical guidelines, with information that is collected by the Patient Empowerment Platform as well as the Home Monitoring Platform. With input from WP6 the task developed a specification of how passively collected data can satisfy the various conditions of decision-making, allowing the pathways to automatically progress using the collected data, and offer recommendations. The task also identified the data types missing to make decisions in line with the guidelines, and review with WP6 how actively collected data such as patient reported outcomes can be used to fill the gap and result in decisions. As part of this, Task 3.1 liaised with the Clinical Reference Group (CRG) and WP2 to evaluate whether data collection is compliant with the project data handling objectives. These specifications will be implemented within the scope of Task 4.5.

3. Modelling Clinical Practice Guidelines

This deliverable is updated with rules, flowcharts and activity diagram from the Interim M8 Release through to the M16 Final release. Semantic interoperability (coding) allocation, and review by clinicians' disambiguation of concepts and assignments of codes was considered. This was performed by the clinical reference group. Rules are documented with a rule-based modelling approach.

3.1 Rule-Based modelling (automation) approach

A rule-based model a collection of rules defined to be processed by general-purpose simulation and analysis tools to result in a variety of outcomes and perform deterministic or stochastic simulation.(3)

In rule-based (rule-based automation) (4) the system uses human-made rules to record, sort and manipulate data by simulating human intelligence. They require a collection of facts or source of data, and a set of rules to work with (5). The If-Then-Else statements are a common format for rule-based automation. This format allows conditional execution based on the evaluation of an expression and is generally used in non-complex conditional tests. An important advantage of rule-based models is that they are easy and familiar for clinician to use and interact. So, we used it as the base format to develop our CIGs.

3.2 UML activity diagram and flowchart formation approach

The Unified Modelling Language (UML) is a general-purpose modelling language (6) and UML Diagrams can be grouped into two main types, structural and behavioural. These approaches were used when necessary to achieve higher understanding of guidelines and appropriate care pathways as complementary approaches in CAREPATH project.

3.2.1 When to Use Activity Diagrams

Activity Diagrams describe how activities are coordinated to provide a service which can be at various levels of abstraction. Typically, an event needs to be achieved by some operations, particularly where the operation is

intended to achieve several different things that require coordination, or how the events in an individual use case relate to one another where activities may overlap and require coordination. They are also suitable for modelling how a collection of use cases coordinates to represent business workflows, an example of how an activity diagram for this might be developed is given below:

1. Identify candidate use cases, through the examination of business workflows
2. Identify pre- and post-conditions (the context) for use cases
3. Model workflows between/within use cases
4. Model complex workflows in operations on objects
5. Model in detail complex activities in a high-level activity Diagram

An activity diagram is an important behavioural diagram in UML, used to describe dynamic aspects of the system. Activity diagrams are an advanced version of flow charts that model the flow from one activity to another.

Below in Figure 2, we show an example flowchart of Antidiabetic medication flow for Diabetes CDS service, based on CAREPATH master guideline.

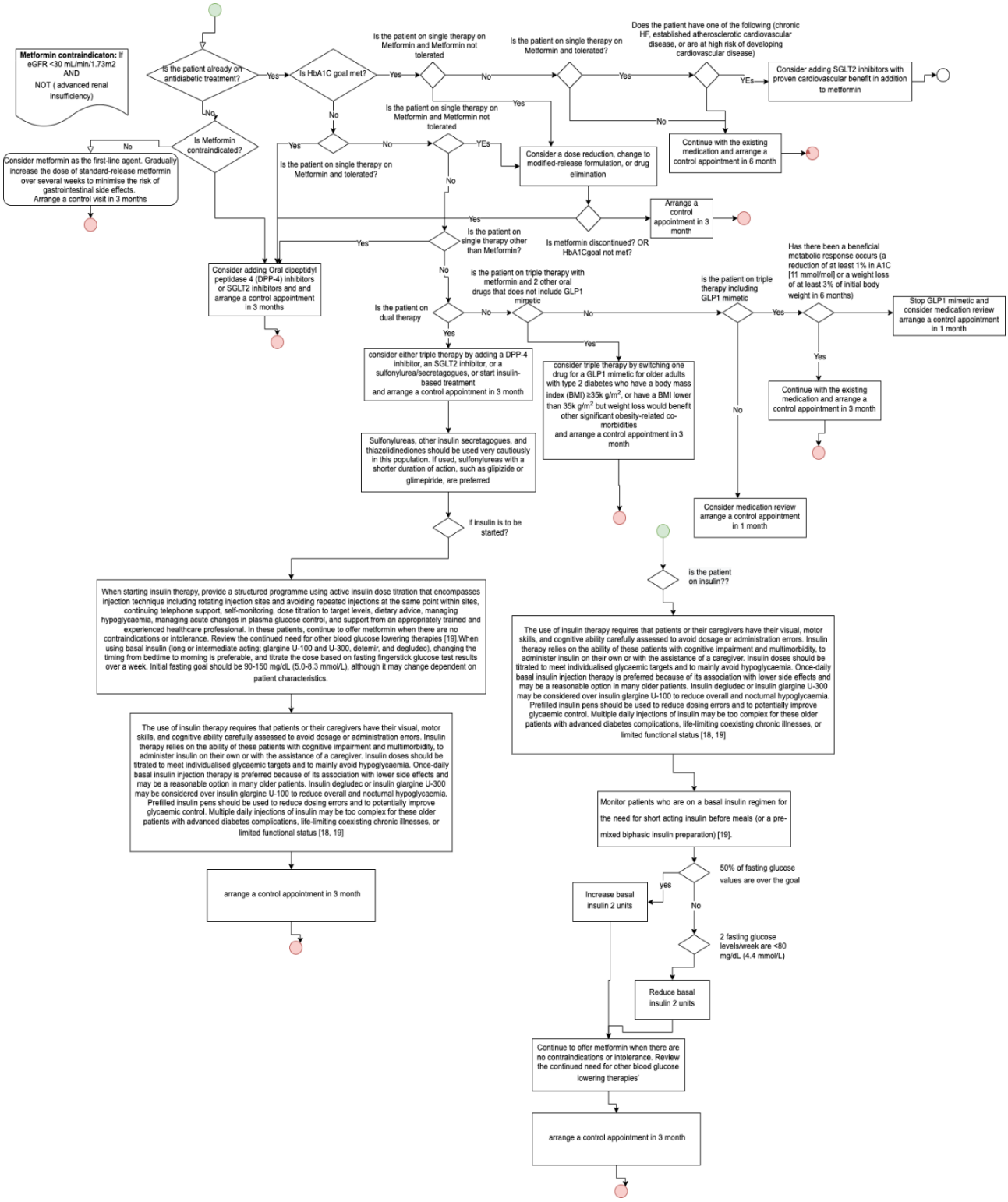

Figure 2- Antidiabetic medication flow

4. Review and Validation of Models

The clinical reference group, primarily supported by the local sites, examined the guidelines and the scenarios of use to identify where the guidelines may fall short of information. Clinicians needed to understand the gaps and conflicts between single disease guidelines and offer an integrated guideline covering the main conditions being investigated within CAREPATH. This involves another subprocess including identification of care plan, and medication conflicts which needed to be reconciled. Reconciliation happened at various levels: a) guideline, static and documented reconciliation, b) CDS based dynamic reconciliation e.g., drug to drug interactions and c) clinical expertise and judgment reconciliation when the professional need to assess the plan and discuss it with other experts to find consensus. The project completed a and b (to an extent) and we offer the tools for c). Task 3.1 does not provide any clinical content but facilitates validation of the consolidated guidelines through providing the rule-based guideline models for review by the CRG.

4.1 Reference Guidelines

The development of the clinical guidelines and best practices for improved management of older patients with dementia and multimorbidity was performed in CAREPATH Work Package 6 [WP6]. Clinical partners within the consortium were the working group for this section of the project. In this context, it was necessary to identify evidence in existing guidelines to extract and consolidate into an overarching consensus guideline that could then be formulated into a computer interoperable rule. The conditions and diseases decided to be covered were frailty, sarcopenia, physical exercise, nutrition and hydration, commonly used drugs, diabetes, heart failure, Chronic Obstructive Pulmonary Disease (COPD), Chronic Kidney Disease (CKD), stroke, coronary artery disease, and hypertension. Also included were multimorbidity and co-morbidity guidelines, guidelines covering dementia and Alzheimer's disease, and behavioural guidelines.

CAREPATH also includes the implementation of a polypharmacy and drug-drug interaction module as part of its CDS, which is going to be implemented in Task 3.2 in parallel to holistic guideline implementation in CDS module.

4.2 Role of CRG

The analysis work of the guidelines identified in D6.1 has been performed in Task 6.2. By detailed analysis of the texts the CRG has studied the relevant guidelines from D6.1 and selected those relevant to be included in the CAREPATH CDSS. They will also support the development of rules and flowcharts for the CAREPATH guidelines. The CRG/sites undertook the following activities:

1. Summarized the result of the reviewed guidelines with reference to the original clinical guideline/chapter for validation.
2. Made a joint agreement of what recommendations should be used and note any local variations to be considered.
3. Review and confirmed the annotations used in the models, disambiguating potential medical concepts covered by the same term. Code annotation will also contribute to accurate translation of content for deployment in each pilot site.
4. The representatives of each pilot site on the CRG distributed the guideline models to appropriate stakeholders in their pilot site, approving the guidelines for deployment, or suggesting customizations.

4.2.1 Develop rules and flowchart diagrams

The clinical partners cooperated in developing if-else-then programming rules and where needed, flows structured in decision trees for the clinical guidelines, with help and feedback from technical partners. These rules and flowcharts represent all the decision making of the collated guidelines.

4.2.2 Review of formalized guidelines

The CRG reviews the formalised guidelines produced by technical partners to assure their validity/interpretation.

5. Methodological approach for development of CIGs

To achieve high levels of improved patient outcome and clinical adherence, the process of translating CPGs into CDSSs should be pursued with sophisticated methodologic considerations. This section describes the methodological aspect of this process and the relevant considerations.

Three phases should be completed to accomplish the patient-centred computer interpretable guideline (CIG) modelling, which include conceptual modelling phase, interpretable modelling phase and localization phase (Figure 3).

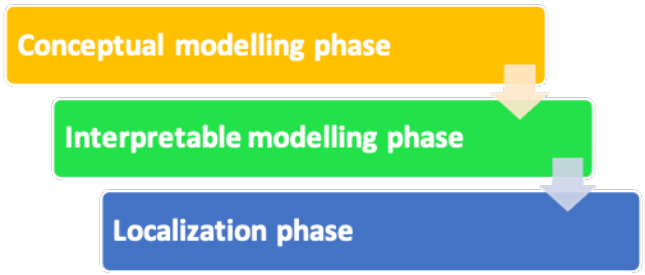

Figure 3- Patient-centred computer interpretable guideline (CIG) modelling phases

5.1 Conceptual modelling phase

Conceptual modelling phase is the first step in the modelling process. We construct a conceptual model and business process based on the holistic clinical guideline developed by the clinicians through D6.2 in the CAREPATH project. In this phase, we intend to format the consensus guideline as small chunk of human readable/Understandable sentences, statements, rules, flowcharts and diagrams.

These sentences, statements, rules, flowcharts, and diagrams are then implemented in the system through human readable decision rules, system and users' states and actions. Guidelines in this phase should be prepared for the next steps where they will become both readable by human and transformable to computer interpretable rules. They also need to be appropriate for technical aspects of local adoption by different healthcare pilot sites throughout the project. Clinicians should provide necessary explanations, evidence and documents to facilitate developing CIGs and validate the final output.

The conceptual model is presented as clearly noted questions for clarification and later basic IF-THEN-ELSE rules should be replaced showing all components, including actions, decisions, patient state and execution state in a non-technical format. The inputs to the decision points as patient data should be clearly identified. The output should be later approved by the project's clinical reference group to assure their validity. Details such as patient data elements and sources, clinical actions output format and guideline technical flow are not needed to be addressed at this stage, whereas ontologic and standard term binding should be specified by setting the references to standard terminologies, controlled vocabularies and coding systems.

5.2 Interpretable modelling phase

When the conceptual modelling phase is completed, the technical team would be ready to start formulating the output and move towards the development of the interpretable model of the CDS.

In the first step of this phase, CDS are implemented through rule-based models. A rule-based model identifies and formulates relationships between the CDS module to be developed and the clinical approaches. It could be easily used to specify the boundaries, audiences, sources and involved parts and platforms of the system and the different interactions implemented in the realization of clinical and medical requirements. Logical rules are particularly helpful to establish a dialog between clinicians and developers, and helpful as a basic tool used to formalize functional requirements of the system.

We start with our holistic, integrated guideline as our main source of actions. Every rule must be linked to at least one actor and cover at least one added value in the target health management process. By the means of these models, technical partners are able to demonstrate categorized system pathways, triggers (e.g., adding a new patient, prescribing a drug, ordering a laboratory test, or entering a new problem on the problem list etc.), inputs (e.g., patient demographics, patient test results, drugs lists, states), interventions and outputs.

In the second step of interpretable modelling phase, where a higher business understanding is needed, business process models are developed, which are defined as a sequence of actions carried out by different actors working together to deliver a tangible result and achieve the expected added value. Generally, in UML-based approaches, business processes are routinely represented using activity diagrams. However, in CAREPATH, we prefer to use Business Process Modelling Notation (BPMN), which is easier to use and being understandable by various stakeholders. In the CAREPATH project methodology, we use business processes in combination with guideline flowcharts to extract more details about what has been determined from rules. These may include but are not limited to decision tree pathway identification, the trigger event in any decision node, switching and changing in states and actors and the expected results or targeted objectives. The input and output parameters of CDSs is conceptualized based on the guidance of CDS Hooks specification.

The third step is about extracting rules and actions definition and implementation tables. Because refined texts generally describe the business and not the IT system, there is a need to translate any nodes and pathways into rules and action records format. It would be preferable to present them in preformatted templates.

5.3 Localization phase

At this phase, models are ready to be implemented as pilot CDS and then should be customized based on the clinicians' opinion for different settings of pilot sites in implementation phase. This should be done in collaboration with the technical team and with consideration of legislative and ethical issues. When adaptation is completed, the final implementation can begin.

Localization consists of adaptation of inputs and outputs of CDS module and contents in accordance with the language, cultural and other specifications of the intended target settings.

6. Process and steps for development of CIGs in CAREPATH

In CAREPATH, we intend to elaborate the holistic, integrated clinical guideline for implementation in Clinical Decision Support (CDS) through a customized rule-based approach. The CDS modelling process is an organized, technical methodology with a formal demonstrated model as an output. The technical team performs CDS modelling by means of rule-based approach, and if necessary, flowcharts or business processes diagrams.

The conceptualizing phase, which was the most fundamental step in master guideline analysis, starts with the content classification process.

6.1 Preliminary Phase in CAREPATH CIG development process

Technical partners participated and collaborated in the process and meetings for developing master narrative draft guideline along with clinicians, to address the areas of conflict and technical feasibility questions regarding conversion of the narrative guideline into a clinically interoperable digital guideline. This activity helped achieving an optimal clinical master guideline and made the opportunity to reach a better understanding on the process and goals of the tasks among different teams. There were several coding systems applicable in this task, including ICD and SNOMED. We developed the process based on ICD system of coding as it was more often used by our partners in the pilot sites, widely present in the EHRs and more familiar for our partner clinicians.

Another important point to discuss and conclude before running into the process of analysing the master guideline, was the application of common standard and internationally accepted coding systems in electronic patient record and within the rules. The joint use of standard coding systems, along with formal and conceptual homogenization of data, provides the possibility of automatic identification of many elements required in CDSS and prevents multiple questions from the patients, caregivers, and the clinicians. By using these codes, the early warning system will also work more efficiently. So, among WP3 meetings, this issue raised and finally agreed to send and receive data based on three international coding systems as follows:

- ICD-10 (International Classification of Diseases) which is a globally used diagnostic tool for epidemiology, health management and clinical purposes. The ICD is maintained by the World Health Organization, which is the directing and coordinating authority for health within the United Nations System.
- ATC codes (Anatomical Therapeutic Chemical) and classification which was developed in Norway as a modification and extension of the European Pharmaceutical Market Research Association (EphMRA) classification system. In ATC coding system a unique code assigned to a medicine according to the organ or system it works on and how it works.
- LOINC (Logical Observation Identifiers Names and Codes) which is a database and universal standard for identifying medical laboratory observations.

6.2 Conceptual modelling phase in CAREPATH

6.2.1 Decision/Command Block classification and extraction process

In the first step, master guideline content was classified based on concept relation and context similarity. After overviewing and holistic analysis of the master guideline, technical partners decided to put the main classification axis on co-morbidities. This decision was made because the structural formation of the D6.2 was based on morbidities in CAREPATH project. The main strengths behind this approach were:

- Each section could be assigned to the relevant specialists to be evaluated for maximum validity in the formulation process.

- The responsible partners and persons in final document preparation of each section were simply identifiable and available for later help through content analysis.
- This classification was in accordance with D6.2.
- Statements, conditions and actions in these sections were completely coherent within base morbidity.
- Continuity of content was completely logical and was kept intact.

Based on this classification approach master guideline document classified to below mentioned sections:

- Mild Cognitive Impairment or Mild Dementia management
- Physical Exercise
- Nutrition and Hydration
- Commonly used drugs
- Frailty and Sarcopenia
- Coronary Artery Disease
- Heart Failure
- Hypertension
- Diabetes
- Chronic Kidney Disease
- Chronic Obstructive Pulmonary Disease
- Stroke
- Caregiver support

Then these sections were distributed to technical partners for the next level content analysis. Through this level, content of each section was fragmented to small chunks of human readable/Understandable statements. In this process, all the contents were kept without any additions, deletions, or changes. These separated parts were all complete sentences and totally meaningful based on original content.

Original Guideline	Fragmented Guideline
Section 16 - Stroke	
Stroke **16.1 Assessment:** • Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24). **16.2 Diagnosis:** • In patients suspected of having a stroke or TIA, Computed Tomography or Magnetic Resonance Imaging of the brain is recommended to confirm the diagnosis of symptomatic ischaemic cerebral vascular disease (23). • In older adults with cryptogenic stroke, echocardiography with or without contrast is reasonable to evaluate for possible cardiac sources of or transcardiac pathways for cerebral embolism (23). If there is not a contraindication to anticoagulation, long-term rhythm monitoring with mobile cardiac outpatient telemetry, implantable loop recorder, or other approach is reasonable to detect intermittent arrhythmia (23). **16.3 Management:** 16.3.1 General recommendations: ○ Consider referral to a rehabilitation specialist when having new neurological impairments and functional limitations, for in-depth assessment and management (24). ○ In older adults with an ischaemic stroke or TIA and obstructive sleep apnea, treatment with positive airway pressure (e.g., continuous positive airway pressure) can be beneficial for improved sleep apnoea, BP, sleepiness, and other apnoea related outcomes (23). ○ In multimorbid older adults with cognitive impairment, and with a TIA or non-disabling ischaemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, carotid endarterectomy should be considered, and risk-benefit evaluated, to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%. It is reasonable to select carotid endarterectomy over carotid artery stenting to reduce the periprocedural stroke rate (23). 16.3.2 Pharmacological recommendations: ○ Antiplatelet Therapy for Secondary Stroke Prevention: For patients with ischaemic stroke or TIA, antiplatelet therapy is recommended for long-term	**Assessment** Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24). **Diagnostic** In patients suspected of having a stroke or TIA, Computed Tomography or Magnetic Resonance Imaging of the brain is recommended to confirm the diagnosis of symptomatic ischaemic cerebral vascular disease (23). In older adults with cryptogenic stroke, echocardiography with or without contrast is reasonable to evaluate for possible cardiac sources of or trans cardiac pathways for cerebral embolism (23). If there is not a contraindication to anticoagulation, long-term rhythm monitoring with mobile cardiac outpatient telemetry, implantable loop recorder, or other approach is reasonable to detect intermittent arrhythmia (23). **Management** **General recommendations** Consider referral to a rehabilitation specialist when having new neurological impairments and functional limitations, for in-depth assessment and management (24). In older adults with an ischaemic stroke or TIA and obstructive sleep apnea, treatment with positive airway pressure (e.g., continuous positive airway pressure) can be beneficial for improved sleep apnoea, BP, sleepiness, and other apnoea related outcomes (23). In multimorbid older adults with cognitive impairment, and with a TIA or non-disabling ischaemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, carotid endarterectomy should be considered, and risk-benefit evaluated, to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%. It is reasonable to select carotid endarterectomy over carotid artery stenting to reduce the periprocedural stroke rate (23). **Management** **Pharmacological recommendations** Antiplatelet Therapy for Secondary Stroke Prevention: For patients with ischaemic stroke or TIA, antiplatelet therapy is recommended for long-term secondary stroke prevention to reduce the risk of recurrent stroke and other vascular events unless there is an indication for anticoagulant therapy (24). Antiplatelet therapy should be started as soon as possible after brain imaging has excluded haemorrhage, within 24 hours of symptom onset (ideally within 12 hours) (24). For long-term secondary stroke prevention, either acetylsalicylic acid (80-325 mg daily), or clopidogrel (75 mg daily), or combined acetylsalicylic acid and

Figure 4- Fragmentation process sample (Stroke guideline)

6.2.2 Comprehensive and semantic analysis process

When the text fragmenting process was finished, we proceeded to the second step, which was to identify the terms, sentences and parts about which there was ambiguity or question and needed clarification and explanation. Therefore, the cases with such characteristics were identified and highlighted. Also, questions or points of ambiguity regarding the extracted items were mentioned in detail as notes in the template table to be sent to the experts.

Fragmented Guideline	Guideline Fragment of Interest	Notes for experts	CRGs feedback	Possible Framework of Refined Guideline
Section 16 - Stroke				
Assessment				
Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24).	Patients at risk of stroke	How is this risk calculated? How is this risk expressed (e.g. percentage vs stratification levels)? How is this risk stored in the EHR? What is the cut off for the risk to be "high"? Does this differ between different patient characteristics e.g. age/ethnicity?		
	Stroke or transient ischemic attack	ICD-10 code?		
	should be assessed for	How should these assessments be carried out? In what order should they be carried out? At what point in the pathway should they be carried out? Do any assessments require referral to other services? How is the result of these assessments recorded in the EHR? What should happen as a result of these assessments? Do they feed into any other guidelines or affect targets? Shall we just send a notification to clinician?		
	vascular disease risk factors	What exact risk factors are of interest here?		
Diagnostic				
In patients suspected of having a stroke or TIA, Computed Tomography or Magnetic Resonance Imaging of the brain is recommended to confirm the diagnosis of symptomatic ischaemic cerebral vascular disease (23).	In patients suspected of having a stroke or Transient Ischaemic Attack (TIA)	The wording of this guideline suggests it is something that should occur when the patient presents to the ED with symptoms of a stroke/TIA. If this is correct, how should the primary care CDSS user interact with this guideline? Is there anything they should follow-up on?		
		Is it just a recommendation with no further action through CDSM?		
In older adults with cryptogenic stroke, echocardiography with or without contrast is reasonable to evaluate for possible cardiac sources of or trans cardiac pathways for cerebral embolism (23). If there is not a contraindication to anticoagulation, long-term rhythm monitoring with mobile cardiac outpatient telemetry, implantable loop	cryptogenic stroke	Is there any ICD-10 code for it?		
	If there is not a contraindication to anticoagulation	Should we provide its contraindications?		

Figure 5- Point extraction process sample (Stroke guideline)

6.2.3 Clinical partners' feedback analysis

In third step, all analysed guidelines were shared with clinical partners to review and provide feedback on. As expected, this output resulted in the following changes:

- Some sections were changed in the master guideline.
- Some responses and advice were provided on how to handle some issues and points.
- Some resources and tools were suggested by clinicians to facilitate working with ambiguous parts.

Fragmented Guideline	Guideline Fragment of Interest	Notes for experts	CRGs feedback	Possible Framework of Refined Guideline
Section 16 - Stroke				
Assessment				
Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24).	Patients at risk of stroke	How is this risk calculated? How is this risk expressed (e.g. percentage vs stratification levels)? How is this risk stored in the EHR? What is the cut off for the risk to be "high"? Does this differ between different patient characteristics e.g. age/ethnicity?		
	Stroke or transient ischemic attack	ICD-10 code?		
	should be assessed for	How should these assessments be carried out? In what order should they be carried out? At what point in the pathway should they be carried out? Do any assessments require referral to other services? How is the result of these assessments recorded in the EHR? What should happen as a result of these assessments? Do they feed into any other guidelines or affect targets? Shall we just send a notification to clinician?		
	vascular disease risk factors	What exact risk factors are of interest here?		

Figure 6- Sample analysed guideline to share (Stroke guideline)

6.3 Interpretable modelling phase in CAREPATH

6.3.1 Rule development process

After CRG review and following receiving feedbacks, at fourth step simple non-technical if-then-else rules were developed.

Fragmented Guideline	Guideline Fragment of Interest	Notes for experts	CRGs feedback	Possible Framework of Refined Guideline
Section 16 - Stroke				
Assessment				
Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24).	Patients at risk of stroke	How is this risk calculated? How is this risk expressed (e.g. percentage vs stratification levels)? How is this risk stored in the EHR? What is the cut off for the risk to be "high"? Does this differ between different patient characteristics e.g. age/ethnicity?	The number of known risk factors for vascular diseases is several hundred. Some of these are of particular medical importance because they have a comparatively large, well-documented effect, are easy to measure and can be influenced preventively if necessary. These include, for example, blood pressure, cholesterol, diabetes mellitus or family history of vascular disease, age and gender, behavioural factors such as smoking, physical inactivity and malnutrition. It is true that physiological parameters such as blood pressure or blood lipids are easy to measure and therefore particularly conspicuous. However, they are actually only the last step in a causal chain that has an effect on arteriosclerosis, which in turn begins with social conditions, for example. These include genetic factors, class affiliation and living conditions, advertising of tobacco products, physical inactivity and malnutrition - to name just a few examples. The global risk approach takes into account the fact, well proven in many prospective cohort studies (e.g. [20- 23]), that the risk for cardiovascular events results from the joint effect of various risk factors. A person with one highly elevated and otherwise normal risk factor may have a lower risk than a person with several risk factors that are each only moderately elevated [15]. Considering only the single risk factor instead of the overall risk when making treatment decisions can lead to both over- and under-treatment [13]. Finally it is better to ask clinician to decide in this regard.	
	Stroke or transient ischemic attack	ICD-10 code?		
	should be assessed for	How should these assessments be carried out? In what order should they be carried out? At what point in the pathway should they be carried out? Do any assessments require referral to other services? How is the result of these assessments recorded in the EHR? What should happen as a result of these assessments? Do they feed into any other guidelines or affect targets? Shall we just send a notification to clinician?		
	vascular disease risk factors	What exact risk factors are of interest here?		

Figure 7- Sample of received feedbacks (Stroke guideline)

The above mentioned format is not only easy for clinicians to catch up with, but also are useable for technical partners in implementation phase.

Fragmented Guideline	Guideline Fragment of Interest	Notes for experts	CRGs feedback	Possible Framework of Refined Guideline
Section 16 - Stroke				
Assessment				
Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24).	Patients at risk of stroke	How is this risk calculated? How is this risk expressed (e.g. percentage vs stratification levels)? How is this risk stored in the EHR? What is the cut off for the risk to be "high"? Does this differ between different patient characteristics e.g. age/ethnicity?		IF [the CAREPATH CDSS identifies a patient [at risk of stroke] AND (stroke OR TIA)] THEN [The CAREPATH CDSS should notify clinicians to assess the patient for vascular disease risk factors ? and lifestyle management issues ? (diet, sodium intake, exercise, weight, alcohol intake, and smoking)]
	Stroke or transient ischemic attack	ICD-10 code?		
	should be assessed for	How should these assessments be carried out? In what order should they be carried out? At what point in the pathway should they be carried out? Do any assessments require referral to other services? How is the result of these assessments recorded in the EHR? What should happen as a result of these assessments? Do they feed into any other guidelines or affect targets? Shall we just send a notification to clinician?		
	vascular disease risk factors	What exact risk factors are of interest here?		

Figure 8- Simple/Draft developed rules sample (Stroke guideline)

Developed rules were shared with clinical responsible partners for further review. Comments and feedbacks were applied as amendment in the rules for final verification and approval with clinicians in point-to-point meetings.

6.3.2 Rule verification and approval process

Finally, point-to-point meetings between technical and clinical partners were held to finalize the rules and discuss some remaining details. In these meetings, an exchange of ideas and consensus regarding the method and step-by-step interaction and performance of the CDS module in the CAREPATH project was also carried out, and the technical and clinical partners agreed on all of them.

Guideline	Guideline Fragment of Interest	Notes	Possible Framework of Refined Guideline	CRGs feedback
Section 16 - Stroke				
Assessment				
Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24).	Patients at risk of stroke	How is this risk calculated? How is this risk expressed (e.g. percentage vs stratification levels)? How is this risk stored in the EHR? What is the cut off for the risk to be "high"? Does this differ between different patient characteristics e.g. age/ethnicity?	IF [Patient at risk of stroke (AICP) OR With (history of [STROKE] (AICP) OR History of [transient ischemic attack] ICD-10-CM: G45)] THEN [*Clinician should* ' *Perform the assessment for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking)* ']	
	Stroke or transient ischemic attack	ICD-10 code?		
	should be assessed for	How should these assessments be carried out? In what order should they be carried out? At what point in the pathway should they be carried out? Do any assessments require referral to other services? How is the result of these assessments recorded in the EHR? What should happen as a result of these assessments? Do they feed into any other guidelines or affect targets? Shall we just send a notification to clinician?		
	vascular disease risk factors	What exact risk factors are of interest here?		
Diagnostic				
In patients suspected of having a stroke or TIA, Computed Tomography or Magnetic Resonance Imaging of the brain is recommended to confirm the diagnosis of symptomatic ischaemic cerebral vascular disease (23).	In patients suspected of having a stroke or Transient Ischaemic Attack (TIA)	The wording of this guideline suggests it is something that should occur when the patient presents to the ED with symptoms of a stroke/TIA. If this is correct, how should the primary care CDSS user interact with this guideline? Is there anything they should follow-up on?	IF [Patient at risk of stroke (AICP)] THEN [*Recommend a Referral to Neurologist or A&E department to confirm the diagnosis of symptomatic ischemic cerebral vascular disease*]	
	Is it just a recommendation with no further action through CDSM?			
In older adults with cryptogenic stroke, echocardiography with or without contrast is reasonable to evaluate for possible cardiac sources of or trans cardiac pathways for cerebral embolism (23).	cryptogenic stroke	Is there any ICD-10 code for it?		Removed
	Should we clarify its contraindications?			

Figure 9- Sample refined rules (Stroke guideline)

Also, whenever and wherever the need was felt, a flowchart or business process diagram showing the step-by-step progress of the guideline and decision points and other related sections was also prepared and reviewed with clinical colleagues for better understanding and the possibility of further discussion.

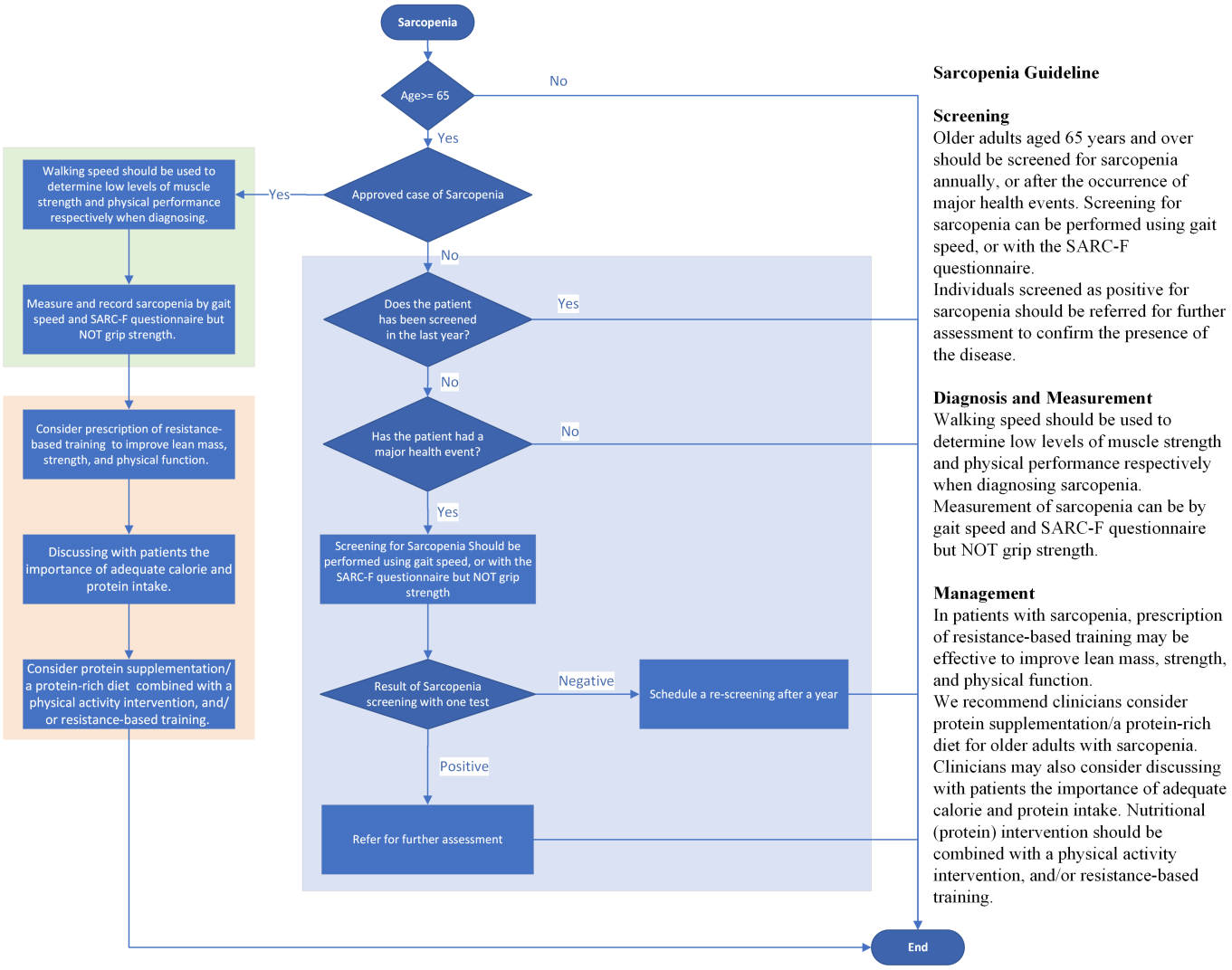

Figure 10- Sample flowchart for further discussion (Sarcopenia guideline)

Regarding the diseases and morbidities, where it was important to apply step by step and consecutive stages of diagnosis and treatment, modelling based on decision tree and flowchart was prepared to help with the future implementation.

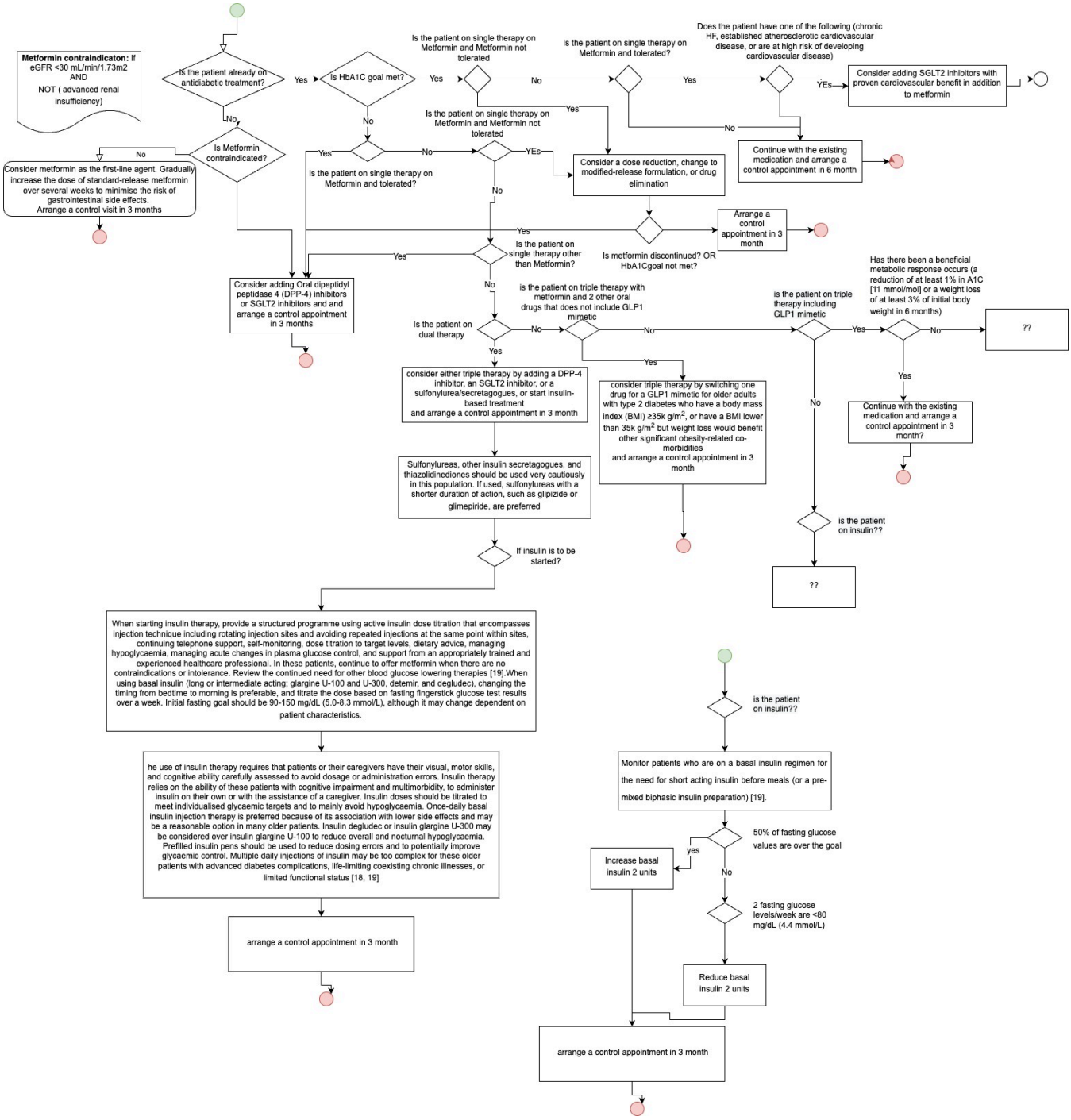

Figure 11- Sample care plan flowchart (Diabetes guideline)

At the end, all the developed and refined rules, the standard included codes (ICD-10/ATC/LOINC), decisions, proposed actions, and progress pathways of the guidelines in the CDS module were approved by the clinical team of the CAREPATH project.

The final rule-based model covers all the decisions, actions, and states of the users of the CAREPATH holistic master guideline, which was decided by the CRG to be of enough importance and necessity to be implemented in the CDSM to facilitate and improve the patient care process while avoiding burnout and fatigue of the users.

6.4 Localization phase in CAREPATH project

The rules should be customised for local adaptation by different pilot sites through the implementation phase of the project. When implementation starts, some adjustments will be needed based on characteristics of different settings. This should be done in collaboration with the technical team and with consideration of legislative and ethical issues. When adaptation is completed, the final implementation can begin. Localization consists of adaptation of inputs and outputs of CDS module and contents in accordance with the language, cultural and other specifications of the intended target settings.

7. Conclusions

This deliverable describes the process and technologies used for modelling clinical guidelines as computer interpretable guidelines in task 3.1 which defines as “Patient-Oriented Computer Interpretable Clinical Guideline Modelling”. It also covers an overview of master clinical guideline delivered by WP6 in D6.2. Validation and Verification modelling approaches are also defined as part of the CAREPATH project. Finally, the step-by-step CAREPATH process of developing CIGs from the master clinical guideline are explained. A final collection of rules to be implemented in CDS module are provided in this deliverable.

The process of developing a computer interpretable integrated clinical guideline required a long list of considerations and decisions. Strong collaboration between clinical and technical teams and reciprocal activities were needed to complete the task in an appropriate way. Differences in standards used by target systems, variability of local rules and regulations, inconsistency between guidelines and definition, need for unprecedented data and heterogeneity of the stakeholders were all issues that contributed to the complexity of this step. Remarkable collaborative activities were required to finalize it. We present a state-of-art work in developing the model to adapt to the intercorrelation of multi-morbidities and their guidelines in mild cognitive impairment (MCI) and mild dementia patient management, for the first time.

It should be noted that the current CIGs are provided based on the latest version of master clinical guideline available at this time (D6.2 version 1v5). As the Clinical Guidelines used in CAREPATH may experience revisions and changes throughout the time, the development of CIGs is an ongoing task in its nature and the present collection of rules can eventually be revised and updated according to the changes introduced into clinical practice in future.

8. References

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9. Appendices

9.1 Mild Cognitive Impairment or Mild Dementia management

All reference numbers in this section are according to deliverable D6.2 1v5.

Mild Cognitive Impairment or Mild Dementia management	
Guideline	Possible Framework of Refined Guideline
Cognitive screening tools exist specifically for the early identification of MCI, like de Montreal Cognitive Assessment (MoCA) (15).	IF [The first visit] THEN [*Recommend Clinician that* *'Cognitive screening tools exist specifically for the early identification of MCI, like de Montreal Cognitive Assessment (MoCA)'*]
For patients with Mild Cognitive Impairment (MCI), clinicians should assess for the presence of functional impairment related to cognition before giving a diagnosis of dementia and a medical evaluation for MCI risk factors that are potentially modifiable.	IF [Patient HAS Mild Cognitive Impairment (MCI) (AICP)] THEN [*Clinician should Perform the assessment* *'Assess for the presence of functional impairment related to cognition before giving a diagnosis of dementia and a medical evaluation for MCI risk factors that are potentially modifiable. A careful sleep history, including assessment of sleep time, insomnia, daytime sleepiness, napping, and REM sleep behaviour disorder may facilitate identification of pre-clinical dementia, or high risk of developing dementia, and should be included in the assessments '*]
A careful sleep history, including assessment of sleep time, insomnia, daytime sleepiness, napping, and REM sleep behaviour disorder may facilitate identification of pre-clinical dementia, or high risk of developing dementia, and should be included in the assessments (15).	Included in previous rule.

There is strong evidence that slower gait speed is associated with future dementia, in population studies. When gait speed (cut-off gait speed below 0.8m/s) is coupled with cognitive impairment (subjective or objective) the risk is higher. We recommend testing gait speed in clinics in those patients with MCI or mild dementia (15).	IF [Patient HAS Mild Cognitive Impairment (MCI) (AICP)] THEN [*Recommend every 6 month to Clinician to Perform* *'There is strong evidence that slower gait speed is associated with future dementia, in population studies. So We recommend testing gait speed in clinics in those patients with MCI or mild dementia* *'*] IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Gait speed < 0.8 m/s]] THEN [*Set a risk alert* *'Patient is at higher risk for future dementia* *'*]
Assess for vascular risk factors, and manage them as prevention of cerebrovascular pathology, that may impact on the progression of dementia (16).	IF [[

	Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [The first visit]] THEN [*Recommend Clinician to Perform* *'Assess for vascular risk factors, and manage them as prevention of cerebrovascular pathology, that may impact on the progression of dementia* *'*]
When using assessment scales to determine the severity of cognitive impairment, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the results and make any adjustments they consider appropriate (17).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [The first visit]] THEN [*Recommend Clinician that*

	‘ *When using assessment scales to determine the severity of cognitive impairment, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the results and make any adjustments they consider appropriate* ‘]
If a personality, behaviour or mood change has been observed, an objective assessment of the behavioural and psychological symptoms of dementia with the patient and a family member using the short version of the Neuropsychiatric Inventory, Mild Behavioural Impairment Checklist, or if a mood change has been observed with the Patient Health Questionnaire-9, should be performed (15).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [personality, behaviour or mood change (AICP)]] THEN [*Clinician should Perform the assessment* *‘An objective assessment of the behavioural and psychological symptoms of dementia with the patient and a family member using the short version of the Neuropsychiatric Inventory, Mild Behavioural Impairment Checklist, or if a mood change has been observed with the Patient Health Questionnaire-9, should be performed* ‘]
If the diagnosis is uncertain and Alzheimer's disease is suspected, consider either (10,17):	IF [[Patient HAS

o FDG-PET (fluorodeoxyglucose-positron emission tomography- Computed Tomography). o Perfusion SPECT (Single-Photon Emission Computed Tomography) if FDG-PET is unavailable, or o Examining cerebrospinal fluid for either total tau or total tau and phosphorylated-tau 181 and either amyloid β 1-42 or amyloid β 1-42, and amyloid β 1-40. If a diagnosis cannot be made after one of these tests, consider using the other one.	(Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [(The diagnosis is uncertain) (AICP) AND (Alzheimer's disease is suspected) (AICP)]] THEN [*Clinician should Perform* *‘* *If the diagnosis is uncertain and Alzheimer's disease is suspected, Consider either:* *o FDG-PET (fluorodeoxyglucose-positron emission tomography- Computed Tomography).* *o Perfusion SPECT (Single-Photon Emission Computed Tomography) if FDG-PET is unavailable, or* *o Examining cerebrospinal fluid for either total tau or total tau and phosphorylated-tau 181 and either amyloid β 1-42 or amyloid β 1-42, and amyloid β 1-40.* *If a diagnosis cannot be made after one of these tests, consider using the other one.* *Do not use Apolipoprotein E genotyping or electroencephalography to diagnose Alzheimer's disease* *‘*]
Do not use Apolipoprotein E genotyping or electroencephalography to diagnose Alzheimer's disease.	Included in previous rule.

When assessing the severity of Alzheimer's disease (cognitive impairment) and the need for treatment, healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so (17).	IF [Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] THEN [*Recommend Clinician that* *'* *When assessing the severity of cognitive impairment and the need for treatment, healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so* *'*]
Before starting non-pharmacological or pharmacological treatment for distress in people living with dementia, conduct a structured assessment to: explore possible reasons for their distress and check for and address clinical or environmental causes (for example pain, infections, delirium or inappropriate care). Identify events (e.g. shopping at busy market) or factors (e.g. going out alone) that may precede, trigger, or enhance problem behaviours. Modify these triggers if possible (17,18).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild Dementia (AICP))] AND [Prescription changed for • AChE inhibitors [N06DA] • Memantine [N06DX01] • Antipsychotics [N05A] • Valproate [N03AG01] • Diazepam [N05BA01] • Melatonin [N05CH01]

	]] THEN [*Recommend Clinician that* ‘ *Before starting non-pharmacological or pharmacological treatment for distress in people living with dementia, conduct a structured assessment to: explore possible reasons for their distress and check for and address clinical or environmental causes (for example pain, infections, delirium or inappropriate care). Identify events (e.g. shopping at busy market) or factors (e.g. going out alone) that may precede, trigger, or enhance problem behaviours. Modify these triggers if possible* ‘]
Ask older adults with MCI or mild dementia whether they wish to know the diagnosis and with whom it should be shared. Tailor the explanation of the illness so that they can understand and retain the information, and give basic information like “dementia is an illness of the brain and tends to get worse over time”, “although there is no cure, there is much that can be done to help and support the person and the family”, or “many specific concerns and behaviours can be managed as they arise” (18).	IF [Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age > 65] AND [The first visit]] THEN [*Recommend Clinician to* ‘

	Ask older adults with MCI or mild dementia whether they wish to know the diagnosis and with whom it should be shared. Tailor the explanation of the illness so that they can understand and retain the information, and give basic information like "dementia is an illness of the brain and tends to get worse over time", "although there is no cure, there is much that can be done to help and support the person and the family", or "many specific concerns and behaviours can be managed as they arise" *'*]
Ensure that patients and family members or carers (as appropriate) have access to a memory service or equivalent hospital- or primary-care-based multidisciplinary dementia service (17).	IF [Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] THEN [*Recommend Clinician to* *'* *Ensure that patients and family members or carers (as appropriate) have access to a memory service or equivalent hospital- or primary-care-based multidisciplinary dementia service* *'*]
Plan for ADL in a way that maximises independent activity, enhances function, helps to adapt and develop skills, and minimises the need for support. Facilitate functioning and participation in the community involving people and their carers in planning and implementation of these interventions. Assist in liaison with available social resources. Advise recreational activities tailored to severity of cognitive impairment. Refer for occupational therapy, if available (18).	IF [Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] THEN [

	Recommend Clinician to *‘* *Ensure that patients and family members or carers (as appropriate) have access to a memory service or equivalent hospital- or primary-care-based multidisciplinary dementia service.* *Plan for ADL in a way that maximises independent activity, enhances function, helps to adapt and develop skills, and minimises the need for support. Facilitate functioning and participation in the community involving people and their carers in planning and implementation of these interventions. Assist in liaison with available social resources. Advise recreational activities tailored to severity of cognitive impairment.* *Keep the environment at home safe to reduce the risk of falling and injury.* *‘*] IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [NOT referred before]] THEN [*Clinician should refer the patient for* *‘* *“Occupational therapy”, if available ‘*]

Keep the environment at home safe to reduce the risk of falling and injury (18).	Included in previous rule.
In older adults with MCI, recommend cognitive interventions when considered (10). Assess for behavioural and neuropsychiatric symptoms in MCI and mild dementia, and treat with both pharmacologic and nonpharmacologic approaches when indicated (10). As initial and ongoing management, offer psychosocial and environmental interventions to reduce distress in people living with MCI or dementia (17).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age > 65]] THEN [*Recommend Clinician to* *‘* *In older adults with MCI, recommend cognitive interventions when considered. Assess for behavioural and neuropsychiatric symptoms in MCI and mild dementia, and treat with both pharmacologic and nonpharmacologic approaches when indicated. As initial and ongoing management, offer psychosocial and environmental interventions to reduce distress in people living with MCI or dementia.* *‘*]
Encourage carers to improve cognitive functioning of older adults with mild dementia using interventions like providing regular orientation information, use of materials such as newspapers, radio, or TV programmes, family albums and household items to promote communication, to orient them to current events, to stimulate memories, and to enable people to share and value their experiences. Use simple short sentences to make verbal communication clear. Try to minimize	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR

competing noises, such as radio, TV, or other conversation. Listen carefully to what the person has to say. Keep things simple, avoid changes to routine, and, as far as possible, avoid exposing the person to unfamiliar and bewildering places (18). Do not try to train cognitive capacity by, for example, confronting the patient with calculating or memorizing exercises, because it causes stress and therefore worthens the situation.	Mild dementia (AICP))] AND [Age>65]] THEN [*Recommend Carers to* *'* *Encourage carers to improve cognitive functioning of older adults with mild dementia using interventions like providing regular orientation information, use of materials such as newspapers, radio, or TV programmes, family albums and household items to promote communication, to orient them to current events, to stimulate memories, and to enable people to share and value their experiences. Use simple short sentences to make verbal communication clear. Try to minimize competing noises, such as radio, TV, or other conversation. Listen carefully to what the person has to say. Keep things simple, avoid changes to routine, and, as far as possible, avoid exposing the person to unfamiliar and bewildering places (18). Do not try to train cognitive capacity by, for example, confronting the patient with calculating or memorizing exercises, because it causes stress and therefore worthens the situation. '*]
In multimorbid older adults with MCI or mild dementia, and behavioural and neuropsychiatric symptoms, consider environmental adaptations such as appropriate seating, safe wandering areas, signs (e.g. 'no exit' sign on the street door or signpost to toilet). Encourage soothing, calming, or distracting strategies. Suggest an activity the person enjoys (e.g. going for a walk, listening to music, engaging in conversation), especially when feeling agitated (18).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age>65

	] AND [New neuropsychiatric symptoms (AICP)]] THEN [*Recommend Carers to* *'* *Encourage carers to improve cognitive functioning of older adults with mild dementia using interventions like providing regular orientation information, use of materials such as newspapers, radio, or TV programmes, family albums and household items to promote communication, to orient them to current events, to stimulate memories, and to enable people to share and value their experiences. Use simple short sentences to make verbal communication clear. Try to minimize competing noises, such as radio, TV, or other conversation. Listen carefully to what the person has to say. Keep things simple, avoid changes to routine, and, as far as possible, avoid exposing the person to unfamiliar and bewildering places (18). Do not try to train cognitive capacity by, for example, confronting the patient with calculating or memorizing exercises, because it causes stress and therefore worthens the situation. '*]
Ensure that older adults living with MCI or mild dementia have access to psychosocial and environmental interventions for distress when having behavioural and neuropsychiatric symptoms (17).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age > 65]]

	THEN [*Recommend Clinician to* *‘* *Ensure that older adults living with MCI or mild dementia have access to psychosocial and environmental interventions for distress when having behavioural and neuropsychiatric symptoms ‘*]
For older adults living with MCI or mild dementia who have sleep problems, consider a personalized multicomponent sleep management approach that includes sleep hygiene education, exposure to daylight, exercise and personalized activities (17).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age > 65] AND [Sleep problems (AICP)]] THEN [*Recommend Clinician to* *‘* *consider a personalized multicomponent sleep management approach that includes sleep hygiene education (PEP), exposure to daylight, exercise and personalized activities ‘*]

Assess the impact on the carer and the carer's needs to ensure necessary support and resources for their family life, employment, social activities, and health. When people living with dementia or their carers have a primary care appointment, assess for any emerging dementia-related needs and ask them if they need any more support (17). Encourage the carers to seek help if they are experiencing difficulty or strain in caring for their loved one. Provide information to the carer regarding dementia, keeping in mind the wishes of the person with dementia. Provide training and support in specific skills, e.g. managing difficult behaviour, if necessary. To be most effective, elicit active participation, e.g. role play. Consider providing practical support when feasible, e.g. home-based respite care. Explore whether the person qualifies for any disability benefits or other social/financial support (government or non-governmental) (18).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) ? (AICP) OR Mild dementia (AICP))] AND [Age > 65] AND [The first visit]] THEN [*Recommend Clinician to* *'* *Assess the impact on the carer and the carer's needs to ensure necessary support and resources for their family life, employment, social activities, and health.* *When people living with dementia or their carers have a primary care appointment, assess for any emerging dementia-related needs and ask them if they need any more support (17). Encourage the carers to seek help if they are experiencing difficulty or strain in caring for their loved one. Provide information to the carer regarding dementia, keeping in mind the wishes of the person with dementia. Provide training and support in specific skills, e.g. managing difficult behaviour, if necessary. To be most effective, elicit active participation, e.g. role play. Consider providing practical support when feasible, e.g. home-based respite care. Explore whether the person qualifies for any disability benefits or other social/financial support (government or non-governmental).* *'*]

For patients with MCI, clinicians should perform serial assessments over time to monitor for changes in cognitive status (10).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP))] THEN [*Clinician should Perform the assessment over time Two options (6 month and 12 month) to 'monitor for changes in cognitive status* *'* AND [*Suggest Setting appointment to 'monitor for changes in cognitive status'*] AND *Recommend Clinician that* *'* *Tracking response to treatment and change over time should be individualized and requires a multi-dimensional approach. It should not rely on a single tool or clinical domain and requires caregiver or reliable informant input. Clinical response should be based on the assessment of the following clinical domains: cognition, functional autonomy, behaviour, as well as caregiver burden.* AND *Set appointment to visit and clinically assess patient every 6 to 12 month.* *Patients with behavioural symptoms of dementia may need more frequent reassessment. Not all domains need to be assessed at every visit, but all domains must be evaluated at least annually* *'*]

Tracking response to treatment and change over time should be individualized and requires a multi-dimensional approach. It should not rely on a single tool or clinical domain and requires caregiver or reliable informant input. Clinical response should be based on the assessment of the following clinical domains: cognition, functional autonomy, behaviour, as well as caregiver burden. The frequency of clinical visits depends on the individual patients and circumstances but typically varies between 6 to 12 months. Patients with behavioural symptoms of dementia may need more frequent reassessment. Not all domains need to be assessed at every visit, but all domains must be evaluated at least annually (15).	Included in previous rule.
Wean patients from medications that can contribute to cognitive impairment (where feasible and medically appropriate) and treat modifiable risk factors that may be contributing (10). Consider discontinuation of opioids in multimorbid older adults with mild dementia in whom there are no signs or symptoms of pain or no clear indication, or suspicion of side effects (16).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age > 65]] THEN [*Recommend Clinician to* *'* *Wean patients from medications that can contribute to cognitive impairment (where feasible and medically appropriate) and treat modifiable risk factors that may be contributing '*] IF [

	[Patient HAS (Mild dementia (AICP))] AND [NO (signs or symptoms of pain or clear indication, or suspicion of side effects)] AND [Age > 65] AND [Opioids [N02A] in prescription]] THEN [*Recommend Clinician to* *'* *Consider discontinuation of opioids* [N02A] *in multimorbid older adults with mild dementia in whom there are no signs or symptoms of pain or no clear indication, or suspicion of side effects '*]
Counsel the patients and families that there are no pharmacologic or dietary agents currently shown to have symptomatic cognitive benefit in MCI, and may choose not to offer acetylcholinesterase (AChE) inhibitors. If clinicians choose to offer cholinesterase inhibitors, they must first discuss with patients the fact that this is an off-label	IF [Patient HAS (Mild Cognitive Impairment (MCI) (AICP))] THEN

prescription not currently backed by empirical evidence (10).	[*Recommend Clinician to* *'Counsel the patients and families that there are no pharmacologic or dietary agents currently shown to have symptomatic cognitive benefit in MCI, and may choose not to offer acetylcholinesterase (AChE) inhibitors.* *'*] IF [Patient HAS (Mild Cognitive Impairment (MCI) (AICP)) AND [AChE inhibitors [N06DA] prescribed]] THEN [*Recommend Clinician to* *'First discuss with patients the fact that this is an off-label prescription not currently backed by empirical evidence.* *If prescribing an AChE inhibitor* [N06DA] *, treatment should normally be started with the drug with the lowest acquisition cost. However, an alternative AChE inhibitor could be prescribed if it is considered appropriate when taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles* *'*]
The three AChE inhibitors donepezil, galantamine and rivastigmine as monotherapies are recommended as options for managing mild to moderate Alzheimer's disease.	IF [Patient HAS (Mild to moderate Alzheimer's (ICD-10: G30) disease (AICP))

Memantine monotherapy is recommended only as an option for managing Alzheimer's disease for people with moderate Alzheimer's disease who are intolerant of or have a contraindication to AChE inhibitors or severe Alzheimer's disease. Prescribers should only start treatment with AChE inhibitors or memantine on the advice of a clinician who has the necessary knowledge and skills (17).	] THEN [*Recommend Clinician that* *'The three AChE inhibitors* [N06DA] *donepezil* [N06DA02]*, galantamine* [N06DA04] *and rivastigmine* [N06DA03] *as monotherapies are recommended as options for managing mild to moderate Alzheimer's disease. '*] IF [[Patient HAS (Moderate Alzheimer's (ICD-10: G30) disease (AICP))] AND [(intolerant of or have a contraindication to AChE inhibitors [N06DA] or severe Alzheimer's disease (AICP))] [THEN [*Recommend Clinician that* *'* *Memantine* [N06DX01] *monotherapy is recommended only as an option for managing Alzheimer's disease for people with moderate Alzheimer's disease who are intolerant of or have a contraindication to AChE inhibitors or severe Alzheimer's disease. Prescribers should only start treatment with AChE inhibitors or memantine on the advice of a clinician who has the necessary knowledge and skills* *'*]

If prescribing an AChE inhibitor, treatment should normally be started with the drug with the lowest acquisition cost. However, an alternative AChE inhibitor could be prescribed if it is considered appropriate when taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles (17).	Previously covered
Do not stop AChE inhibitors in people with Alzheimer's disease because of disease severity alone (17).	IF [Patient HAS (Alzheimer's (ICD-10: G30) disease (AICP)) AND [AChE inhibitors [N06DA] prescription removed]] THEN [*Recommend Clinician that* *'Do not stop AChE inhibitors* [N06DA] *in people with Alzheimer's disease because of disease severity alone (17). '*]
In older adults with MCI or mild dementia with behavioural and neuropsychiatric symptoms, only offer antipsychotics when at risk of harming themselves or others or experiencing agitation, hallucinations or delusions that are causing them severe distress.	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Age > 65

When using antipsychotics, use the lowest effective dose and use them for the shortest possible time. Except in cases of delirium, avoid haloperidol and use risperidone or quetiapine. Reassess the person at least every 6 weeks, to check whether they still need medication. Monitor the person for extrapyramidal symptoms. Stop treatment with antipsychotics if the person is not getting a clear ongoing benefit from taking them and after discussion with the person taking them and their family members or carers (as appropriate) (17,18).	] AND [behavioural and neuropsychiatric symptoms (AICP)] AND [antipsychotics [N05A] prescribed]] THEN [*Recommend Clinician to* *'In older adults with MCI or mild dementia with behavioural and neuropsychiatric symptoms, only offer antipsychotics when at risk of harming themselves or others or experiencing agitation, hallucinations or delusions that are causing them severe distress. When using antipsychotics, use the lowest effective dose and use them for the shortest possible time.* *Stop treatment with antipsychotics if the person is not getting a clear ongoing benefit from taking them and after discussion with the person taking them and their family members or carers (as appropriate) (17,18).'* AND *Set appointment every 6 weeks to 'Check whether they still need medication. Monitor the person for extrapyramidal symptoms.'*]
Do not offer valproate or diazepam to manage agitation or aggression in people living with dementia, unless it is indicated for another condition (17,18).	IF [[Patient HAS (Dementia (AICP))] AND [Valproate [N03AG01] or Diazepam [N05BA01] prescribed

	] AND [agitation or aggression (AICP)]] THEN [*Recommend Clinician that* *'Do not offer valproate* [N03AG01] *or diazepam* [N05BA01] *to manage agitation or aggression in people living with dementia, unless it is indicated for another condition (17,18). '*]
Do not routinely offer antidepressants to manage mild to moderate depression in people living with MCI or mild dementia, unless they are indicated for a pre-existing severe mental health problem (17).	IF [[Patient HAS (Mild Cognitive Impairment (MCI) (AICP) OR Mild dementia (AICP))] AND [Antidepressants [N06A] prescribed]] THEN [*Recommend Clinician that* *'Do not routinely offer antidepressants* [N06A] *to manage mild to moderate depression in people living with MCI or mild dementia, unless they are indicated for a pre-existing severe mental health problem (17). '*]

Do not offer melatonin to manage insomnia in people living with Alzheimer's disease (17).	IF [Patient HAS (Alzheimer's (ICD-10: G30) disease (AICP)) AND [melatonin [N05CH01] prescribed]] THEN [*Recommend Clinician that* *'Do not offer melatonin to manage insomnia in people living with Alzheimer's disease (17). '*]

9.2 Morbidity-based formulated outputs

All reference numbers in this section are according to deliverable D6.2 1v5.

9.2.1 Physical Exercise

Guideline	Rules after revision
Structured exercise programmes supervised by qualified trainers should be implemented when feasible for older adults with multimorbidity and cognitive impairment to improve physical fitness and quality of life. VIVIFRAIL or Otago programmes may be suitable for this population. Setting specific exercise goals, problem solving potential barriers to physical activity, providing information on where and when to exercise, and self-monitoring should be performed collaboratively between the older patient with multimorbidity and cognitive impairment and the healthcare team to increase physical activity	*Notify the clinician that:* • Structured exercise programmes supervised by qualified trainers should be implemented when feasible for older adults with multimorbidity and cognitive impairment to improve physical fitness and quality of life. VIVIFRAIL or Otago programmes may be suitable for this population • Setting specific exercise goals, problem solving potential barriers to physical activity, providing information on where and when to exercise, and self-monitoring should be performed collaboratively between the older patient with multimorbidity and cognitive impairment and the healthcare team to increase physical activity
Regular performance of up to moderate intensity (i.e., breathing faster but able to hold a conversation) continuous exercise is recommended in patients with stable chronic heart failure, particularly in those with reduced LVEF, to improve physical function and quality of life, and to decrease hospitalisation	IF the patient has [chronic heart failure] OR [reduced LVEF] THEN Notify the clinician that • 'Regular performance of up to moderate intensity (i.e., breathing faster but able to hold a conversation) continuous exercise is recommended in patients with stable chronic heart failure, particularly in those with reduced LVEF, to improve physical function and quality of life, and to decrease hospitalisation.' • Recommend assigning Vivifrail exercise programme to patient
Increased physical activity with a structured exercise programme is recommended for adults with elevated BP or hypertension	IF the patient has [hypertension] OR [elevated BP] THEN Notify the clinician that 'Increased physical activity with a structured exercise programme is recommended for adults with elevated BP or hypertension' AND Recommend assigning Vivifrail exercise programme to patient] -
Avoid sedentary behaviors.	Notify the clinician that:

Light-intensity physical activity, even as little as 15 minutes a day, is likely to produce benefits [13].	'Sedentary behaviors should be avoided. Light-intensity physical activity, even as little as 15 minutes a day, is likely to produce benefits ' AND Recommend assigning Vivifrail exercise programme to patient
Older adults with diabetes should perform resistance exercise at least twice a week and preferably 3 times per week in addition to aerobic exercise. They should ideally accumulate a minimum of 150 minutes of moderate-to-vigorous intensity aerobic exercise each week, spread over at least 3 days of the week, with no more than 2 consecutive days without exercise, to improve glycaemic control. Smaller amounts (90–140 minutes/week) of exercise or planned physical activity can also be beneficial but to a lesser extent for glycaemic control. Interval training (short periods of vigorous exercise alternating with short recovery periods at low-to-moderate intensity or rest from 30 seconds to 3 minutes each) can be recommended to people willing and able to perform it to increase gains in cardiorespiratory fitness.	IF the patient has [Diabetes]] THEN Notify the clinician that: • 'Older adults with diabetes should perform resistance exercise at least twice a week and preferably 3 times per week in addition to aerobic exercise AND Recommend assigning Vivifrail exercise programme to patient
Techniques like step count monitoring with a pedometer or accelerometer can be considered in combination with physical activity counselling, support, and goal setting to support and reinforce increased physical activity.	Not to be implemented in Carepath

9.2.2 Nutrition and Hydration

Guideline	Rules after revision
Nutritional and hydration care for older persons with multimorbidity and cognitive impairment should be both individualised and comprehensive in order to ensure adequate nutritional intake, maintain or improve nutritional status, and improve clinical outcomes, and quality of life.	Notify clinician that: • Nutritional and hydration care for older persons with multimorbidity and cognitive impairment should be both individualised and comprehensive in order to ensure adequate nutritional intake, maintain or improve nutritional status, and improve clinical outcomes, and quality of life.
Nutritional interventions should be part of a multi-modal and multi-disciplinary team intervention in order to support adequate dietary intake, maintain or increase body weight, and improve functional and clinical outcomes.	IF [(BMI > 30 AND (MNA>= 12 OR MUST < 1)) OR ((BMI>=21 OR BMI<=30) AND (MNA <12 OR MUST>=1)) OR (BMI<21 AND (MNA<12 OR MUST>=1))] THEN [Notify clinician that: • Nutritional Intervention is required. Nutritional interventions should be part of a multi-modal and multi-disciplinary team intervention]
Older adults with malnutrition or at risk of malnutrition and with eating dependency should be offered nutritional information, education, and individualised nutritional counselling, as part of a comprehensive intervention concept in order to improve awareness of and knowledge about nutritional problems, and/or mealtime assistance, in order to support adequate dietary intake	IF [[Age > 60] AND (With malnutrition (AICP) OR At risk of malnutrition (AICP)) AND With eating dependency] THEN [[PEP: Nutritional care Plan]

	AND [Notify clinician to: • Offer nutritional information, education, and individualised nutritional counselling, as part of a comprehensive intervention concept • Refer for: specialised assessment and intervention]]
Fortified food should be offered.	Not to be implemented in Carepath
Healthcare professionals and informal caregivers should be offered nutritional education in order to ensure awareness of and basic knowledge of nutritional problems and thus promote adequate dietary intake of older persons with malnutrition or at risk of malnutrition.	To be included in AICP
Patients should be advised to eat a healthy balanced diet containing vegetables, legumes, fresh fruits, low-fat dairy products, wholegrains, fish, and unsaturated fatty acids (especially olive oil), and to have a low consumption of red meat and saturated fatty acids.	Included in SESCAM Diet Plan. To be included in AICP
The Mediterranean diet includes many of these nutrients and foods	Included in SESCAM Diet Plan. To be included in AICP
Guiding value for energy intake in this population is 30 kcal/kg/day, and protein intake should be at least 1 g protein/kg/day; these values should be individually adjusted with regard to nutritional status, physical activity level, disease status, and tolerance [14].	Not to be implemented in Carepath
Strategies to support adequate fluid intake should be developed including the older person themselves. These strategies should include high availability of drinks, varied choice of drinks, frequent offering of drinks, caregiver awareness of the need for adequate fluid intake, and caregiver support for drinking. Older women should be offered at least 1.6 L of drinks each day, while older men should be offered at least 2.0L of drinks each day unless there is a clinical condition that requires a different approach.	Included in SESCAM Diet Plan. To be included in AICP
Neither simple signs and tests commonly used to assess low-intake dehydration such as skin turgor, mouth dryness, weight change, urine color or specific gravity, nor	Not to be implemented in Carepath

bioelectrical impedance, should be used to assess hydration status in this population.	
Oral Nutritional Supplementation (ONS) when needed, should provide at least 400 kcal/day including 30 g or more of protein/day, and should be fibre-containing products.	• Not to be implemented in Carepath
During periods of exercise, adequate amounts of energy and protein should be provided in order to maintain body weight, and to maintain or improve muscle mass.	Not to be implemented in Carepath
When needing hospitalization, multimorbid older persons with cognitive impairment and malnutrition, or at risk of malnutrition, should receive a multi- component non-pharmacological intervention that includes hydration and nutritional management, to prevent geriatric syndromes like delirium or functional decline. They should be offered ONS, in order to improve dietary intake and body weight, and to lower the risk of complications and readmission.	IF [Patient needs hospitalization (AICP)] THEN [Notify clinician: • When needing hospitalization, multimorbid older persons with cognitive impairment and malnutrition, or at risk of malnutrition, should receive a multi-component non-pharmacological intervention that includes hydration and nutritional management, to prevent geriatric syndromes like delirium or functional decline. They should be offered ONS, in order to improve dietary intake and body weight, and to lower the risk of complications and readmission.]
After discharge, this population should continue to be offered ONS in order to improve dietary intake and body weight, and to lower the risk of functional decline.	IF [Patient has been discharged in the past 1 month (AICP)] THEN [Notify clinician: • That, this population after discharge should continue to be offered ONS in order to improve dietary intake and body weight, and to lower the risk of functional decline.]
If weight reduction is considered in multimorbid older persons with obesity and cognitive impairment, dietary interventions should be combined with physical exercise whenever possible in order to preserve muscle mass.	IF [Patient has been discharged in the past 1 month (AICP)] THEN [Notify clinician: • That, if weight reduction is considered in multimorbid older persons with obesity and cognitive impairment, dietary interventions should be combined with

	physical exercise whenever possible in order to preserve muscle mass.]
Volume depletion following fluid and salt loss with vomiting or diarrhea should be assessed by checking a set of signs. A person with at least four of the following seven signs is likely to have moderate to severe volume depletion: confusion, non-fluent speech, extremity weakness, dry mucous membranes, dry tongue, furrowed tongue, or sunken eyes [14].	IF [[Age > 60] AND [(Volume depletion following fluid and salt loss (AICP) [AND HAS (Vomiting OR Diarrhea))]] THEN [Notify clinician: • That, patient Need fast clinical assessment and should be assessed by usual healthcare team or even by emergency service.]
Reduce salt intake to <6 g per day in patients with cardiovascular risk factors.	IF [[Age > 60] AND [(Hypertension (AICP) OR Heart Failure (AICP) OR Chronic Kidney Disease (AICP) (ICD-10: N18))]] THEN [Notify clinician: • To reduce patient's salt intake to <6 g per day]

9.2.3 Commonly used drugs

Guideline	Rules after revision
Managing When oral anticoagulation is initiated in a patient with Atrial Fibrillation (AF) who is eligible for a Direct Oral Anticoagulant (DOAC), a DOAC is recommended in preference to a Vitamin K Antagonist (VKA). In patients who are eligible for a DOAC, apixaban 2.5/5 mg BD, dabigatran 110/150 mg BD, rivaroxaban 15/20 mg OD, or edoxaban 30/60 mg OD should be offered based on age, renal function, and weight.	• IF the patient has [AF] (AICP) (ICD-10: I48) and has [VKA] [B01AA] (AICP) and not [DOAC] [B01AF] (AICP) in his prescription list • Notify the Clinician that • 'Consider change to DOAC. DOAC specially recommended instead of VKA when: - Hypersensibility or contraindication for AVK use - Past history of cerebral haemorrhage - Ischemic stroke at high risk for haemorrhagic transformation - AVK treatment with controlled INR ratio, and episodes of severe thromboembolic disease - Inability to achieve INR between 2.0 and 3.0, although good adherence to VKA treatment - Inability to access INR controls - Glomerular filtration rate < 30 ml/min rivaroxaban, edoxaban, or dabigatran not indicated, use AVK. Glomerular filtration rate < 25 ml/min apixaban not indicated, use AVK.' Polypharmacy Rules: STOPP C6 "B01AC*" hasICDPrefix("I25.1"), hasICDPrefix("I60"),hasICDPrefix("I61"),hasICDPrefix("I62"), hasICDPrefix("I63"),hasICDPrefix("I64"),hasICDPrefix("I65"), hasICDPrefix("I66"),hasICDPrefix("I67"),hasICDPrefix("I68"), hasICDPrefix("I69"),icd=="I73.9" "B01AA*","B01AE*", "B01AF*" STOPP C6: Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (No added benefit from dual therapy). STOPP C8 "B01AA*","B01AE*","B01AF*" STOPP C8: Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (e.g. thrombophilia) for > 6 months, (no proven added benefit). STOPP C9 "B01AA*","B01AE*","B01AF*" hasICDPrefix("I26") STOPP C9: Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (e.g. thrombophilia) for > 12 months (no proven added benefit).

	START A1 TRUE icd == "I48.2" START A1: Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation. START A2 TRUE icd == "I48.2" START A2: Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated.
Concomitant use of a Proton Pump Inhibitor (PPI) is recommended in patients receiving aspirin monotherapy, dual antiplatelet therapy (DAPT), or oral anticoagulant (OAC) monotherapy who are at high risk of gastrointestinal bleeding.	• IF the Patient has • one of the following in his/her prescription list [Aspirin monotherapy, dual antiplatelet therapy (DAPT), or oral anticoagulant (OAC) monotherapy] • • THEN • • *Notify clinician that* 'Concomitant use of a Proton Pump Inhibitor (PPI) is recommended in patients receiving aspirin monotherapy, dual antiplatelet therapy (DAPT), or oral anticoagulant (OAC) monotherapy who are at high risk of gastrointestinal bleeding.' AND *Recommend Starting Medication (Proton Pump Inhibitor (PPI))* Polypharmacy Rules: START A2 TRUE icd == "I48.2" START A2: Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated. START A3 TRUE hasICDPrefix("I25.1"), hasICDPrefix("I60"), hasICDPrefix("I61"), hasICDPrefix("I62"), hasICDPrefix("I63"), hasICDPrefix("I64"), hasICDPrefix("I65"), hasICDPrefix("I66"), hasICDPrefix("I67"), hasICDPrefix("I68"),hasICDPrefix("I69"),icd== "I73.9"START A3: Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.
Statins are recommended in all patients, regardless of age, for the secondary prevention of cardiovascular events in patients with Chronic Coronary Syndromes.	• IF the Patient has one of the following conditions [Chronic Coronary Syndromes] • THEN

If a patient's goal is not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended. For patients at very high risk who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with a PCSK9 inhibitor is recommended.	• Notify clinician that 'Statins are recommended in all patients, regardless of age, for the secondary prevention of cardiovascular events in patients with Chronic Coronary Syndromes. ' AND • Recommend Starting Medication (Statins) • •
	• IF the Patient has one of the following conditions [Chronic Coronary Syndromes] AND on [Statin] AND [LDL-C] >=70 mg/dL • THEN • *Notify the clinician that* 'If a patient's goal is not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.' AND • Recommend Starting Medication (ezetimibe) • •
	• IF the Patient has one of the following conditions [Chronic Coronary Syndromes] AND on [Statin AND ezetimibe] AND [Lipid Goal not achieved, [LDL-C] >=70] AND ((has [Stroke] and [one of the major atherosclerotic cardiovascular disease (coronary artery disease, carotid artery stenosis, peripheral artery disease, or atherosclerotic renal artery stenosis)]) OR (has [Stroke] and [multiple high-risk conditions (hypertension, diabetes, dyslipidaemia, thromboembolic disease)]) • THEN *Notify the clinician that* 'For patients at very high risk who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with a PCSK9 inhibitor is recommended.' • AND • Recommend Starting Medication (PCSK9 inhibitor) •

	•
The sodium-glucose co-transporter 2 (SGLT2) inhibitors empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with diabetes and cardiovascular disease.	• IF the patient has [Diabetes] OR [Heart Failure] OR [cardiovascular disease: I25.1, I25.5, I25.9, I65.29, I70.1, I73.9, G45.9, G45.8, I67.82, I63.9] • • THEN • *Notify the clinician that* 'The sodium-glucose co-transporter 2 (SGLT2) inhibitors empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with diabetes and cardiovascular disease.' AND • Recommend Starting medication (Sodium-glucose co-transporter 2 (SGLT2) inhibitors (empagliflozin, canagliflozin or dapagliflozin)] • • • IF the patient has [CKD] and [eGFR]>25ml/min • • THEN • *Notify the clinician that* 'The sodium-glucose co-transporter 2 (SGLT2) inhibitors (dapagliflozin) are recommended for patients with CKD when glomerular filtration rate is > 25 ml/min, but if treatment was begun with this GFR, the drug can be maintained until dialysis' AND • Recommend Starting medication (Sodium-glucose co-transporter 2 (SGLT2) inhibitors (dapagliflozin)] • • • • Polypharmacy rules: START F1 TRUE hasICDPrefix("E08"), hasICDPrefix("E09"), hasICDPrefix("E10"), hasICDPrefix("E11"), hasICDPrefix("E13")

	"START F1: ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment. • " •
In periods of acute immobilisation, like during a hospitalisation, thromboembolism prophylaxis, for instance with low molecular weight heparin (LMWH), is recommended in patients not already anticoagulated and with no contraindication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism [10].	IF the patient needs [*acute immobilization (AICP)] and not [contraindication to anticoagulation]* *Notify the clinician that* 'In periods of acute immobilisation, like during a hospitalisation, thromboembolism prophylaxis, for instance with low molecular weight heparin (LMWH), is recommended in patients not already anticoagulated and with no contraindication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism [10]' AND *Recommend Starting medication (anticoagulation therapy)* *We will put info boxes for the definition of the following to AICP:* *- acute immobilization: e.g. during a hospitalisation, thromboembolism prophylaxis, for instance with low molecular weight heparin (LMWH),* *-Contraindication to anticoagulation':* - Active bleeding - Recent bleeding (2 weeks): intracerebral haemorrhage, gastrointestinal bleeding, respiratory, urogenital, or pericarditis - Uncontrolled severe hypertension - Haemorrhagic retinopathy - Cerebral aneurism - Impossibility to warrant anticoagulation control: Cognitive or mental disorders - Recent cerebral surgery *Haemostatic impairment with high haemorrhagic risk: Hepatic insufficiency with coagulopathy; blood haemorrhagic dyscrasia; thrombocytopenia (platelets < 50.000/ mm3; increased fibrinolytic activity (e.g. following lung, prostate or uterus surgery); treatment with fibrinolytics*

9.2.4 Frailty and Sarcopenia

Guideline	Rules after revision
Assessment Frailty is a marker of future dementia and should be assessed in multimorbid older adults with MCI (15). Multimorbid older adults with MCI or mild dementia should be screened for sarcopenia and frailty annually, or after the occurrence of major health events. Screening for sarcopenia can be performed using clinical suspicion, or with the SARC-F questionnaire. Screening for frailty can be performed using the FRAIL instrument, or performance measurements like gait speed or the Short Physical Performance Battery (SPPB). Individuals screened as positive for sarcopenia or frailty should be referred for further assessment to confirm the presence of the disease.	IF [(First time visit in CAREPATH) OR (Today – Date of last sarcopenia screening >= 365 day) OR (Patient has [*hospitalization*] (with or without [*surgery*]) OR (long [*immobilization*] at home (for example after a [*fracture*] or [*acute disease*]))]] THEN [*Clinician should Perform [Screening] for* • [Sarcopenia] using SARC-F questionnaire but NOT grip strength • [Frailty] using Freid's frailty phenotype, or FRAIL] IF [(SARC-F result >= 4)] THEN [*Recommend a Referral to Geriatrician or Physician for confirmation*] IF [(Frailty screening == POSITIVE)] THEN [*Recommend a Referral to Geriatrician or Physician for confirmation*] %We should provide tool and a brief explanation about via AICP%
Diagnosis	IF [(SARC-F result >= 4)

Walking speed should be used to determine low levels of muscle strength and physical performance respectively when diagnosing sarcopenia. Measurement of sarcopenia can be by gait speed and SARC-F questionnaire but NOT grip strength.	OR (Frailty screening == POSITIVE)] THEN [*Clinician should Perform the [SPPB] measure as part of the visit to determine low levels of physical performance.* *AND* *Clinician should Perform [grip strength test] as part of the visit to determine low levels of muscle strength.*]
Management In patients with sarcopenia, prescription of resistance-based training may be effective to improve lean mass, strength, and physical function. We recommend clinicians consider protein supplementation/a protein-rich diet for older adults with sarcopenia. Clinicians may also consider discussing with patients the importance of adequate calorie and protein intake. Nutritional (protein) intervention should be combined with a physical activity intervention, and/or resistance-based training.	IF [(ICD-10-CM: M62.84 == POSITIVE) OR (Frailty diagnosis == Confirmed)] THEN [*Notify the Clinician that '* *Prescription of resistance-based training may be effective to improve lean mass, strength, and physical function.* *Nutritional (protein) intervention should be combined with a physical activity intervention, and/or resistance-based training.* *Consider protein supplementation/a protein-rich diet* *Consider discussing with patients the importance of adequate calorie and protein intake* ']

9.2.5 Coronary Artery Disease

Guideline	Rules after revision
Non-invasive functional imaging for myocardial ischaemic or coronary computed tomography angiography is recommended as the initial test to diagnose Coronary Artery Disease (CAD) in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.	IF [[ICD-10-CM: I20-I25 OR IS (Symptomatically a probable case of [CAD] OR (Symptomatic now)) (AICP)] AND (Patient has not been referred before)] THEN [*Recommend a Referral to (Cardiologist) for Coronary Artery Disease Assessment (CAD)*] If not done before *
Functional imaging for myocardial ischaemia is recommended if coronary computed tomography angiography has shown CAD of uncertain functional significance or is not diagnostic.	No automation required
Invasive coronary angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood, severe symptoms refractory to medical therapy or typical angina at a low level of exercise, and clinical evaluation that indicates high event risk.	*Recommend assessing patient risk class using SCORE2-OP (https://u-prevent.com/calculators/score2)* **(MED-Calc)** *OR* ***based on clinical assessment*** **(AICP)** IF [Risk class >= (High risk or Very High Risk) AND (Patient has not been referred before)] THEN [*Recommend a Referral to (Cardiologist) for Coronary Artery Disease Assessment (CAD)*]
Invasive functional assessment must be available and used to evaluate stenoses before revascularisation, unless very high grade (>90% diameter stenosis) [13].	Not applicable in CAREPATH
Risk stratification is recommended based on clinical assessment and the result of the diagnostic test initially employed to diagnose CAD. In symptomatic patients with a high- risk clinical profile, invasive coronary	IF [Risk class >= (High risk or Very High Risk) AND Patient is symptomatic **(AICP)**

angiography complemented by invasive physiological guidance is recommended for cardiovascular risk stratification, particularly if the symptoms are responding inadequately to medical treatment and revascularisation is considered for improvement of prognosis [13].	] THEN [*Recommend a Referral to (Cardiologist) for cardiovascular Assessment.* AND *Notify the Clinician to ' prevent the development of cardiovascular disease with:* • Education • Lifestyle modifications (healthy weight) • Cessation of smoking • Physical activity • Prescribing medications • Evidence-based interventions (best evidence, clinical experience, patient values/preferences) ']
Comprehensive risk profiling and multi-disciplinary management, including treatment of major co-morbidities such as hypertension, hyperlipidaemia, diabetes, anaemia, and obesity, as well as smoking cessation and lifestyle modification, are recommended [13].	IF [Risk class >= (High risk or Very High Risk) AND Patient is SMOKER (AICP) AND (Patient is not on Smoking cessation plan)] THEN [*Set a goal for (Smoking cessation plan).* AND *Recommend clinician to prescribe* nicotine delivering patch ??]
Improvement of lifestyle factors in addition to appropriate pharmacological management is recommended in patients with CAD. Cognitive behavioural interventions are recommended to help individuals achieve a healthy lifestyle [13].	
Exercise-based cardiac rehabilitation is recommended as an effective means for patients with chronic coronary syndromes to achieve a healthy lifestyle and manage risk factors [13].	IF [ICD-10-CM: I25] THEN [*Recommend clinician to plan for Exercise-based cardiac rehabilitation to achieve a healthy lifestyle and manage risk factors*]

Short-acting nitrates are recommended for immediate relief of angina. Initial first-line treatment with the combination of a beta-blocker and a dihydropyridine Calcium Channel Blocker (CCB) should be considered, to control heart rate and symptoms. Long-acting nitrates should be considered as a second-line treatment option when the initial therapy is contraindicated, poorly tolerated, or inadequate to control angina symptoms. When long-acting nitrates are prescribed, a nitrate-free or low-nitrate interval should be considered to reduce tolerance. Beta-blockers are recommended in patients with left ventricular (LV) dysfunction or systolic heart failure [13].	IF [patient HAS [(effort angina) (AICP) AND (no existing prescription for a short-acting nitrate) (AICP)] THEN [*Notify the Clinician that '* • In patient with effort angina Short-acting nitrates are recommended for immediate relief (Check contraindications before use). • Initial first-line treatment with the combination of a β-blocker and a dihydropyridine calcium channel blocker (CCB) should be considered, to control heart rate and symptoms. *Recommend clinician to refer patient to A&E if symptom remained and notify that* • Long-acting nitrates should be considered as a second-line treatment option when the initial therapy is contraindicated, poorly tolerated, or inadequate to control angina symptoms. When long-acting nitrates are prescribed, a nitrate-free or low-nitrate interval should be considered to reduce tolerance. • β-blockers are recommended in patients with left ventricular dysfunction or systolic heart failure • Nicorandil (C01DX16), ranolazine (C01EB18), ivabradine (C01EB17), or trimetazidine (C01EB15) should be considered as a next-line treatment to reduce angina frequency and improve exercise tolerance in subjects who cannot tolerate, have contraindications to, or whose symptoms are not adequately controlled by β-blockers, CCBs, and long-acting nitrates. • Ivabradine (C01EB17) should be considered in patients with sinus rhythm, left ventricular ejection fraction ≤ 35%, and a resting heart rate > 70 bits per minute. • '
Nicorandil, ranolazine, ivabradine, or trimetazidine should be considered as a second-line treatment to reduce angina frequency and improve exercise tolerance in subjects who cannot tolerate, have contraindications to, or whose symptoms	Combined with previous rule

are not adequately controlled by beta-blockers, CCBs, and long-acting nitrates. Ivabradine should be considered in patients with sinus rhythm, left ventricular ejection fraction (LVEF) ≤35%, and a resting heart rate >70 BPM [13].	
Aspirin 75-100 mg daily is recommended in patients with CAD. Clopidogrel 75 mg daily is recommended as an alternative to aspirin in patients with aspirin intolerance. Adding a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with a high risk of ischaemic events and without high bleeding risk [13].	IF [ICD-10: I20-I25 AND (Aspirin 75-100 mg daily (B01AC06), Clopidogrel 75 mg daily (B01AC04) NOT in prescription list)] THEN [*Recommend clinician to 'prescribe Aspirin 75-100 mg daily (B01AC06), Clopidogrel 75 mg daily (B01AC04) is recommended as an alternative to aspirin in patients with aspirin intolerance.* *Adding a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with a high risk of ischemic events and without high bleeding risk* *'*]
Clopidogrel 75 mg daily following appropriate loading (e.g., 600 mg or >5 days of maintenance therapy) is recommended, in addition to aspirin, for 6 months following coronary stenting, irrespective of stent type, unless a shorter duration (1-3 months) is indicated due to risk or the occurrence of life-threatening bleeding [13].	IF [patient HAS [(History of coronary stenting in the past 6 month) (AICP) AND NOT (Clopidogrel 75 mg daily (B01AC04) in PL)] THEN [*Recommend Clinician to add '* *Clopidogrel 75 mg daily (B01AC04) following appropriate loading (e.g., 600 mg or >5 days of maintenance therapy) is recommended, in addition to aspirin, for 6 months following coronary stenting, irrespective of stent type, unless a shorter duration (1-3 months) is indicated due to risk or the occurrence of life-threatening bleeding '*]
Angiotensin-Converting Enzyme (ACE) inhibitors or Angiotensin II Receptor Blockers (ARBs) are recommended in patients with chronic coronary syndromes at very high risk of cardiovascular events, or in patients with concomitant conditions like heart failure, hypertension, or diabetes. An ARB is recommended as an alternative in patients who do not tolerate ACE inhibition, or an angiotensin receptor-	IF [[[Risk class >= (Very High Risk) AND [chronic coronary syndromes] (AICP) OR (ICD-10-CM: I25)] OR [

neprilysin inhibitor in patients with persistent symptoms despite optimal medical therapy [13].	patients with concomitant conditions like (heart failure (ICD-10-CM: I50), hypertension (ICD-10-CM: I15), or diabetes (ICD-10-CM: E08-13).] AND not prescribed before] THEN [*Recommend Clinician to add ' Angiotensin-Converting Enzyme (ACE) inhibitors or Angiotensin II Receptor Blockers (ARBs). An ARB is recommended as an alternative in patients who do not tolerate ACE inhibition, or an angiotensin receptor-neprilysin inhibitor in patients with persistent symptoms despite optimal medical therapy '*]
A Mineralocorticoid Receptor Antagonist, spironolactone, or eplerenone is recommended in patients who remain symptomatic despite adequate treatment with an ACE inhibitor and beta-blocker, to reduce morbidity and mortality [13].	IF [Patient is symptomatic **(AICP)** AND (adequate treatment with an ACE inhibitor and β-blocker) **(AICP)**] THEN [*Recommend Clinician to add 'A mineralocorticoid receptor antagonist (MRA), spironolactone* (C03DA01) *, or eplerenone* (C03DA04) *is recommended in patients who remain symptomatic despite adequate treatment with an ACE inhibitor and β-blocker, to reduce morbidity and mortality '*]

9.2.6 Heart Failure

Guideline	Rules after revision
Because very high levels of NT-proBNP carry a poor prognosis, refer people with suspected heart failure (HF) and an NTproBNP level above 2,000 ng/litre (236 pmol/litre) urgently, to have specialist assessment and transthoracic echocardiography within 2 weeks, and in 6 weeks if NT-proBNP levels are between 400 and 2,000 ng/litre (47 to 236 pmol/litre). Review alternative causes for symptoms of HF in people with NTproBNP levels below 400 ng/litre. If there is still concern that the symptoms might be related to HF, discuss with an expert physician in HF [15].	IF [Patient is suspected to Heart Failure (AICP) AND [NTproBNP level (LOINC: 83108-1, 33763-4) > 2,000 ng/litre (236 pmol/litre)]] THEN [*Recommend an urgent Referral to (Specialist) for specialist assessment and transthoracic echocardiography within 2 weeks*] IF [Patient is suspected to Heart Failure (AICP) AND [400 < NTproBNP level (LOINC: 83108-1, 33763-4) < 2,000 ng/litre (47 - 236 pmol/litre)]] THEN [*Recommend a Referral to (Specialist) for specialist assessment and transthoracic echocardiography within 6 weeks*] IF [Patient is suspected to Heart Failure (AICP) AND [NTproBNP level (LOINC: 83108-1, 33763-4) < 400 ng/litre (47 pmol/litre)]] THEN [*Recommend clinician to 'Review alternative causes for symptoms of HF and If there is still concern that the symptoms might be related to HF, discuss with an expert physician in HF'*]
When a diagnosis of HF has been made, assess severity, aetiology, precipitating factors, type of cardiac dysfunction, and correctable causes. Perform transthoracic echocardiography to exclude valve disease, assess the systolic (and diastolic) function of the LV, and detect intracardiac shunts [15].	IF [New case of Heart Failure ICD-10: I50] THEN [*Recommend clinician to 'Assess severity, etiology, precipitating factors, type of cardiac dysfunction, and correctable causes.',* AND *Recommend clinician to 'Perform NYHA classification (AICP) (New York Health Association) to assess the severity of heart failure'* *'* AND *Recommend clinician to 'Perform transthoracic echocardiography to exclude valve disease, assess the systolic (and diastolic) function of the LV, and detect intracardiac shunts'*

<table>
<tr>
<td></td>
<td>AND
Recommend clinician to ‘Perform cardiac dysfunction classification by LVEF’ OR by entering LVEF measure (AICP)’
Table 4. Classification of HF by LVEF
<table>
<tr><th>Type of HF According to LVEF</th><th>Criteria</th></tr>
<tr><td>HFrEF (HF with reduced EF)</td><td>LVEF ≤40%</td></tr>
<tr><td>HFimpEF (HF with improved EF)</td><td>Previous LVEF ≤40% and a follow-up measurement of LVEF >40%</td></tr>
<tr><td>HFmrEF (HF with mildly reduced EF)</td><td>LVEF 41%–49%
Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)</td></tr>
<tr><td>HFpEF (HF with preserved EF)</td><td>LVEF ≥50%
Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)</td></tr>
</table>
AND
Recommend clinician to ‘Perform Self-management education for patients with HF and their caregivers, to decrease hospitalization and mortality. It should commence soon after diagnosis, be patient-centered, appropriate to their level of health literacy, culturally appropriate, and revised throughout the person’s life’

]
]</td>
</tr>
<tr>
<td>Self-management education for patients with HF and their caregivers is recommended, to decrease hospitalisation and mortality. It should commence soon after diagnosis, be patient-centred, appropriate to their level of health literacy, culturally appropriate, and revised throughout the person’s life [9;10].</td>
<td>Covered before</td>
</tr>
<tr>
<td>Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in people with HF, and titrated (up and down) according to need following the initiation of subsequent heart failure therapies. People who have HF with preserved ejection fraction (HFpEF) should be offered a low to medium dose of loop diuretics (for example, less than 80 mg furosemide per day).</td>
<td>IF
[
People with HF (ICD-10: I50)
AND
Patient is NOT on diuretics
]
THEN
[
Recommend clinician that ‘</td>
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Combination of a loop diuretic with thiazide-type diuretic should be considered in patients with resistant oedema who do not respond to an increase in loop diuretic doses *(McDonagh, 2018)*. People whose HF does not respond to this treatment will need further specialist advice [15].	• Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in people with HF, and titrated (up and down) according to need following the initiation of subsequent heart failure therapies. IF [preserved ejection fraction (HFpEF)] THEN [*Recommend clinician that '* • People who have HF with preserved ejection fraction (HFpEF) should be offered a low to medium dose of loop diuretics (for example, less than 80 mg furosemide [C03CA01] per day).] AND *Recommend start Medication (Diuretics)*] IF [People with HF (ICD-10: I50) AND Patient is on diuretics AND Patient is NOT on loop diuretics AND preserved ejection fraction (HFpEF)] THEN [*Recommend clinician that '* • People who have HF with preserved ejection fraction (HFpEF) should be offered a low to medium dose of loop diuretics (for example, less than 80 mg furosemide [C03CA01] per day). AND *Recommend start Medication (Loop Diuretics)*] IF [People with HF (ICD-10-CM: I50) AND Patient is NOT on thiazide-type diuretics (in combination with loop diuretics) AND preserved ejection fraction (HFpEF) AND Edema (AICP) is present] THEN [*Recommend clinician that '*

	• Combination of a loop diuretic with thiazide-type diuretic should be considered in patients with resistant oedema who do not respond to an increase in loop diuretic doses (McDonagh, 2018). AND *Recommend clinician to 'Refer patient for further specialist advice if does not respond to treatment with Combination of a loop diuretic and thiazide-type diuretics'*]
ACE inhibitors or ARB are recommended in patients with left ventricle systolic dysfunction to decrease the risk of developing HF (11). Measure serum sodium and potassium, and assess renal function, before and 1 to 2 weeks after starting an ACE inhibitor/ARB, and after each dose increment (25).	IF [left ventricle systolic dysfunction (ICD-10: I50.1) AND Patient is NOT on (ACE-inhibitor OR ARB)] THEN [*Recommend start Medication (ACE inhibitors or ARB) to decrease the risk of developing HF in patients with left ventricle systolic dysfunction.* AND *Recommend clinician 'Measure serum sodium and potassium, and assess renal function, before and 1 to 2 weeks after starting an ACE inhibitor/ARB, and after each dose increment.'* AND *Recommend clinician 'Assess renal function, before and 1 to 2 weeks after starting an ACE inhibitor/ARB, and after each dose increment.'.* AND ?? *Recommend adding an Appointment/Reminder to check lab works/results before 2 weeks.*] IF (list should be provided) [ACE inhibitors started or dose increment in prescription OR ARB started or dose increment in prescription] THEN [*Recommend clinician 'Measure serum sodium and potassium, and assess renal function, before and 1 to 2 weeks after starting an ACE inhibitor/ARB, and after each dose increment.'* AND *Recommend clinician 'Assess renal function, before and 1 to 2 weeks after starting an ACE inhibitor/ARB, and after each dose increment.'.* AND ?? *Recommend adding an Appointment/Reminder to check lab works/results before 2 weeks*]
Introduce beta-blockers in all patients with HFrEF associated with a moderate or severe reduction in LVEF (LVEF ≤40%) unless contraindicated or not tolerated, and	IF [Heart Failure ICD-10: I50 AND LVEF =< 40% (HFrEF)

once stabilised with no or minimal clinical congestion on physical examination to decrease mortality and decrease hospitalisation [9]. Introduce beta-blockers in a "start low, go slow" manner. Assess heart rate and clinical status after each titration. Measure blood pressure before and after each dose increment of a beta-blocker [15]. Specifically, use bisoprolol, carvedilol, metoprolol (controlled release or extended release), or nebivolol [9].	] THEN [*Recommend clinician to 'Prescribe beta-blockers (e.g. Bisoprolol* (C07AB07), *carvedilol* (C07AG02), *sustained-release metoprolol succinate* (C07AB02) or nebivolol (C07AB12)) *unless contraindicated or not tolerated, and once stabilised with no or minimal clinical congestion on physical examination to decrease to reduce mortality and hospitalization',* AND *Recommend clinician to 'Introduce beta-blockers in a "start low, go slow" manner. Assess heart rate and clinical status after each titration'* AND *Recommend clinician 'Measure blood pressure before and after each dose increment of a beta-blocker'.*]
Offer a Mineralocorticoid Receptor Antagonist, in addition to an ACE inhibitor (or ARB) and beta-blocker, to people who have HF with reduced ejection fraction (HFrEF) if they continue to have symptoms of heart failure. Measure serum sodium and potassium, and assess renal function, before and after starting a Mineralocorticoid Receptor Antagonist and after each dose increment [15].	IF [Heart Failure ICD-10: I50 AND LVEF =< 40% (HFrEF) AND NYHA class II-IV AND Patient is on [ACE inhibitor (or ARB) and beta-blocker]] THEN [*Recommend clinician to 'Prescribe a Mineralocorticoid Receptor Antagonist, in addition to an ACE inhibitor (or ARB) and beta-blocker,* AND *Recommend clinician to 'Measure serum sodium and potassium (should be < 5.0 mEq/L), and assess renal function (eGFR should be >30 mL/min/1.73 m^2) , before and after starting a Mineralocorticoid Receptor Antagonist and after each dose increment.'*] IF [Mineralocorticoid Receptor Antagonist started or dose increment in prescription] THEN [*Recommend clinician to 'Measure serum sodium and potassium (should be < 5.0 mEq/L), and assess renal function (eGFR should be >30 mL/min/1.73 m^2) , before and after starting a Mineralocorticoid Receptor Antagonist and after each dose increment.'*]
SGLT2 inhibitors (dapagliflozin, empagliflozin, canagliflozin, and sotagliflozin) are recommended in patients with HFrEF or HFpEF irrespective of diabetes presence, to reduce hospitalisations for HF, major cardiovascular events, end-stage renal dysfunction, and cardiovascular death [10].	IF [Heart Failure ICD-10: I50] THEN [*Recommend clinician to 'Prescribe SGLT2 inhibitors (dapagliflozin* (A10BK01) *, empagliflozin* (A10BK03) *, canagliflozin* (A10BK02) *, and sotagliflozin* (A10BK06 *) in patients with HFrEF or HFpEF irrespective*

	of diabetes presence, to reduce hospitalizations for HF, major cardiovascular events, end-stage renal dysfunction, and cardiovascular death,]
Every multimorbid older adult with mild cognitive impairment or mild dementia with non- valvular atrial fibrillation (NV-AF), benefits from OAC irrespective of the risk of stroke or CHA_2DS_2-VASc score, unless specific contraindication for OAC exists. In case of sinus rhythm, anticoagulation should be considered for those with a history of thromboembolism, LV aneurysm, or intracardiac thrombus [15]. In patients with moderate or severe mitral stenosis or mechanical prosthetic heart valves, AVK should be prescribed instead of DOACs [10].	IF [[Atrial Fibrillation] (ICD-10-CM: I48) AND non- valvular atrial fibrillation (NV-AF) (AICP)] THEN [*Recommend clinician to 'Prescribe OAC irrespective of the risk of stroke or CHA2DS2-VASc score, unless specific contraindication for OAC exists,*] IF [sinus rhythm (AICP) AND History of thromboembolism, LV aneurysm, or intracardiac thrombus (AICP)] THEN [*Recommend clinician to 'Prescribe anticoagulation for those with a history of thromboembolism, LV aneurysm, or intracardiac thrombus,*] IF [moderate or severe (AICP) [mitral stenosis] AND mechanical prosthetic heart valves (AICP)] THEN [*Recommend clinician to 'Prescribe AVK (e.g. Warfarin* (B01AA03) *and Acenocoumarol* (B01AA07) *) instead of DOACs,*]
In patients with HFrEF (LVEF <45%) associated with persistent symptoms despite optimised therapy, iron studies should be performed and, if the patient is iron deficient (ferritin <100 mcg/L or transferrin saturation <20%), treatment with intravenous ferric carboxymaltose should be considered [9;10].	IF [persistent symptoms despite optimised therapy (AICP) AND LVEF =< 40% (HFrEF)] THEN [*Recommend clinician to 'Perform, iron studies,'* AND *[* IF [iron deficient (AICP) OR

	Ferritin < 100 mcg/L (LOINC:2276.4)??? OR Transferrin saturation (LOINC: 86913-1) < 20%] THEN [*Recommend clinician to 'consider treatment with intravenous ferric carboxymaltose '*]
Monitor the response to titration of medicines closely in people who have HF and Chronic Kidney Disease (CKD), considering the increased risk of hyperkalaemia. For people who have HF and CKD with an eGFR below 30 ml/min/1.73 m^2, consider liaising with a renal physician [15].	IF [Heart Failure ICD-10: I50 AND Chronic Kidney Disease (CKD) ICD-10-CM: I18] THEN [*Recommend clinician to 'Monitor the response to titration of medicines closely in people who have HF and Chronic Kidney Disease (CKD), considering the increased risk of hyperkalemia.,* AND IF [eGFR < 30 ml/min/1.73 m2] THEN [*Recommend clinician to 'consider liaising with a renal physician'*]

9.2.7 Hypertension

Guideline	Rules after revision
Age alone must never be a barrier to antihypertensive treatment because high blood pressure (BP) is an important risk factor even at the most advanced ages. However, in this population, concerns do exist about potential poor tolerability, and even harmful effects of BP-lowering interventions in people in whom mechanisms for preserving BP homeostasis and vital organ perfusion may be more frequently impaired. Consequently, the decision to treat hypertension must take into account the patient's clinical condition, concomitant treatments, and frailty [16]	No rule, can be provided by default for all patients
BP measurements in the community setting are recommended to confirm the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counselling or clinical interventions. BP should be categorised as normal, high-normal (BP 130-139/85-89 mmHg), or Grade 1 (BP 140-159/90-99 mmHg), 2 (BP 160-179/100-109 mmHg), or 3 (BP ≥180/110 mmHg) hypertension to prevent and treat high BP [16].	IF the patient does not have [*Hypertension*] diagnosis yet AND if the *Patient has not been sent home for diagnosis confirmation* AND IF [*BP measurement*] is below 130/85 THEN the patient should be categorized as [*normotensive*] ELSE IF [*BP measurement*] is between130-139/85-89 mmHg THEN the Patient should be categorized as [*high-normal*] ELSE IF [*BP measurement*] is higher that 139/89 mmHg THEN *Recommend* *-Self measurement of BP for 2 –4 weeks* *-Follow appointment to confirm the diagnosis after 2-4 weeks* ELSE IF the patient does not have [*Hypertension*] diagnosis yet AND if the *Patient [has been sent home for diagnosis confirmation]* IF [*BP measurement]* is below 130/85 THEN the Patient should be categorized as [*normotensive*] ELSE IF [*BP measurement]* is between130-139/85-89 mmHg THEN the Patient should be categorized as [*high-normal*] ELSE IF [*BP measurement]* is between 140-159/90-99 mmHg THEN Recommend the patient should be categorized as *[Grade 1 hypertension]* -Recommend adding a Diagnosis (hypertension) ELSE IF [*BP measurement]* is between 160-179/100-109 mmHg THEN recommend *Recommend the patient should be categorized as [Grade 2 hypertension]* -Recommend adding a Diagnosis (hypertension) ELSE IF [*BP measurement]* is ≥180/110 mmHg THEN

	Recommend the Patient should be categorized as [Grade 3 hypertension] -Recommend adding a Diagnosis (hypertension) *Recommend Referral to emergency services OR* *Seek Advice from specialists (e.g. Renal experts)*
Lifestyleadvice should be offered to every patient with high-normal, or Grade 1, 2, or 3 hypertension [16].	IF the patient is categorized as [*high-normal*] OR [*Grade 1 hypertension]* OR [G*rade 2 hypertension*] OR [G*rade 3 hypertension]* THEN *Recommend Regular physical activity of a minimum of 150 minutes per week over 5 days a week* *Recommend Diet (Salt Restriction)* *Recommend assigning Education Material (Hypertension Education Material) to the patient* IF the patient is categorized as [*high-normal*] OR *[Grade 1 hypertension] OR [Grade 2 hypertension] OR [Grade 3 hypertension] AND [smoking]* *Recommend a Goal for (Smoking Cessation)*
The evidence supports the recommendation that multimorbid older patients with cognitive impairment (>65 years, including patients over 80 years) should be offered BP-lowering treatment if their systolic BP (SBP) is ≥160 mmHg. There is also justification to now recommend BP-lowering treatment for older patients (aged >65 but not >80 years) at a lower BP (i.e., Grade 1 hypertension: SBP = 140–159 mmHg). SBP should be targeted to between 130 and 140 mmHg, and diastolic BP (DPB) to <80 mmHg. Treated SBP should not be targeted to <120 mmHg. Drug treatment is not recommended for older adults with high-normal BP [16].	IF the patient is [*high-normal]* AND [*Age*] >65 years THEN *Notify the clinician that 'Drug treatment is not recommended for older adults with high-normal BP'* ELSE IF the patient's ([*SBP*] is ≥160 mmHg AND [*Age*] >65 year) OR ([*SBP*] is between 140–159 mmHg AND [not >80 years) AND does not have [*Antihypertensive drugs]* THEN Recommend HbA1C Goal BP GOAL should be set as between 130 and 140 mmHg, and diastolic BP (DPB) to <80 mmHg *AND* *Flow should continue with DRUG TREATMENT* ELSE IF the patient's ([*SBP*] is ≥160 mmHg AND [*Age*] >65 year) OR ([*SBP*] is between 140–159 mmHg AND [not >80 years) AND already on [*Antihypertensive drugs]* THEN Recommend HbA1C Goal BP GOAL should be set as between 120 and 140 mmHg, and diastolic BP (DPB) to <80 mmHg

	AND *Flow should continue with DRUG TREATMENT* ELSE *Notify the clinician that 'Drug treatment is not recommended'*
Antihypertensive treatment may also be considered in frail older patients if tolerated [16]	No action now…
In multimorbid older adults with cognitive impairment, it may be appropriate to initiate treatment with monotherapy, and by means of once daily drug treatment, as a rule. When combination therapy is used, it is recommended that this is initiated at the lowest available doses.	See Figures
The possible occurrence of adverse reactions, particularly relating to postural BP, should be closely monitored and symptoms of possible hypotensive episodes checked by ambulatory BP monitoring (ABPM).	IF the patient has *[Hypertension] AND is on [Antihypertensive Drugs]* THEN *Notify the Clinician that 'The possible occurrence of adverse reactions, particularly relating to postural BP, should be closely monitored and symptoms of possible hypotensive episodes checked by ambulatory BP monitoring (ABPM)'*
The concomitant use of other appropriate antihypertensive drugs that may elevate the hypotensive effects should be monitored [11, 16].	IF the patient has *[Hypertension] AND is on [Antihypertensive Drugs]* THEN *Notify the Clinician that 'The concomitant use of other appropriate antihypertensive drugs that may elevate the hypotensive effects should be monitored [11, 16].'*
The impact of BP-lowering on the well-being of the patient should be closely monitored due to the increased risk of adverse events (e.g., injurious falls) with lower BP values potentially being more pronounced in this population [16]	IF the patient has *[Hypertension] AND is on [Antihypertensive Drugs]* THEN *Notify the Clinician that 'The impact of BP-lowering on the well-being of the patient should be closely monitored due to the increased risk of adverse events (e.g., injurious falls) with lower BP values potentially being more pronounced in this population [16]'* In AICP we will allow the physician to record number of falls in the last monitoring period (i.e. since the last visit
Adults initiating a new or adjusted drug regimen for hypertension should have a follow-up evaluation of adherence and response to treatment at monthly intervals until control is achieved [12].	This has been integrated to the drug recommendation flow: [IF CAREPATH CDSS hypertensive drug treatment flow recommends new drug or a dose change of an existing drug] THEN *Recommend a Follow-up Appointment after 1 month for* follow-up evaluation of adherence and response to treatment.
Renal function should be frequently assessed to detect possible increase in serum creatinine and reductions in eGFR as a result of BP-related reductions in renal perfusion [16].	This has been integrated to the drug recommendation flow: [IF CAREPATH CDSS hypertensive drug treatment flow recommends new drug or a dose change of an existing drug] THEN *Recommend Lab test for (eGFR) and (serum creatinine) (after a month) together with the follow-up evaluation*
Tolerance of antihypertensive treatment (potential of adverse reactions or adverse	This has been integrated to the drug recommendation flow:

events such as reduced organ perfusion arising from excessive hypotensive effects) varies depending on the condition and the magnitude or rate of blood pressure reduction in individual cases. Care needs to be taken in the process of achieving the goal of antihypertensive treatment in these patients, as well as the tolerability of antihypertensive treatment after achievement of the goal	[IF CAREPATH CDSS hypertensive drug treatment flow recommends new drug or a dose change of an existing drug] THEN *Notify the clinician that 'Tolerance of antihypertensive treatment (potential of adverse reactions or adverse events such as reduced organ perfusion arising from excessive hypotensive effects) varies depending on the condition and the magnitude or rate of blood pressure reduction in individual cases.* *Care needs to be taken in the process of achieving the goal of antihypertensive treatment in these patients, as well as the tolerability of antihypertensive treatment after achievement of the goal'*
Weight loss is recommended to reduce BP in adults with elevated BP or hypertension and overweightness or obesity [12].	IF the (patient's [*BP measurement*] is between 140-159/90-99 mmHg OR patient has OR [*hypertension*] diagnosis)) AND (patients [*BMI*] is over 25) THEN *Recommend setting a Goal for weight loss in case it works for the patient*
For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs [12].	See Figure 1- Figure 7 based on Table 1 and Table 2 of the refined guideline
Unless required for concomitant diseases, loop diuretics and alpha-blockers should be avoided because of their association with injurious falls [16].	See Figure 1- Figure 7 based on Table 1 and Table 2 of the refined guideline
Simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended to treat adults with hypertension [12].	IF the patient is on [*ARB*] AND [*ACEI*] THEN *Notify the clinician that 'Simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended to treat adults with hypertension [12]'*
In those with CKD (stage 3 or higher, or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio, or the equivalent in the first morning void]), treatment with an ACE inhibitor is reasonable to slow kidney disease progression [12].	IF the patient has [*Hypertension*] AND ([*CKD Stage 3,4,5*] OR ([*CKD Stage 1,2*] AND [*Albumin per 24 hours*]>=300 mg/g) OR [*Albumin/Creatinine Ratio in Urine*]>=300mg/g) THEN *Notify the clinician that 'In those with CKD (stage 3 or higher, or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio, or the equivalent in the first morning void]), treatment with an ACE inhibitor is reasonable to slow kidney disease progression [12].'*
Resistant hypertension is more frequent in this population. Secondary causes must be ruled out when BP recommended treatment strategy fails to lower SBP and DBP values to <140	IF the patient has [*Hypertension*] AND has 3 or more [*Antihypertensive drugs*] and [*BP measurement*] over 140/90 mmHg THEN

mmHg and/or <90 mmHg, respectively, and the inadequate control of BP is confirmed by ABPM, or home BP monitoring in patients whose adherence to therapy has been confirmed. The recommended treatment strategy should include appropriate lifestyle measures and treatment with optimal or best-tolerated doses of three or more drugs, which should include a diuretic, typically an ACE inhibitor or an ARB, and a CCB [16].	*Notify the clinician that* 'Resistant hypertension is more frequent in this population. Secondary causes must be ruled out when BP recommended treatment strategy fails to lower SBP and DBP values to <140 mmHg and/or <90 mmHg, respectively, and the inadequate control of BP is confirmed by ABPM, or home BP monitoring in patients whose adherence to therapy has been confirmed. The recommended treatment strategy should include appropriate lifestyle measures and treatment with optimal or best-tolerated doses of three or more drugs, which should include a diuretic typically an ACE inhibitor or an ARB, and a CCB [16].' AND *Recommend Self Monitoring of Blood Pressure twice a day* AND *Recommend a Referral to (Cardiologist) for ruling out secondary causes* *AND* *Recommend a follow up appointment 2-4 weeks after*
In patients with snoring/apnoea, nocturia, nocturnal dyspnoea, night-time cardiovascular events, or resistant hypertension in addition to sleepiness during the daytime, Obstructive Sleep Apnoea (OSA) should be suspected [11].	IF the patient has [*Hypertension*] AND has 3 or more [*Antihypertensive drugs*] AND [*BP measurement*] over 140/90 mmHg AND patient has ([*snoring*]OR [*apnoea*]OR [*nocturia*] OR [*nocturnal dyspnoea*] OR [*sleepiness during the daytime]* OR [*night-time cardiovascular events*]) THEN *Notify the clinician that* 'In patients with snoring/apnoea, nocturia, nocturnal dyspnoea, night-time cardiovascular events, or resistant hypertension in addition to sleepiness during the daytime, Obstructive Sleep Apnoea (OSA) should be suspected [11].' AND *Recommend consider referring to respiratory clinicians for OSA* *OR* *Recommend consider referring to OSA services*
In hypertensive patients with bronchial asthma, β and αβ- blockers should be avoided [11].	IF the patient with *[hypertension]* AND [*bronchial asthma*] *Notify the clinician that* 'In hypertensive patients with bronchial asthma, β and αβ-blockers should be avoided [11]'
Non-steroidal anti-inflammatory drugs (NSAIDs) raise the blood pressure, mainly in this population of older adults, and antagonise the antihypertensive effects of diuretics, beta-blockers, ACE inhibitors, and ARBs. Therefore, these drugs must be carefully administered [11].	IF the patient is on ([*diuretics*] OR [*beta-blockers*] OR [*ACE inhibitors*] OR [*ARBs*]) THEN *Notify the clinician that* 'Non-steroidal anti-inflammatory drugs (NSAIDs) raise the blood pressure, mainly in this population of older adults, and antagonise the antihypertensive effects of diuretics, beta-blockers, ACE inhibitors, and ARBs. Therefore, these drugs must be carefully administered [11].'
Therapy with glucocorticoids, particularly at higher doses, causes an increase in blood pressure. If their administration is unavoidable, CCBs, ACE inhibitors, ARBs, beta-blockers, diuretics, or Mineralocorticoid Receptor Antagonists should be used [11].	IF the patient is on [*glucocorticoids*] AND (has [*hypertension*] diagnosis OR [*BP measurement*]>140/90) THEN *Notify the clinician that* 'Therapy with glucocorticoids, particularly at higher doses, causes an increase in blood pressure. If their administration

	is unavoidable, CCBs, ACE inhibitors, ARBs, beta-blockers, diuretics, or Mineralocorticoid Receptor Antagonists should be used'
The use of erythropoietin, oestrogen, or sympathomimetic drugs including antidepressants may cause an increase in BP. If BP increases during the use of these drugs, a reduction in the dose or discontinuation of administration should be considered. If they cannot be discontinued, CCBs, ACE inhibitors, ARBs or alpha-blockers should be used [11].	IF the patient is on [*erythropoietin*] OR [*oestrogen*] OR [*sympathomimetic drugs including antidepressants*] AND (has [*hypertension*] diagnosis OR [*BP measurement]*>140/90) THEN *Notify the clinician that* 'The use of erythropoietin, oestrogen, or sympathomimetic drugs including antidepressants may cause an increase in BP. If BP increases during the use of these drugs, a reduction in the dose or discontinuation of administration should be considered. If they cannot be discontinued, CCBs, ACE inhibitors, ARBs or alpha-blockers should be used [11].'
Table 1 presents the drug treatment recommendations for multimorbid older adults with cognitive impairment,	See Figures (Figure12-17)
Table 2 the compelling and possible contraindications to the use of specific antihypertensive drugs in this population [16].	

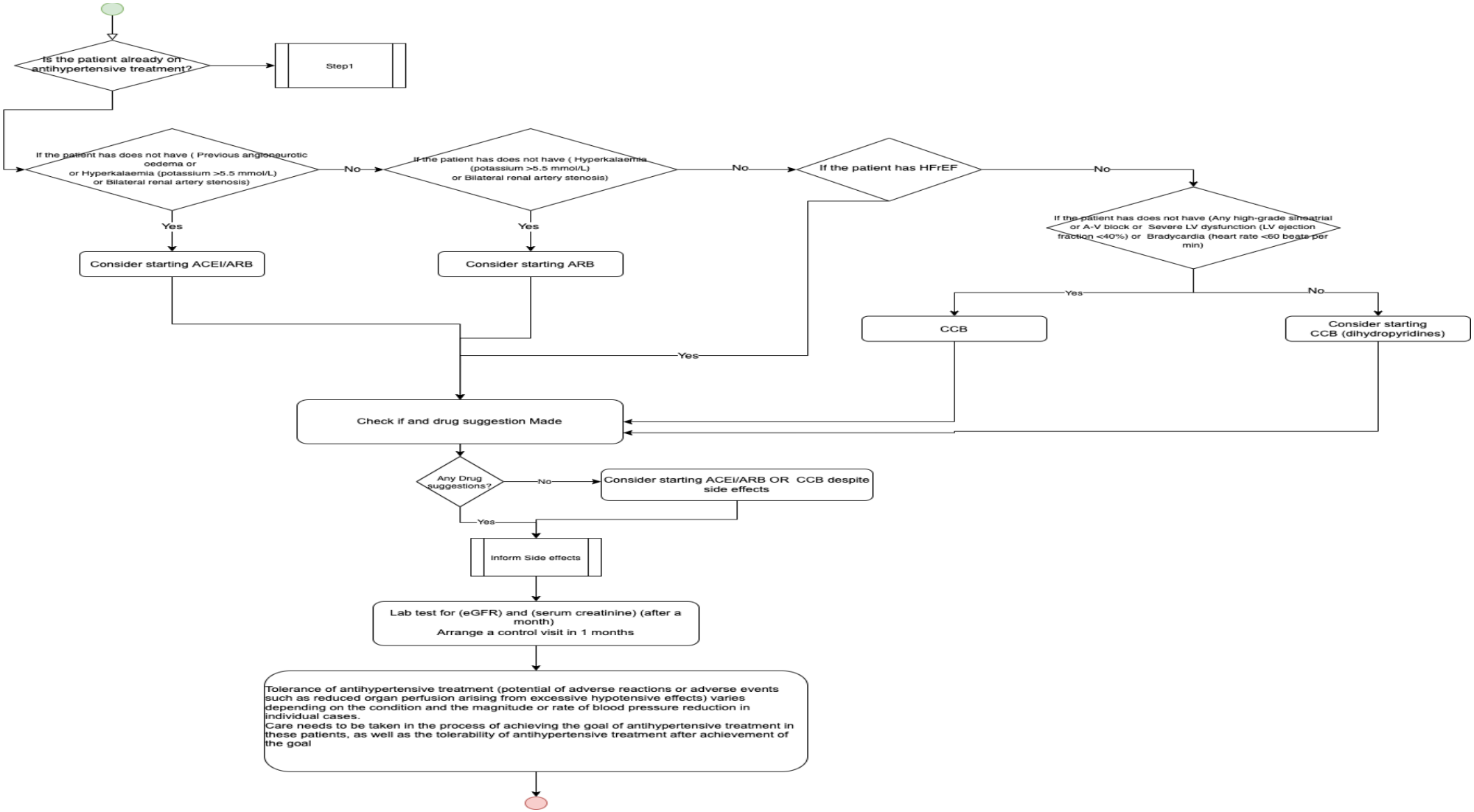

Figure 12- Antihypertensive Drug Algorithm-Initiate Monotherapy

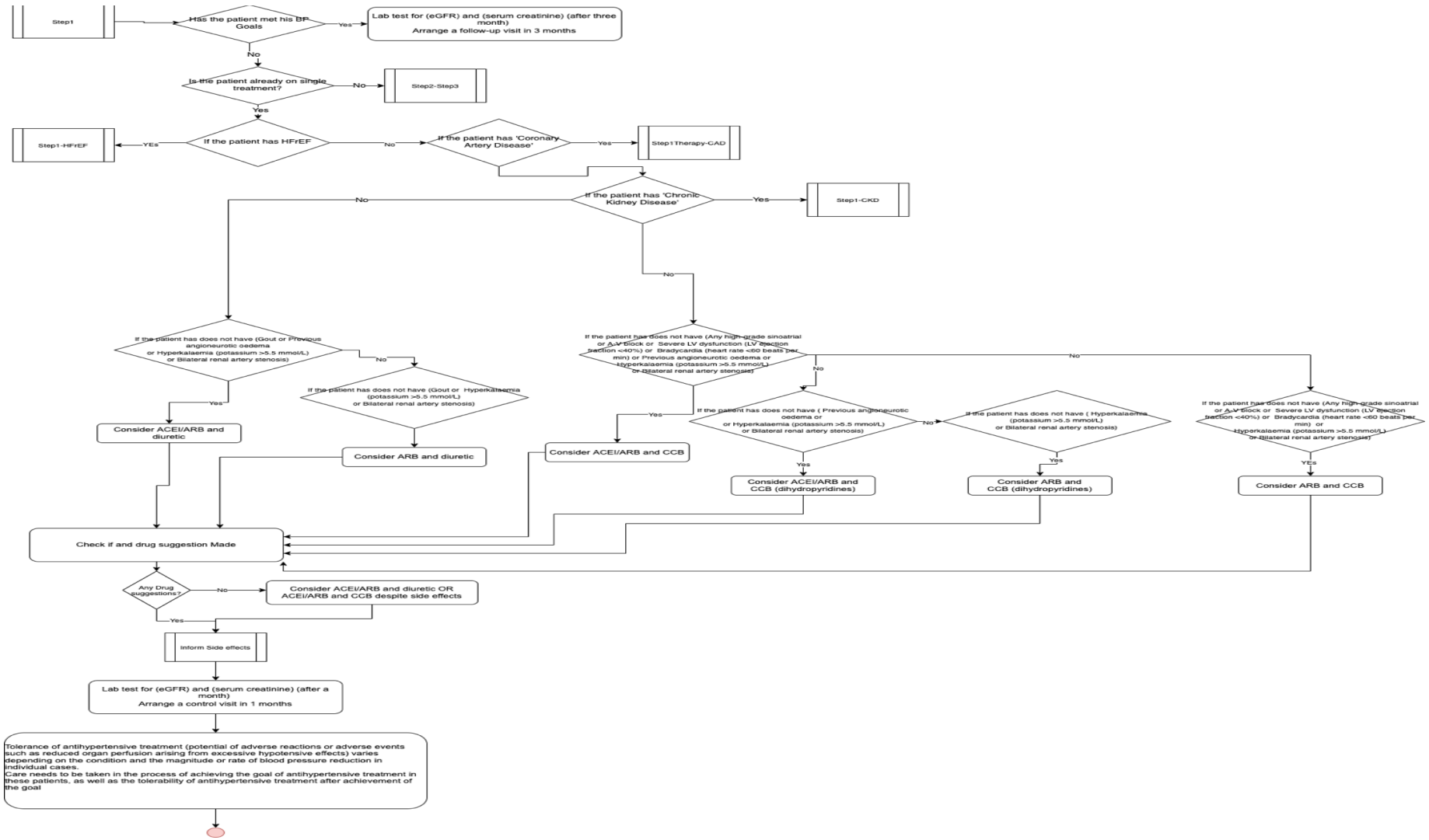

Figure 13- Antihypertensive Drug Algorithm-Step1-Most Patients

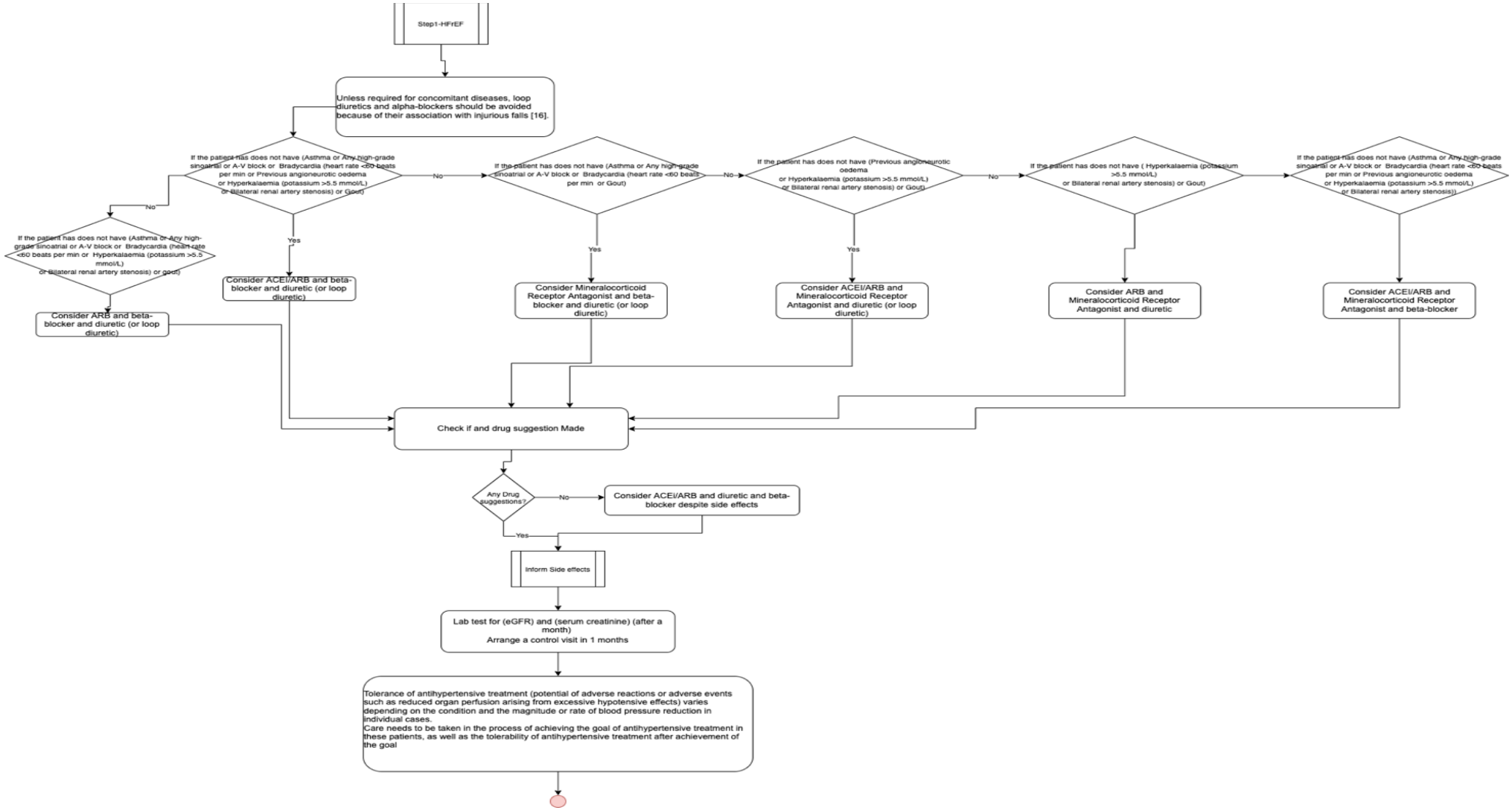

Figure 14- Antihypertensive Drug Algorithm-Step1 - HFrEF Patients

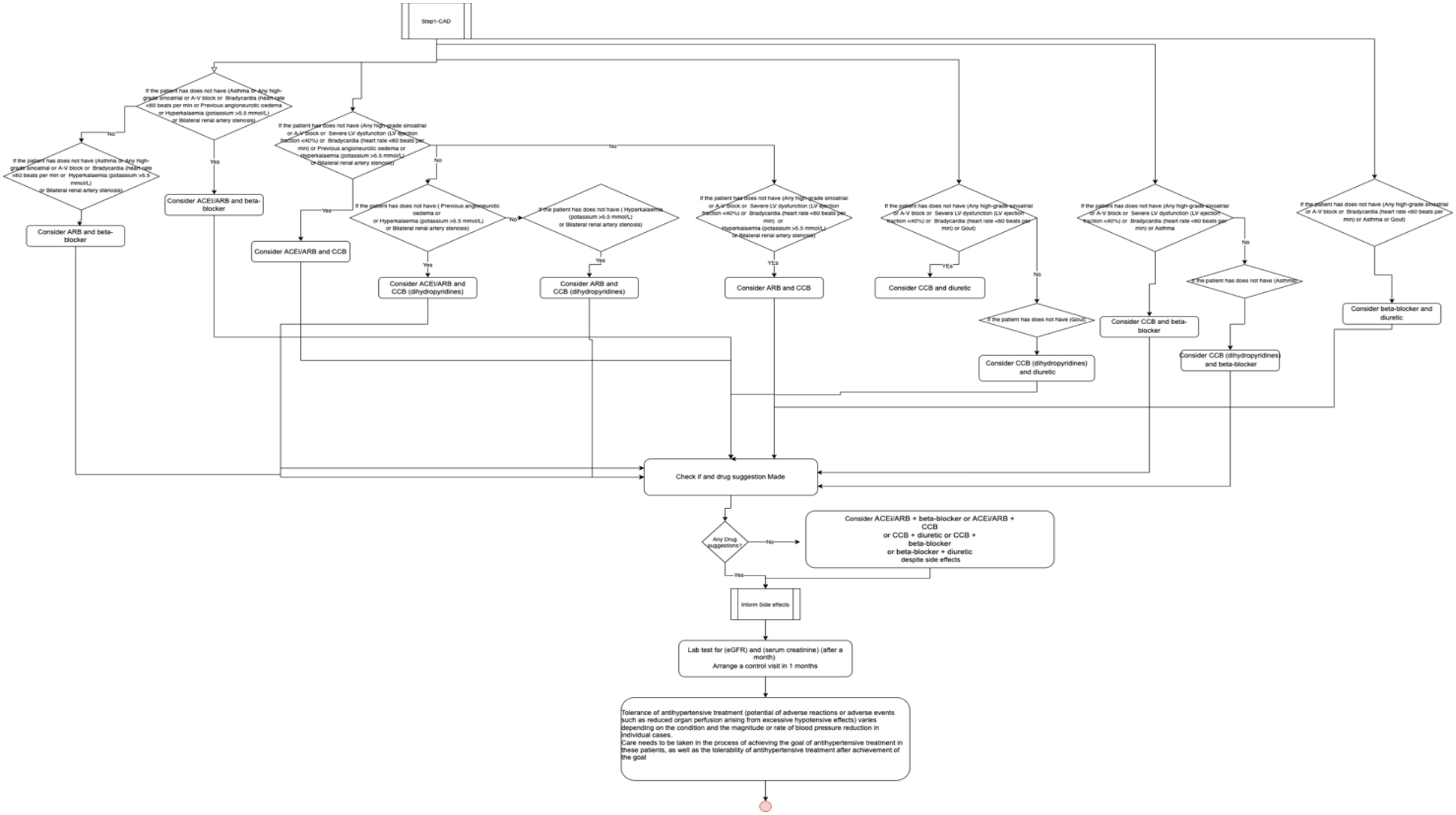

Figure 15- Antihypertensive Drug Algorithm-Step1 - CAD Patients

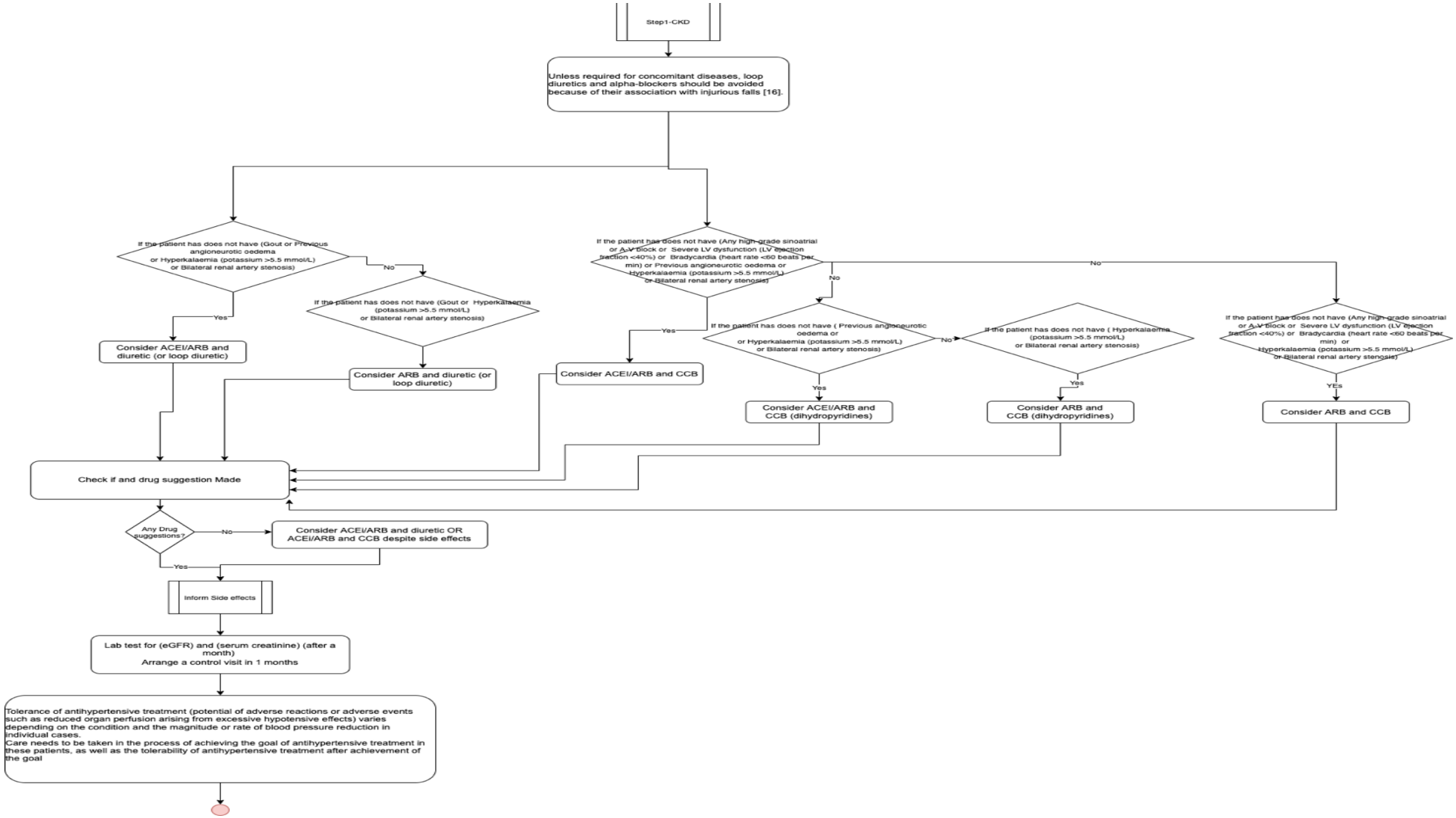

Figure 16- Antihypertensive Drug Algorithm-Step1 - CKD Patients

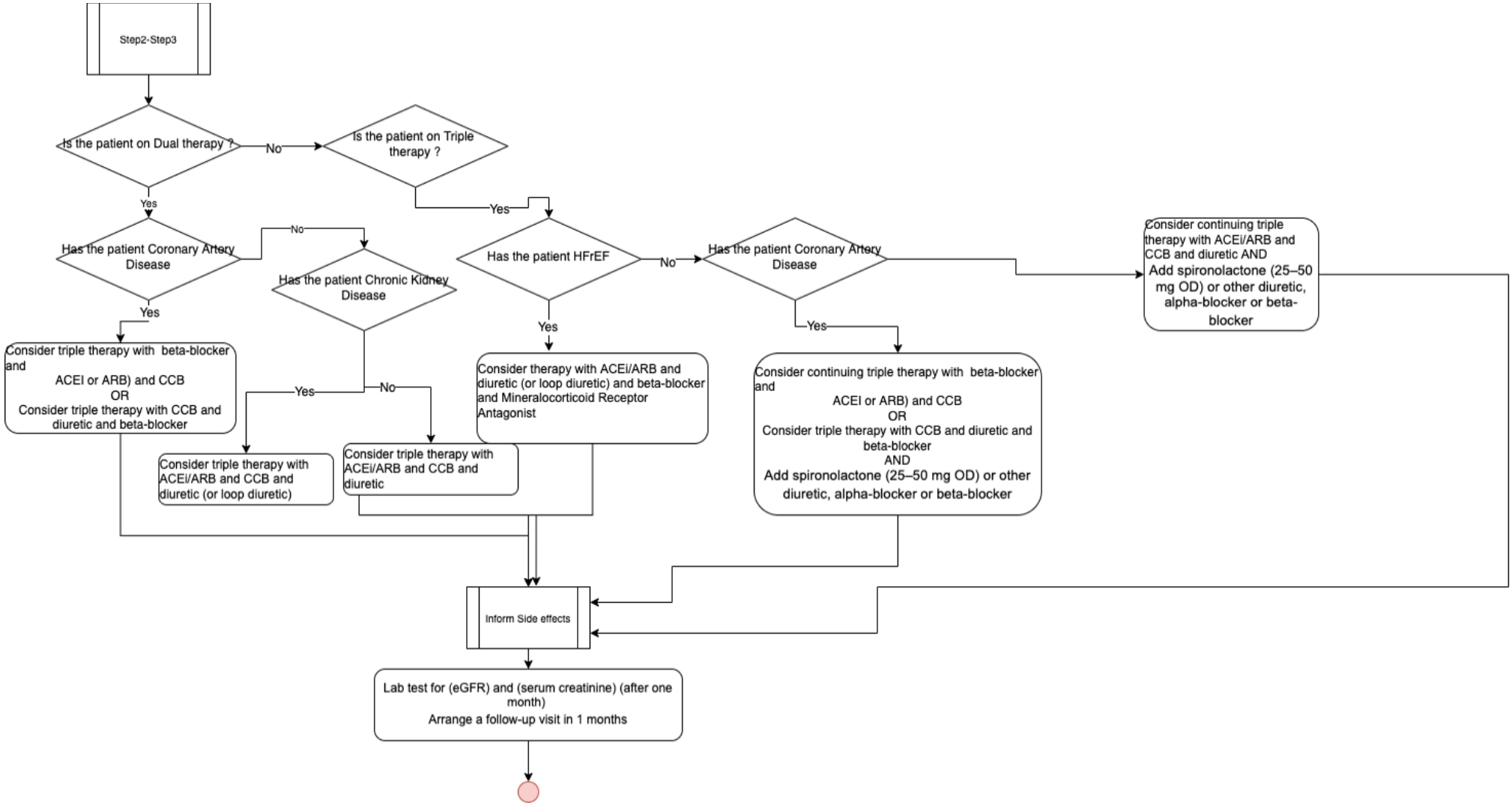

Figure 17- Antihypertensive Drug Algorithm-Step2&3-Adding new drugs when BP Goal not met

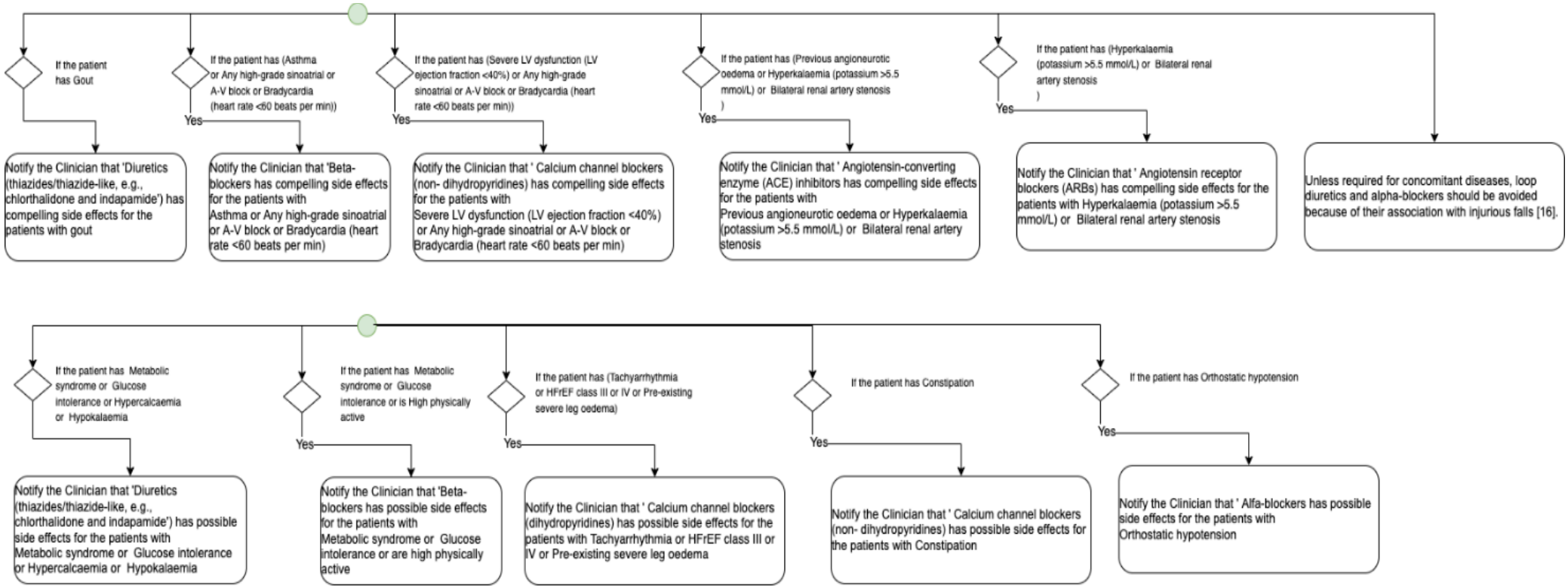

Figure 18- Drug treatment recommendations for multimorbid older adults with cognitive impairment.

9.2.8 Diabetes

Guideline	Rules after revision
It is important to recognize standards of care when treating older people with diabetes [17]. The most important outcomes in multimorbid older adults with cognitive impairment and diabetes are the maintenance of cognitive and functional status, and quality of life [18].	IF the patient has *[Diabetes]* THEN *Notify the Clinician tha*t 'It is important to recognize standards of care when treating older people with diabetes [17]. The most important outcomes in multimorbid older adults with cognitive impairment and diabetes are the maintenance of cognitive and functional status, and quality of life [18].'
Diabetes should be diagnosed by any of the following criteria: fasting plasma glucose (FPG) ≥126 mg/dL (7.0mmol/L), or Hba1c ≥6.5% (48 mmol/mol), **or** 2h plasma glucose (PG) in a 75 g oral glucose tolerance test (OGTT) ≥200 mg/dl (11.1 mmol/L), **or** in a patient with classic symptoms of hyperglycaemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L) [18].	IF the patient does not have *[Diabetes]* diagnosis yet AND IF *[Fasting plasma glucose (FPG)]* ≥126 mg/dL (7.0mmol/L), or *[Hba1c]* ≥6.5% (48 mmol/mol), or [*2h plasma glucose (PG) in a 75 g oral glucose tolerance test (OGTT)]*≥200 mg/dl (11.1 mmol/L), or in a patient with classic symptoms of [*hyperglycaemia]* or *[hyperglycemic crisis]*, a *[random plasma glucose]* ≥200 mg/dL (11.1 mmol/L) THEN *Recommend adding a Diagnosis (Diabetes*)
Pre-diabetes (defined as a state which places individuals at high risk of developing diabetes and its complications) is diagnosed by any of the following criteria: impaired fasting glucose as defined per FPG 100-125 mg/dL (5.6-6.9 mmol/L), **or** impaired glucose tolerance as defined per a 2-h PG during 75 g OGTT 140-199 mg/dL (7.8-11.0 mmol/L), **or** A1C 5.7-6.4% (39-47 mmol/mol).	IF the patient does not have *[Diabetes]* diagnosis yet AND IF *[FPG]* is between 100-125 mg/dL (5.6-6.9 mmol/L), **or** a [*2-h PG during 75 g OGTT] is between* 140-199 mg/dL (7.8-11.0 mmol/L), **or** *[HbA1C]* is between 5.7-6.4% (39-47 mmol/mol). THEN *Recommend adding a Diagnosis (Prediabetes*)
In older adults with pre-diabetes, a structured programme of healthy behaviour interventions that includes moderate weight loss and regular physical activity of a minimum of 150 minutes per week over 5 days a week should be implemented to reduce the risk of type 2 diabetes, and pharmacologic therapy with metformin may be used to reduce the risk of type 2 diabetes. 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. An interprofessional weight management programme is recommended to prevent weight gain and improve cardiovascular risk factors. In healthy patients with obesity, modest weight loss (5-7%) should be considered for its benefits on quality of life, mobility, physical functioning, and cardiometabolic risk factors [18].	IF the patient has [*Prediabetes*] AND *[Age] <80* THEN *Set a Goal for weight loss of [5%] in [3] months* IF the patient has *[Prediabetes]* THEN *Recommend Regular physical activity of a minimum of 150 minutes per week over 5 days a week* IF the patient has *[Prediabetes]* THEN *Recommend starting Medication(Metformin)*
Offer structured education to adults with type 2 diabetes and their family members or	IF the CAREPATH CDSS identifies that the patient is with *[Diabetes]*

carers (as appropriate) at the time of diagnosis, with annual reinforcement and review. Explain to people that structured education is an integral part of diabetes care.	THEN *Recommend assigning Education Material (Diabetes Education Material) to the patient* AND IF *[date of the last diabetes education session]* is older than one year *Recommend adding an Appointment with (Diabetes Nurse?) for diabetes education (this week)?*
Support for self-management should be offered to assist individuals in implementing and maintaining diabetes self-management by offering peer-led support or community support workers, diabetes coaching, or telephone follow-up. Education programmes for multimorbid older adults with type 2 diabetes and cognitive impairment should meet the cultural, linguistic, cognitive, and literacy needs of people in the local area. Self-management Education (SME) interventions may be offered in small group and/or one-on-one settings. Interventions that increase participation and collaboration of the person with diabetes in healthcare decision-making should be used, and those that target the family's ability to cope with stress or diabetes-related conflict should be included when indicated.	IF the patient has recently been diagnosed with *[Diabetes]* THEN *Notify the Clinician that* • Support for self-management should be offered to assist individuals in implementing and maintaining diabetes self-management by offering peer-led support or community support workers, diabetes coaching, or telephone follow-up. • Education programmes for multimorbid older adults with type 2 diabetes and cognitive impairment should meet the cultural, linguistic, cognitive, and literacy needs of people in the local area. Self-management Education (SME) interventions may be offered in small group and/or one-on-one settings. • Interventions that increase participation and collaboration of the person with diabetes in healthcare decision-making should be used, and those that target the family's ability to cope with stress or diabetes-related conflict should be included when indicated.
Programmes incorporating cognitive-behavioural educational interventions, such as problem solving, goal setting, self-monitoring of health parameters, dietary modifications, and physical activity are recommended.	None None None None
The care plan should consider assessment for symptoms of diabetes distress, disabilities, depression, anxiety, disordered eating, visual and hearing impairments, cognitive capacities, and other geriatric syndromes using a Comprehensive Geriatric Assessment (CGA) at the initial visit, at periodic intervals, and when there is a change in disease, treatment, or life circumstance, including caregivers and family members in this assessment.	It seems these will be functionality of AICP rather than CDS suggestions.. Or maybe simple an info card to be presented by the CDS IF the patient has been diagnosed with *[Diabetes]* THEN *Notify the Clinician that* 'The care plan should consider assessment for symptoms of diabetes distress, disabilities, depression, anxiety, disordered eating, visual and hearing impairments, cognitive capacities, and other geriatric syndromes using a Comprehensive Geriatric Assessment (CGA) at the initial visit, at periodic intervals, and when there is a change in disease, treatment, or life circumstance, including caregivers and family members in this assessment.' AND *Recommend a Completion of Comprehensive Geriatric Assessment (CGA)* *OR*

	Recommend Referral to for Comprehensive Geriatric Assessment (CGA)
The living situation and needs of older adults with diabetes and their caregivers should be evaluated to construct a tailored care plan. Impaired social functioning may reduce these patients' quality of life and increase the risk of functional dependency. Social and instrumental support networks that provide instrumental or emotional support for older adults with diabetes should be included in diabetes management discussions and shared decision-making [18].	IF the patient has been diagnosed with *[Diabetes]* THEN *Notify the Clinician that* 'The living situation and needs of older adults with diabetes and their caregivers should be evaluated to construct a tailored care plan. Impaired social functioning may reduce these patients' quality of life and increase the risk of functional dependency. Social and instrumental support networks that provide instrumental or emotional support for older adults with diabetes should be included in diabetes management discussions and shared decision-making [18].'
Referral to an inter-professional team with specialized training may be considered for individuals with type 2 diabetes who are consistently not meeting cardiometabolic targets, and adults with depression and diabetes for collaborative care.	IF the patient has been diagnosed with *[Diabetes] AND* has not met [*HbA1C and/or Cholesterol goals] in two consecutive visits* THEN *Recommend a Referral to Local Specialist Service*
	IF the patient has been diagnosed with *[Diabetes] AND [Depression]* THEN *Recommend a Referral to Local Specialist Service*
Measure A1C levels in adults with type 2 diabetes every 3 to 6 months (tailored to individual needs), until A1C is stable on unchanging therapy, and 6 months once the A1C level and blood glucose lowering therapy are stable	IF the patient has *[Diabetes]* AND *[has met his personalized HbA1C goal]* THEN *Recommend a Follow-up Appointment after 6 months* ELSE *Recommend a Follow-up Appointment after 3 months*
Discuss and agree an individual A1C target with patients and caregivers [19]. Multimorbid older adults with cognitive impairment should have less stringent glycaemic goals than the general population, such as A1C <8.0-8.5% (64-69 mmol/mol). Those who are healthy, with few coexisting chronic illnesses, very low cognitive and functional decline, could have glycaemic goals of A1C <7.0-7.5% (53-58 mmol/mol). However, hyperglycaemia leading to symptoms or risk of acute hyperglycemia complications should be avoided in all patients. Table 1 presents the framework for considering treatment goals in these patients [18].	IF the patient has [*Diabetes*] AND has more than 3 diseases from *[Chronic diseases list]* AND *[mild-to-moderate cognitive impairment]* THEN *Recommend HbA1C Goal (<8.0-8.5% (64-69 mmol/mol))* *AND* *Recommend start Medication (Statin) unless Contraindicated or not tolerated* *AND Recommend Total cholesterol Goal (< 4.0 mmol/litre), and HDL cholesterol Goal (< 1.4 mmol/litre) and total LDL Goal (< 2.0 mmol/litre).* *AND Recommend Blood Pressure Goal <140/90mmHg* ELSE if the patient has [*Diabetes*] AND has less than 3 diseases from [*Chronic diseases list*] AND (Does not have [*Cognitive Impairment]* OR *[low cognitive and functional decline (< 2 IADL Impairments]* THEN *Recommend HbA1C Goal(<7.0-7.5% (53-58 mmol/mol)).* *AND* *Recommend start Medication (Statin) unless contraindicated* *or not tolerated*

	AND Recommend Total cholesterol Goal (< 4.0 mmol/litre), and HDL cholesterol Goal (< 1.4 mmol/litre) and total LDL Goal (< 2.0 mmol/litre). *AND Recommend Blood Pressure Goal <140/90mmHg* ELSE IF the patient has [*Diabetes*] AND [LTC *or end-stage chronic illnesses (such as stage 3-4 heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy)]* OR [*moderate-to-severe cognitive impairment*] OR *[> 2 ADL impairments]* *THEN* *Notify the Clinician tha*t 'Avoid reliance on A1C; glucose control based on avoiding hypoglycaemia and symptomatic hyperglycaemia' AND 'Consider likelihood of benefit with statin' *AND Recommend Blood Pressure Goal <160/90mmHg* *AND* *Notify the Clinician tha*t 'Hyperglycaemia leading to symptoms or risk of acute hyperglycemia complications should be avoided in all patients' *Chronic diseases list:* • arthritis, • cancer, • congestive heart failure, • depression, • emphysema, • falls, • hypertension, • incontinence, • stage 3 or worse chronic kidney disease, • myocardial infarction, • stroke. • mild-to-moderate cognitive impairment

If adults with type 2 diabetes are self-monitoring their capillary blood glucose levels, conduct a structured assessment at least annually. The assessment should include the person's self-monitoring skills, the quality and frequency of testing, checking that the person knows how to interpret the blood glucose results and what action to take, the impact on the person's quality of life, the continued benefit to the person, and the equipment used [19].	IF the patient has [self-monitoring their capillary blood glucose levels] in his Care plan THEN *Notify the Clinician that* 'If adults with type 2 diabetes are self-monitoring their capillary blood glucose levels, conduct a structured assessment at least annually. The assessment should include the person's self-monitoring skills, the quality and frequency of testing, checking that the person knows how to interpret the blood glucose results and what action to take, the impact on the person's quality of life, the continued benefit to the person, and the equipment used [19].'
Discuss with adults with type 2 diabetes the benefits and risks of drug treatment and the options available. Base the choice of drug treatments on the person's individual clinical circumstances, for example co-morbidities, contraindications, weight, risks from polypharmacy, the person's individual preferences and needs, the effectiveness of the drug treatments in terms of metabolic response, cardiovascular and renal protection, time-to-benefit, safety and tolerability of the drug treatment, monitoring requirements, the licensed indications, or combinations available, and costs [19].	IF the patient has [*Diabetes*] AND does not have *[Antidiabetic Medication]* THEN *Notify the Clinician that* 'Discuss with adults with type 2 diabetes the benefits and risks of drug treatment and the options available. Base the choice of drug treatments on the person's individual clinical circumstances, for example co-morbidities, contraindications, weight, risks from polypharmacy, the person's individual preferences and needs, the effectiveness of the drug treatments in terms of metabolic response, cardiovascular and renal protection, time-to-benefit, safety and tolerability of the drug treatment, monitoring requirements, the licensed indications, or combinations available, and costs [19].'
Before initiating pharmacological treatment, assess the person's cardiovascular status and risk to determine whether they have chronic HF, established atherosclerotic cardiovascular disease, or are at high risk of developing cardiovascular disease and chronic kidney disease, to select the most suitable drug regimen [19].	IF the patient has [*Diabetes*] AND does not have *[Antidiabetic Medication]* THEN *Notify the Clinician that* 'Before initiating pharmacological treatment, assess the person's cardiovascular status and risk to determine whether they have chronic HF, established atherosclerotic cardiovascular disease, or are at high risk of developing cardiovascular disease and chronic kidney disease, to select the most suitable drug regimen [19].' We can present the following in AICP screens: • status of established atherosclerotic cardiovascular disease • status chronic kidney disease and ask the physician to set whether the patient has high risk of developing cardiovascular disease or chronic kidney disease.
Diabetes Medication Flow	Medication Flow in Figure 1
Consider metformin as the first-line agent for older adults with type 2 diabetes. It may be used safely in patients with eGFR <30 mL/min/1.73m^2. However, it is contraindicated in patients with advanced renal insufficiency and should be used with	IF the patient has [*Diabetes*] AND has *[no Diabetic Medication]* AND [*eGFR*] <30 mL/min/1.73m2 THEN *Recommend*

caution in patients with impaired hepatic function or heart failure, because of an increased risk of lactic acidosis. Gradually increase the dose of standard-release metformin over several weeks to minimise the risk of gastrointestinal side effects. In case of gastrointestinal side effects, or a reduction in appetite, it may be necessary for a dose reduction, change to modified-release formulation, or drug elimination [18].	*Starting Medication(Metformin (Gradually increase the dose of standard-release metformin over several weeks to minimise the risk of gastrointestinal side effects.)* AND *Assigning Metformin side effect questionnaire to the patient* ELSE [Continue with the algorithm below]
Oral dipeptidyl peptidase 4 (DPP-4) inhibitors and SGLT2 inhibitors have few side effects and could be considered second-line drug classes in this population [18]. In patients with chronic HF, established atherosclerotic cardiovascular disease, or are at high risk of developing cardiovascular disease, offer an SGLT2 inhibitor with proven cardiovascular benefit in addition to metformin. When starting dual therapy with metformin and an SGLT2 inhibitor as first-line therapy, introduce the drugs sequentially, starting with metformin and checking tolerability. Start the SGLT2 inhibitor as soon as metformin tolerability is confirmed [18;19].	See Figure 19
Sulfonylureas, other insulin secretagogues, and thiazolidinediones should be used very cautiously in this population. If used, sulfonylureas with a shorter duration of action, such as glipizide or glimepiride, are preferred [18].	See Figure 19
For adults with type 2 diabetes, if dual therapy with metformin and another oral drug has not continued to control A1C to below the person's individually agreed threshold for further intervention, consider either triple therapy by adding a DPP-4 inhibitor, an SGLT2 inhibitor, or a sulfonylurea/secretagogues, or start insulin-based treatment [19].	See Figure 19
If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated, or contraindicated, consider triple therapy by switching one drug for a GLP1 mimetic for older adults with type 2 diabetes who have a body mass index (BMI) ≥35k g/m^2, or have a BMI lower than 35k g/m^2 but weight loss would benefit other significant obesity-related co-morbidities. Only continue GLP1 mimetic therapy if a beneficial metabolic response occurs (a reduction of at least 1% in A1C [11 mmol/mol] and weight loss of at least 3% of initial body weight in 6 months) [19].	See Figure 19

The use of insulin therapy requires that patients or their caregivers have their visual, motor skills, and cognitive ability carefully assessed to avoid dosage or administration errors. Insulin therapy relies on the ability of these patients with cognitive impairment and multimorbidity, to administer insulin on their own or with the assistance of a caregiver. Insulin doses should be titrated to meet individualised glycaemic targets and to mainly avoid hypoglycaemia. Once-daily basal insulin injection therapy is preferred because of its association with lower side effects and may be a reasonable option in many older patients. Insulin degludec or insulin glargine U-300 may be considered over insulin glargine U-100 to reduce overall and nocturnal hypoglycaemia. Prefilled insulin pens should be used to reduce dosing errors and to potentially improve glycaemic control. Multiple daily injections of insulin may be too complex for these older patients with advanced diabetes complications, life-limiting coexisting chronic illnesses, or limited functional status [18, 19]	See Figure 19
When starting insulin therapy, provide a structured programme using active insulin dose titration that encompasses injection technique including rotating injection sites and avoiding repeated injections at the same point within sites, continuing telephone support, self-monitoring, dose titration to target levels, dietary advice, managing hypoglycaemia, managing acute changes in plasma glucose control, and support from an appropriately trained and experienced healthcare professional. In these patients, continue to offer metformin when there are no contraindications or intolerance. Review the continued need for other blood glucose lowering therapies [19]. When using basal insulin (long or intermediate acting; glargine U-100 and U-300, detemir, and degludec), changing the timing from bedtime to morning is preferable, and titrate the dose based on fasting fingerstick glucose test results over a week. Initial fasting goal should be 90-150 mg/dL (5.0-8.3 mmol/L), although it may change dependent on patient characteristics.	See Figure 19
Increase basal insulin 2 units if >50% of fasting glucose values are over the goal and reduce 2 units if >2 fasting glucose levels/week are <80 mg/dL (4.4 mmol/L) [1].	IF the patient has [Diabetes] AND is on [Insulin] AND >50% of fasting glucose values are over the goal THEN Recommend Increase basal insulin 2 units

	ELSE IF the patient has [Diabetes] AND is on [Insulin] AND >2 fasting glucose levels/week are <80 mg/dL (4.4 mmol/L) THEN reduce basal insulin 2 units
Monitor patients who are on a basal insulin regimen for the need for short acting insulin before meals (or a pre-mixed biphasic insulin preparation) [19].	See Figure 19
Screening for diabetes complications should be individualised in older adults, but the main focus should be on those leading to functional impairment. These patients are less likely to benefit from reducing the risk of microvascular complications and more likely to suffer serious adverse effects from hypoglycaemia. However, patients with poorly controlled diabetes may be subject to acute complications of diabetes, including dehydration, poor wound healing, and hyperglycaemic hyperosmolar coma. Glycaemic goals should, at a minimum, avoid these consequences [18].	IF the patient has been diagnosed with *[Diabetes]* THEN *Notify the Clinician that* 'Screening for diabetes complications should be individualised in older adults, but the main focus should be on those leading to functional impairment. These patients are less likely to benefit from reducing the risk of microvascular complications and more likely to suffer serious adverse effects from hypoglycaemia. However, patients with poorly controlled diabetes may be subject to acute complications of diabetes, including dehydration, poor wound healing, and hyperglycaemic hyperosmolar coma. Glycaemic goals should, at a minimum, avoid these consequences [18]'
Tight glycaemic control in this population is associated with an increased risk of hypoglycaemia. Hypoglycaemia, defined as a glucose level <70mg/dL (3.9 mmol/L), has been linked to increased risk of dementia, and conversely, cognitive decline has also been associated with an increased risk of hypoglycaemia. Patients and their caregivers should be routinely asked about hypoglycaemia and hypoglycaemia unawareness (neuroglycopenic symptoms: dizziness, poor coordination, tiredness, visual disturbance, difficulty concentrating, and autonomic symptoms: sweatiness, pounding heart, trembling, and being nervous/tense). Older patients can also be risk stratified for future risk for hypoglycaemia with validated risk calculators (e.g., Kaiser Hypoglycemia Model, Table 4). An important step in mitigating hypoglycaemia risk is to determine whether the patient is skipping meals or inadvertently repeating doses of their medications [18].	This will be asked via AICP to be routinely recorded in visits? 'How many times has the patient ever had hypoglycemia related utilization in an ED or hospital (0, 1-2, more than or equal to 3)'
	Not to be asked.
	Not to be used in Carepath
	We will record the presence of these in AICP: - Is the patient skipping meals - Is the patient inadvertently repeating doses of their medications
Continuous Glucose Monitoring (CGM) may be an option for older patients with type 2 diabetes using multiple daily injections of insulin, to prevent hypoglycaemia [18].	IF the patient has been diagnosed with *[Diabetes]* AND has [on Insulin] OR [Hypoglycemia] THEN *Notify the Clinician that* 'Continuous Glucose Monitoring (CGM) may be an option for older patients with type 2 diabetes using multiple daily injections of insulin, to prevent hypoglycaemia [18] AND *Recommend Continuous Glucose Monitoring (CGM) to Patient*
	These will be implemented as early warning rules:

Consider the following situations as alert strategies in multimorbid older adults with cognitive impairment: A. Contact providers immediately when low blood glucose levels <70 mg/dL (3.9 mmol/L). B. Contact providers as soon as possible if: I. Glucose values are 70–100 mg/dL (3.9-5.6 mmol/L), as the regimen may need to be adjusted. II. Glucose values are >250 mg/dL (13.9 mmol/L) within a 24 hour period or >300 mg/dL (16.7 mmol/L) over 2 consecutive days. III. Any reading is too high for the glucometer. IV. The patient is sick, with vomiting, symptomatic hyperglycaemia, or poor oral intake.	IF [blood glucose levels] <70 mg/dL (3.9 mmol/L) *Notify the Patient/Informal Care giver tha*t 'Contact providers immediately' IF [blood glucose levels] 70–100 mg/dL (3.9-5.6 mmol/L) *Notify the Patient/Informal Care giver tha*t 'Contact providers as soon as possible as the regimen may need to be adjusted' IF [*blood glucose levels*] 70–100 mg/dL (3.9-5.6 mmol/L) OR *blood glucose levels*] >250 mg/dL (13.9 mmol/L) within a 24 hour period or >300 mg/dL (16.7 mmol/L) over 2 consecutive days OR Any reading is too high for the glucometer *Notify the Patient/Informal Care giver tha*t '*Contact providers as soon as possible as the regimen may need to be adjusted'*
	These will be implemented as early warning rules: IF the patient presents the following symptoms: *[vomiting], [symptomatic hyperglycaemia], or [poor oral intake]* *Notify the Patient/Informal Care giver tha*t 'Contact as soon as possible'
In older adults receiving palliative care, or end-of-life care, the focus should be to avoid hypoglycaemia and symptomatic hyperglycaemia, while reducing the burdens of glycaemic control and management. When organ failure develops, medicines will have to be de-intensified or de-prescribed. For the dying patient, most agents for type 2 diabetes may be omitted [18].	IF the patient has been diagnosed with *[Diabetes] AND [palliative care]* *Notify the Clinician tha*t 'In older adults receiving palliative care, or end-of-life care, the focus should be to avoid hypoglycaemia and symptomatic hyperglycaemia, while reducing the burdens of glycaemic control and management.'
	Not to be implemented
Take the into account relevant national government guidelines in these patients when still driving [19].	If the patient has [Diabetes] THEN Present the following Info Card 'Take the into account relevant national government guidelines in these patients when still driving'
Cognitive behavioural therapy (CBT) can be used to treat depression in individuals with depression, alone or in combination with antidepressant medication, for maintenance treatment to prevent recurrence of depression	If the patient has [*Diabetes*] AND [*Depression*] OR [GDS-4 Score]>=2 THEN *Recommend Referral for CBT* *AND* *Recommend starting Medication [Antidepressant prescription]*
Screening for peripheral neuropathy should be conducted by assessing loss of sensitivity to the 10 g monofilament or loss of sensitivity to vibration at the dorsum of the great toe. The following agents are preferred to relieve painful peripheral	If the patient has [*Diabetes*] THEN *Notify Clinician that* 'Screening for peripheral neuropathy should be conducted by assessing loss of sensitivity to the 10 g monofilament or loss of sensitivity to vibration at the dorsum of the great toe.'

neuropathy in this population: pregabalin, gabapentin, anticonvulsants (carbamazepine or valporate), or antidepressants (duloxetine). Be aware of the increased likelihood of side effects such as orthostatic hypotension, delirium, and functional or cognitive decline when using these drugs [19].	If the patient has [*Diabetes*] AND [peripheral neuropathy] THEN *Recommend starting Medication [pregabalin, gabapentin, anticonvulsants (carbamazepine or valporate), or antidepressants (duloxetine)]* *AND* *Notify the clinician that* 'Be aware of the increased likelihood of side effects such as orthostatic hypotension, delirium, and functional or cognitive decline when using these drugs'
Think about the possibility of autonomic neuropathy affecting the gut in older adults with type 2 diabetes who have unexplained diarrhoea that happens particularly at night [19], and in autonomic neuropathy affecting the bladder in those with unexplained bladder emptying problems [19].	If the patient has [*Diabetes*] AND [unexplained diarrhoea that happens particularly at night] OR unexplained bladder emptying problems THEN *Notify Clinician that* 'Think about the possibility of autonomic neuropathy affecting the gut in older adults with type 2 diabetes who have unexplained diarrhoea that happens particularly at night [19], and in autonomic neuropathy affecting the bladder in those with unexplained bladder emptying problems [19]. AND *Recommend Referral for autonomic neuropathy Diagnosis*
Feet should be tested annually in this population, and where complications arrive, clinicians should refer to relevant guidelines for the management of diabetic foot disease [19].	If the patient has [*Diabetes*] THEN *Notify Clinician that* 'Feet should be tested annually in this population, and where complications arrive, clinicians should refer to relevant guidelines for the management of diabetic foot disease'
Offer older men with type 2 diabetes the opportunity to discuss erectile dysfunction as part of their annual review. Offer education and support, addressing contributory factors such as cardiovascular disease as well as possible treatment options [19].	If the patient has [*Diabetes*] AND [Male] THEN *Notify Clinician that* 'Offer older men with type 2 diabetes the opportunity to discuss erectile dysfunction as part of their annual review. Offer education and support, addressing contributory factors such as cardiovascular disease as well as possible treatment options [19].
Screening and evaluation for diabetic retinopathy should be performed by an experienced vision care professional (optometrist or ophthalmologist) at the time of diagnosis of diabetes. In those with no or minimal retinopathy, the recommended interval for testing is 1–2 years. Arrange emergency review by an ophthalmologist for sudden loss of vision or visual acuity reduction or flashes [19].	IF the patient has [*Diabetes*] THEN *Notify Clinician that* 'Screening and evaluation for diabetic retinopathy should be performed by an experienced vision care professional (optometrist or ophthalmologist) at the time of diagnosis of diabetes. In those with no or minimal retinopathy, the recommended interval for testing is 1–2 years' AND *Recommend Referral (*ophthalmologist*) for retinopathy review* IF the patient has [*Diabetes*] AND [sudden loss of vision] OR [visual acuity reduction] OR [flashes] THEN *Notify Clinician that* 'Arrange emergency review by an ophthalmologist for sudden loss of vision or visual acuity reduction or flashes [19].^ AND *Recommend Referral (*ophthalmologist*) for emergency review*

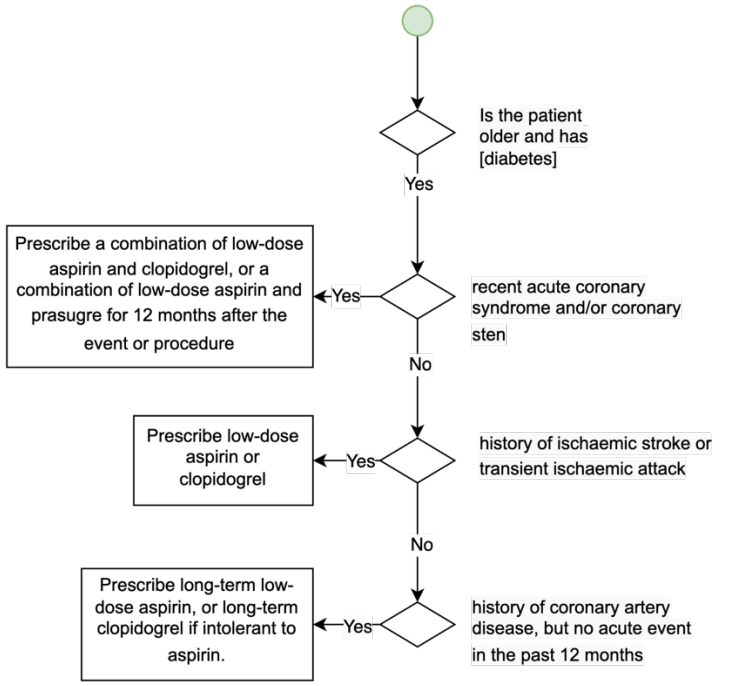

Table 1- Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in multimorbid older adults with diabetes and cognitive impairment

Patient characteristics	Reasonable A1C goal	Fasting or pre-prandial glucose	Bedtime glucose	Blood pressure	Lipids
Complex/ intermediate (multiple co-existing chronic illnesses* or ≥ 2 IADL impairments or mild-to-moderate cognitive impairment)	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or > 2 ADL impairments)	Avoid reliance on A1C; glucose control based on avoiding hypoglycaemia and symptomatic hyperglycaemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<160/90 mmHg	Consider likelihood of benefit with statin

Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is important for treatment individualisation. A patient's health status and preferences may change over time. ADL: activities of daily living; LTC: long-term care. *Co-existing chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. "Multiple" means at least three, but many patients may have five or more. **The presence of a single end-stage chronic illness, such as stage 3-4 heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy.

Modified from: American Diabetes Association. "12. Older adults: standards of medical care in diabetes—2021." Diabetes care 44.Supplement_1 (2021): S168-S179.

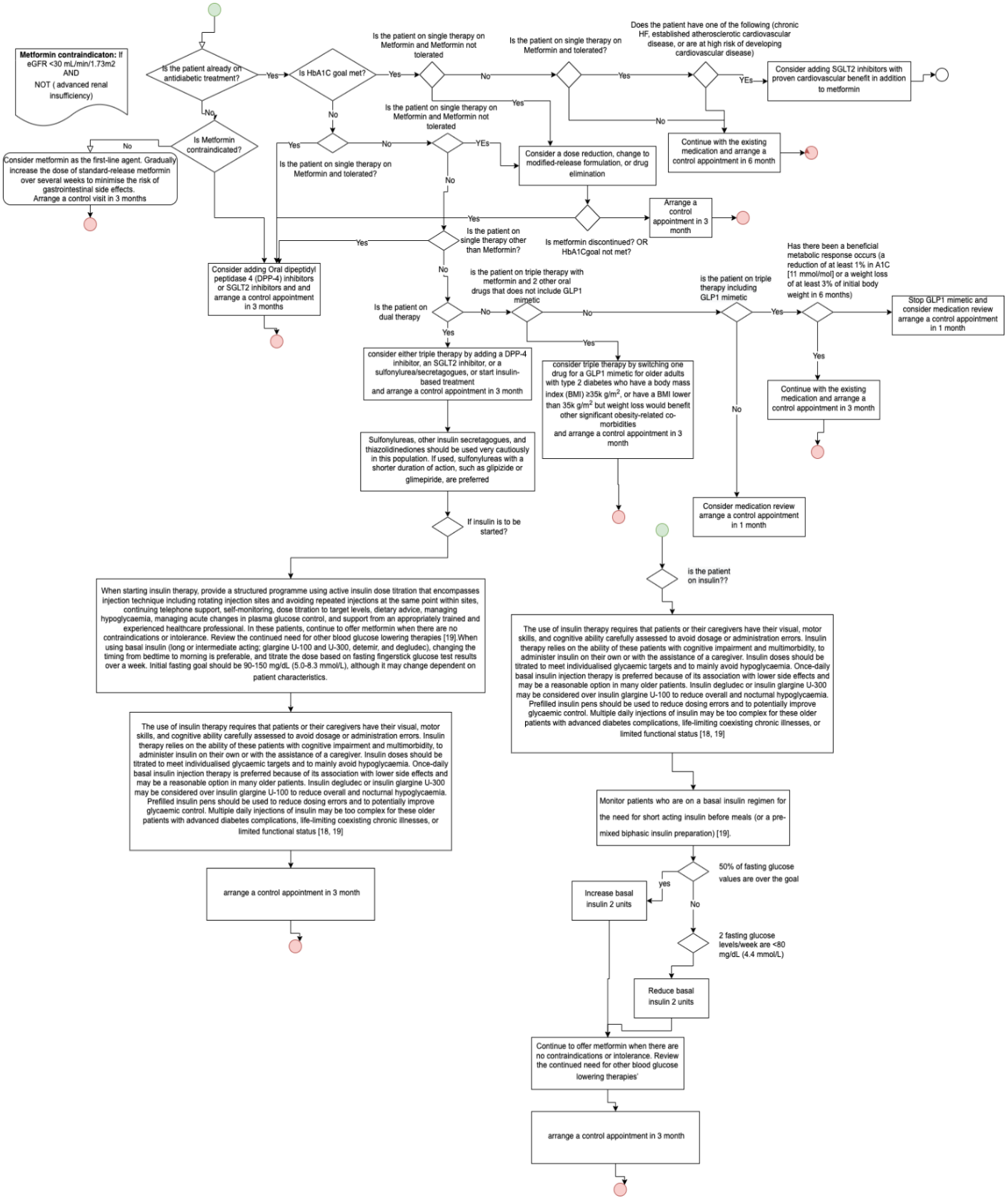

Figure 19- Antidiabetic medication flow

9.2.9 Chronic Kidney Disease

Guideline	Rules after revision
Testing for CKD using eGFR creatinine and urine albumin/creatinine ratio (ACR) should be offered to older adults with multimorbidity and cognitive impairment with any of the following risk factors: diabetes, hypertension, previous episode of acute kidney injury, cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease, or cerebral vascular disease), structural renal tract disease, recurrent renal calculi or prostatic hypertrophy, multi-system diseases with potential kidney involvement, for example systemic lupus erythematosus, gout, or incidental detection of haematuria or proteinuria [21].	IF [NOT eGFR in previous 365 days OR NOT ACR in previous 365 days] THEN [*Recommend clinician to 'Test for CKD using eGFR creatinine* (LOINC: 45066-8) *and urine albumin/creatinine ratio (ACR)* (LOINC: 32294-1) *in older adults with multimorbidity and cognitive impairment with any of the following risk factors: diabetes, hypertension, previous episode of acute kidney injury, cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease, or cerebral vascular disease), structural renal tract disease, recurrent renal calculi or prostatic hypertrophy, multi-system diseases with potential kidney involvement, for example systemic lupus erythematosus, gout, or incidental detection of haematuria or proteinuria* (AICP)]
eGFR creatinine measurement in this population may be less reliable in certain situations like acute kidney injury, oedematous states, muscle wasting disorders, sarcopenia, malnutrition, higher muscle mass, use of ONS with proteins, or in those who have had an amputation [21].	IF [NOT eGFR in previous 365 days OR NOT ACR in previous 365 days] THEN [*Recommend clinician that 'eGFR creatinine measurement in this population may be less reliable in certain situations like acute kidney injury, oedematous states, muscle wasting disorders, sarcopenia, malnutrition, higher muscle mass, use of ONS with proteins, or in those who have had an amputation'*]
Proteinuria should be measured with ACR in older adults with multimorbidity and cognitive impairment. In patients with diabetes, an eGFR of less than 60 ml/min/1.73 m^2, or with an eGFR of 60 ml/min/1.73 m^2 or more if there is a strong suspicion of CKD [21].	
Classify CKD in adults using a combination of GFR (ml/min/1.73 m^2) and ACR (mg/g or mg/mmol) categories (see Table 5) [21].	**GFR categories or stage** IF GFR >= 90 then GFRcat=G1 IF 60 =<GFR< 90 then GFRcat=G2 IF 45 =<GFR =< 59 then GFRcat=G3a IF 30 =<GFR =< 44 then GFRcat=G3b IF 15 =<GFR =< 29 then GFRcat=G4 IF GFR < 15 then GFRcat=G5 (ICD-10-CM: N18.1-9) **Albuminuria category** IF ACR < 30 mg/g (3 mg/mmol) THEN AlbCat= A1

	IF 30 mg/g (3 mg/mmol) =<ACR <299 mg/g (29 mg/mmol) THEN AlbCat= A2 IF 300 mg/g (30 mg/mmol) =<ACR THEN AlbCat= A3
Accelerated progression of CKD can be considered a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months, or a sustained decrease in GFR of 15 ml/min/1.73 m^2 per year [21].	IF [[Current GFR – Previous GFR (One year ago) > Current GFR/4] OR [GFR Cat Changes (In past year)] OR [Current GFR – Previous GFR (One year ago) > 15] THEN *Recommend clinician that 'Accelerated progression of CKD is happening'* *Recommend adding a Diagnosis (Accelerated progression of CKD*), AND *Recommend a Referral to (Nephrologist or Specialist) for specialist assessment.*
Offer a renal ultrasound scan to all adults with CKD who have accelerated progression of CKD, have visible or persistent invisible haematuria, have symptoms of urinary tract obstruction, have a family history of polycystic kidney disease, or have a GFR of less than 30 ml/min/1.73 m^2 (GFR category G4 or G5) [21].	IF [ICD-10-CM: N18 AND [Accelerated progression of CKD OR visible haematuria ICD-10-CM: R31.0 OR AICP OR persistent invisible haematuria ICD-10-CM: N02 OR AICP OR symptoms of urinary tract obstruction (AICP) OR family history of polycystic kidney disease (AICP) OR GFRcat =G4 or =G5)] THEN [*Recommend clinician to 'Request Renal ultrasound'*]
Agree a plan to establish the cause of CKD during an informed discussion with the patient, particularly if the cause may be treatable (for example, urinary tract obstruction, medicines that can adversely affect kidney function, or glomerular disease) [21]. Offer patients with CKD, their family members or carers as appropriate, education and information tailored to the	IF [New case of ICD-10-CM: N18] THEN [*Recommend clinician to 'Agree a plan to establish the cause of CKD during an informed discussion with the patient, particularly if the cause may be treatable (for example, urinary tract obstruction, medicines that can adversely affect kidney function, or glomerular disease). '*

severity and cause of CKD, the associated complications, and the risk of progression. Involve older adults with CKD in the education programme from the outset. Discuss the available treatments, what are their advantages and disadvantages, what complications or side effects may occur, what can people do to manage and influence their own condition, and in what ways could CKD and its treatment affect people's daily life and social activities. Take account of the psychological aspects of coping with CKD and offer adults with CKD access to support, for example, support groups, counselling, or a specialist nurse [21].	AND *Recommend clinician to 'Offer patients with CKD, their family members or carers as appropriate, education and information tailored to the severity and cause of CKD, the associated complications, and the risk of progression.* *Involve older adults with CKD in the education programme from the outset.* *Discuss the available treatments, what are their advantages and disadvantages, what complications or side effects may occur, what can people do to manage and influence their own condition, and in what ways could CKD and its treatment affect people's daily life and social activities.* *Take account of the psychological aspects of coping with CKD and offer adults with CKD access to support, for example, support groups, counselling, or a specialist nurse'*]
Offer dietary advice about potassium, phosphate, calorie, and salt intake appropriate to the severity of CKD. Do not offer low-protein diets (dietary protein intake less than 0.6 to 0.8 g/kg/day). Give information about controlling intake of phosphate-rich foods (in particular, foods with a high phosphate content per gram of protein, as well as food and drinks with high levels of phosphate additives) to control serum phosphate, while avoiding malnutrition by maintaining a protein intake at or above the minimum recommended level [21].	IF [New case of ICD-10-CM: N18] THEN [*Recommend clinician that In CKD patient it is recommended to offer dietary advice about potassium, phosphate, calorie, and salt intake appropriate to the severity of CKD. Do not offer low-protein diets (dietary protein intake less than 0.6 to 0.8 g/kg/day). Give information about controlling intake of phosphate-rich foods (in particular, foods with a high phosphate content per gram of protein, as well as food and drinks with high levels of phosphate additives) to control serum phosphate, while avoiding malnutrition by maintaining a protein intake at or above the minimum recommended level. ,*]
The frequency of eGFR creatinine monitoring should be tailored according to the underlying cause of CKD, the rate of decline in eGFR or increase in ACR, risk factors like heart failure, diabetes and hypertension, changes in the treatment (such as renin– angiotensin–aldosterone system antagonists, NSAIDs and diuretics), intercurrent illness (for example acute kidney injury), and whether they have chosen conservative management of CKD.	IF [ICD-10-CM: N18 [ ] THEN [*Recommend a Follow-up Appointment to monitor eGFR creatinine tailored according to the underlying cause of CKD, the rate of decline in eGFR or increase in ACR, risk factors like heart failure, diabetes and hypertension, changes in the treatment (such as renin– angiotensin–aldosterone system antagonists, NSAIDs and diuretics), intercurrent illness (for example acute kidney injury), and whether they have chosen conservative management of CKD.'*]
In these patients, the chronic use of NSAIDs may be associated with progression of CKD, and acute use is associated with a reversible decrease in	IF [ICD-10-CM: N18 AND

GFR. Great caution must be taken when giving NSAIDs to this population over prolonged periods of time. Monitor the effects on GFR, particularly in people with a low baseline GFR and/or in the presence of other risks for progression [21].	NSAIDs prescribed AND AICP [ ] THEN [*Recommend clinician that 'There should be no subscription of NSAID in the presence of CKD, unless without alternative. Great caution must be taken when giving NSAIDs to this patient over prolonged periods of time. Monitor the effects on GFR, particularly in people with a low baseline GFR and/or in the presence of other risks for progression'* AND *Recommend a Follow-up Appointment to monitor eGFR bi-Weekly'*]
Consider investigating and managing anaemia if the haemoglobin levels falls to 11.0 g/dL or less, or if symptoms attributable to anaemia (such as tiredness, shortness of breath, lethargy, and palpitations) appear. If eGFR is above 60 ml/min/1.73 m^2, investigate other causes of anaemia as it is unlikely to be caused by CKD. If eGFR is between 30 and 60 ml/min /1.73 m^2, investigate other causes of anaemia, but use clinical judgement to decide how extensive this investigation should be, because the anaemia may be caused by CKD. If eGFR is below 30 ml/min/1.73 m^2, think about other causes of anaemia but note that anaemia is often caused by CKD [21].	IF [ICD-10-CM: N18 AND [Hb < 11.0 g/dl OR Suspect to Anemia/Sypmtoms attributable to Anemia [such as tiredness, shortness of breath, lethargy, and palpitations] (AICP)] AND eGFR >= 60 ml/min/1.73 m^2] THEN [*Recommend clinician that 'investigate other causes of anaemia as it is unlikely to be caused by CKD.'*] IF [ICD-10-CM: N18 AND [Hb < 11.0 g/dl OR Suspect to Anemia/Sypmtoms attributable to Anemia [such as tiredness, shortness of breath, lethargy, and palpitations] (AICP)] AND 60 > eGFR >= 30 ml/min/1.73 m^2] THEN [*Recommend clinician that 'investigate other causes of anaemia, but use clinical judgement to decide how extensive this investigation should be, because the anaemia may be caused by CKD.'*] IF [

	ICD-10-CM: N18 AND [Hb < 11.0 g/dl OR Suspect to Anemia/Sypmtoms attributable to Anemia [such as tiredness, shortness of breath, lethargy, and palpitations] (AICP)] AND 30 > eGFR ml/min/1.73 m^2] THEN [*Recommend clinician that 'Think about other causes of anaemia but note that anaemia is often caused by CKD.'*]
Carry out testing to diagnose iron deficiency and determine potential responsiveness to iron therapy and long-term iron requirements every 3 months (every 1 to 3 months for people having haemodialysis). Use a combination of transferrin saturation (<20%) and serum ferritin measurement (<100 mcg/L). Do not routinely measure erythropoietin levels [21].	IF [ICD-10-CM: N18 AND On haemodialysis (AICP)] THEN [*Recommend adding labworks to 'Monitoring Iron deficiency and determine potential responsiveness to iron therapy and long-term iron requirements by testing transferrin saturation and serum ferritin measurement every 1 to 3 months'*] ELSE [*Recommend 'Monitoring Iron deficiency and determine potential responsiveness to iron therapy and long-term iron requirements by testing transferrin saturation and serum ferritin measurement every 3 months'*] IF ??? [transferrin saturation <20% AND serum ferritin <100 mcg/L] THEN [*Recommend adding a Diagnosis (Iron deficieny*) AND *Recommend start Therapy (Iron Therapy)*]
Identify and treat clinically relevant hyperparathyroidism. Determine vitamin D levels, serum parathyroid hormone levels, alkaline phosphatase, serum calcium, and medications that might affect serum calcium and phosphate [21].	

In patients with eGFR <60 mL/min/1.73 m^2, monitoring serum phosphate, calcium, intact parathyroid hormone (iPTH), and 25-hydroxyvitamin D levels is recommended. The frequency of monitoring depends on the eGFR: measure serum phosphate and calcium every 6 to 12 months if eGFR is 30-59 mL/min/1.73 m^2, every three to six months if 15-29 mL/min/1.73 m^2, and every one to three months if <15 mL/min/1.73 m^2. Measure iPTH and vitamin D levels depending on the baseline values and vitamin D treatment [21].	IF [ICD-10-CM: N18 AND eGFR < 60 ml/min/1.73 m^2] THEN [*Recommend clinician to 'Monitoring serum phosphate, calcium, intact parathyroid hormone (iPTH), and 25-hydroxyvitamin D levels.'* IF [ICD-10-CM: N18 AND 30 =<eGFR =< 59 ml/min/1.73 m^2] THEN [*Recommend adding a labworks to 'Monitoring serum phosphate, calcium every 6 to 12 month'* *Recommend adding a labworks to 'Monitoring intact parathyroid hormone (iPTH), and 25-hydroxyvitamin D levels depending on the baseline values and vitamin D treatment'*] IF [ICD-10-CM: N18 AND 15 =<eGFR =< 29 ml/min/1.73 m^2] THEN [*Recommend adding a labworks to 'Monitoring serum phosphate, calcium every 3 to 6 month'* *Recommend adding a labworks to 'Monitoring intact parathyroid hormone (iPTH), and 25-hydroxyvitamin D levels depending on the baseline values and vitamin D treatment'*] IF [ICD-10-CM: N18 AND eGFR < 15 ml/min/1.73 m^2] THEN [*Recommend adding a labworks to 'Monitoring serum phosphate, calcium every 1 to 3 month'* *Recommend adding a labworks to 'Monitoring intact parathyroid hormone (iPTH), and 25-hydroxyvitamin D levels depending on the baseline values and vitamin D treatment'*

	]
Refer older adults with CKD for specialist assessment, taking into account their wishes and multimorbidities, if they have any of the following (30): a. A 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable Kidney Failure Risk Equation) b. An ACR of 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated. c. An ACR of more than 30 mg/mmol (ACR category A3), together with haematuria. d. A sustained decrease in eGFR of 25% or more and a change in eGFR category within 12 months. e. A sustained decrease in eGFR of 15 ml/min/1.73 m2 or more per year. f. Hypertension that remains poorly controlled (above the person's individual target) despite the use of at least 4 antihypertensive medicines at therapeutic doses. g. Suspected renal artery stenosis.	IF [ICD-10-CM: N18 AND [ACR > 70 mg/mmol AND NOT [known to be caused by diabetes ICD-10: E08-E13 AND already appropriately treated]] OR [ACR > 30 mg/mmol (A3) AND Haematuria (AICP) OR Urine blood > 0] OR [Current GFR – Previous GFR (One year ago) > Current GFR/4 OR GFR Cat Changes (In past year)] OR [Current GFR – Previous GFR (One year ago) > 15] OR [Hypertension that remains poorly controlled (above the person's individual target) - despite the use of at least 4 antihypertensive medicines at therapeutic doses. (AICP)] OR [Suspected renal artery stenosis (AICP)]] THEN [*Recommend a Referral to (Specialist)*]
Refer patients with CKD and renal outflow obstruction to urological services [21].	IF [ICD-10-CM: N18 AND [Renal Outflow obstruction] THEN [*Recommend a Referral to (Urological services)*]
Offer an ARB or an ACE inhibitor, titrated to the highest licensed dose that the patient can tolerate, to older adults with	IF [

CKD who have hypertension and an ACR over 30 mg/mmol (ACR category A3 or above), and to older adults with diabetes and an ACR over 3 mg/mmol [21].	ICD-10-CM: N18 AND [[Hypertension (AICP) AND ACR over 30 mg/mmol (ACR category A3 or above)] OR [Diabetes (ICD-10: E08-13) AND ACR over 3 mg/mmol] THEN [*Recommend prescription of (ARB or ACE-inhibitor titrated to the highest licensed dose that the patient can tolerate)*]
Measure serum potassium concentrations and estimate the GFR before starting rennin- angiotensin system antagonists. Repeat these measurements between 1 and 2 weeks after starting rennin-angiotensin system antagonists and after each dose increase. Do not routinely offer a rennin-angiotensin system antagonist to adults with CKD if their pre- treatment serum potassium concentration is greater than 5.0 mmol/L. In these cases, assess for and treat any other factors that promote hyperkalaemia and recheck serum potassium concentration.	IF [(rennin- angiotensin system antagonists) drug list is going to be provided started OR dosage increase] THEN [*Recommend adding labworks 'Check serum potassium concentrations and estimate the GFR before starting rennin-angiotensin system antagonists.'* *Recommend adding labworks 'Repeat serum potassium concentrations measurements between 1 and 2 weeks after starting rennin-angiotensin system antagonists and after each dose increase.'*] IF [ICD-10-CM: N18 AND [(rennin- angiotensin system antagonists) started OR dosage increase] AND [serum potassium concentration > 6.0 mmol/L] THEN [*Recommend clinician that 'Do not routinely offer a rennin-angiotensin system antagonist to adults with CKD if their pre-treatment serum potassium concentration is greater than 5.0 mmol/L. In these cases, assess for and treat any other factors that promote hyperkalaemia and recheck serum potassium concentration.'*]

Stop rennin-angiotensin system antagonists in adults if the serum potassium concentration increases to 6.0 mmol/L or more and other medicines known to promote hyperkalaemia have been discontinued.	IF [(rennin- angiotensin system antagonists) drug list AND serum potassium concentration > 5.0 mmol/L] THEN [*Recommend clinician to 'Stop rennin-angiotensin system antagonists if the serum potassium concentration increases to 6.0 mmol/L or more and other medicines known to promote hyperkalaemia have been discontinued..'*]
If there is a decrease in eGFR or increase in serum creatinine after starting or increasing the dose of rennin-angiotensin system antagonists, but it is less than 25% (eGFR) or 30% (serum creatinine) of baseline, repeat the test in 1 to 2 weeks. Do not modify the rennin-angiotensin system antagonist dose if the change in eGFR is less than 25% or the change in serum creatinine is less than 30% [21].	IF [(rennin- angiotensin system antagonists) drug list started OR dosage increase (AICP) AND [Current GFR – Previous GFR (before rennin- angiotensin system antagonists prescription) < Current GFR/4] OR [Serum creatinine (Current) - Serum creatinine (before rennin-angiotensin system antagonists prescription) < Serum creatinine (before rennin- angiotensin system antagonists prescription) * 0.3]] THEN [*Recommend clinician that 'Do not modify the rennin-angiotensin system antagonist dose if the change in eGFR is less than 25% or the change in serum creatinine is less than 30% and repeat the tests'* *Recommend adding labworks 'Repeat eGFR and serum creatinine measurements in 1 to 2.weeks'*]
Offer antiplatelet medicines for the secondary prevention of cardiovascular disease but be aware of the increased risk of bleeding [21].	IF [ICD-10-CM: N18 AND [NO antiplatelet medicines [B01AC]] [THEN [*Recommend clinician that 'Offer antiplatelet medicines for the secondary prevention of cardiovascular disease but be aware of the increased risk of bleeding'*]

ESA (erythropoietic stimulating agent) therapy should not be started in the presence of absolute iron deficiency without also managing the iron deficiency. ESAs need not be administered if the prognosis is likely to negate the benefits of correcting the anaemia.	IF [ICD-10-CM: N18 AND ESA (erythropoietic stimulating agent) [B03XA] AND serum ferritin <100 mcg/L] THEN [*Recommend stopping prescription 'ESA (erythropoietic stimulating agent) therapy should not be started in the presence of absolute iron deficiency without also managing the iron deficiency* *ESAs need not be administered if the prognosis is likely to negate the benefits of correcting the anaemia..'* AND *Recommend start Therapy (Iron deficiency management)*]
If a trial of ESA therapy is carried out, assess the effectiveness of the trial after an agreed interval, and agree with the patient and caregiver if appropriate whether or not to continue ESA therapy.	IF [ICD-10-CM: N18 AND ESA (erythropoietic stimulating agent) [B03XA]] THEN [*Recommend effectiveness assessment interval setting 'If a trial of ESA therapy is carried out, assess the effectiveness of the trial after an agreed interval, and agree with the patient and caregiver if appropriate whether or not to continue ESA therapy.'*]
The dose and frequency of ESA should be adjusted to keep the rate of Hb increase between 1.0 and 2.0 g/dL/month.	IF [ICD-10-CM: N18 AND ESA (erythropoietic stimulating agent) [B03XA]] THEN [*Recommend setting a therapy goal 'The dose and frequency of ESA should be adjusted to keep the rate of Hb increase between 1.0 and 2.0 g/dL/month'*]
Maintain the Hb range between 10.0 and 12.0 g/dL. Avoid blood transfusions, if possible, in people with anaemia of CKD in whom kidney transplant is a treatment option [21].	IF [ICD-10-CM: N18 AND anaemia of CKD (AICP) AND Kidney transplant is a treatment option (AICP)] THEN

	[*Recommend clinician to set a goal to 'Maintain the Hb range between 10.0 and 12.0 g/dL (Latest one show). Avoid blood transfusions, if possible, in people with anaemia of CKD in whom kidney transplant is a treatment option*]
Offer iron therapy to older adults with anaemia of CKD who are receiving ESAs to maintain transferrin saturation greater than 20% and serum ferritin level greater than 100 mcg/L (unless serum ferritin is greater than 800 mcg/L). Most adults will need 500 to 1,000 mg of iron in a single or divided dose depending on the preparation. High-dose and low-frequency iron is a maximum of 2 infusions, with a minimum of 500 mg of iron in each infusion, and low dose and high frequency is more than 2 infusions with 100 mg to 200 mg of iron in each infusion. Offer oral iron therapy only if intravenous iron therapy is contraindicated or the patient chooses not to have intravenous iron therapy after discussing the relative efficacy and side effects of oral and intravenous iron therapy. Once the transferrin saturation is greater than 20%, and serum ferritin level is greater than 100 mcg/L, offer maintenance iron. Carry out routine monitoring of iron stores to prevent iron overload using serum ferritin at intervals of 1 to 3 months [21].	IF [ICD-10-CM: N18 AND ESA (erythropoietic stimulating agent) [B03XA] AND serum ferritin <800 mcg/L AND Anaemia (AICP)] THEN [*Recommend start Therapy (Iron deficiency management-Iron therapy) to maintain transferrin saturation greater than 20% and serum ferritin level greater than 100 mcg/L (unless serum ferritin is greater than 800 mcg/L).* *Most adults will need 500 to 1,000 mg of iron in a single or divided dose depending on the preparation.* *High-dose and low-frequency iron is a maximum of 2 infusions, with a minimum of 500 mg of iron in each infusion, and low dose and high frequency is more than 2 infusions with 100 mg to 200 mg of iron in each infusion.* *Offer oral iron therapy only if intravenous iron therapy is contraindicated or the patient chooses not to have intravenous iron therapy after discussing the relative efficacy and side effects of oral and intravenous iron therapy* *Once the transferrin saturation is greater than 20%, and serum ferritin level is greater than 100 mcg/L, offer maintenance iron.* *Carry out routine monitoring of iron stores to prevent iron overload using serum ferritin at intervals of 1 to 3 months. '*]
Treat hyperphosphatemia when values are persistently and progressively higher than normal (>4.5 mg/dL) in non-dialysis CKD patients. Begin with dietary phosphate restriction of 900 mg/day. Phosphate restriction should primarily include processed foods and colas, and not high-biologic-value foods such as meat and eggs. Food additives (as are found in processed foods) and medications are an important source of dietary phosphate.	IF [ICD-10-CM: N18 AND persistently (more than one measurement) Phosphate > 4.5 mg/dL AND [progressively (more than previous measurement) Phosphate (AICP)] AND Non-dialysis CKD (AICP) OR EHR

Patients should receive education on the absorbability of phosphate from different foods. A more vegetarian-based diet in order to control phosphate could be advised. If hyperphosphatemia persists, phosphate binders should be prescribed. Non calcium-containing binders like sevelamer, lanthanum, sucroferric oxyhydroxide, and ferric citrate, are preferred over calcium-containing binders like calcium carbonate and calcium acetate, although the increased cost and restricted availability of the first agents make calcium-containing binders an acceptable alternative in some circumstances [21, 22].	] THEN [*Recommend clinician to 'Treat hyperphosphatemia when values are persistently and progressively higher than normal (>4.5 mg/dL) in non-dialysis CKD patients.* *Begin with dietary phosphate restriction of 900 mg/day. Phosphate restriction should primarily include processed foods and colas, and not high-biologic-value foods such as meat and eggs.* *Food additives (as are found in processed foods) and medications are an important source of dietary phosphate.'* *Recommend assigning Education Material (absorbability of phosphate from different foods.) to the patient.'* *Recommend clinician to 'Advise a more vegetarian-based diet in order to control phosphate'*] IF [ICD-10-CM: N18 AND persistently (more than 4 measurement) Phosphate > 4.5 mg/dL AND [progressively (more than previous measurement) Phosphate (AICP) OR] AND Non-dialysis CKD (AICP) OR EHR AND Diatery Advised ***] THEN [*Recommend clinician to prescribe , phosphate binders 'If hyperphosphatemia persists, phosphate binders should be prescribed. Non calcium-containing binders like sevelamer, lanthanum, sucroferric oxyhydroxide, and ferric citrate, are preferred over calcium-containing binders like calcium carbonate and calcium acetate, although the increased cost and restricted availability of the first agents make calcium-containing binders an acceptable alternative in some circumstances'*]
Consider oral sodium bicarbonate supplementation for adults with eGFR < 30 ml/min/1.73 m2 and a serum bicarbonate concentration of < 20 mmol/liter (30).	IF [ICD-10-CM: N18 AND eGFR < 30 ml/min/1.73 m2 AND serum bicarbonate concentration of < 20 mmol/liter]

	THEN [*Recommend clinician to prescribe oral sodium bicarbonate supplementation'*]
Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in adults with a GFR of 30 ml/min/1.73 m^2 or more. Offer colecalciferol or ergocalciferol to treat vitamin D deficiency in patients with CKD and vitamin D deficiency. If vitamin D deficiency has been corrected and symptoms of CKD such as mineral and bone disorders persist, offer calcitriol (1-25 dihydroxycholecalciferol) to people with a GFR of less than 30 ml/min/1.73 m^2.	IF [Patient is in risk of Osteoprosis (AICP) AND eGFR > 30 ml/min/1.73 m^2 AND Bisphosphonates NOT in medication list [M05BA]] THEN [*Recommend clinician to prescribe bisphosphonates for the prevention and treatment of osteoporosis*] IF [vitamin D deficiency (AICP) OR Serum 25(OH)D < 25 nmol/L AND colecalciferol [A11CC05] or ergocalciferol [A11CC01] NOT in medication list] THEN [*Recommend clinician to prescribe colecalciferol(A11CC05) or ergocalciferol (A11CC01) to treat vitamin D deficiency.*] IF [ICD-10-CM: N18 AND corrected vitamin D deficiency [Current Serum 25(OH)D > 50 nmol/L AND Previous Serum 25(OH)D in past 6 month < 50 nmol/L AND colecalciferol (A11CC05) or ergocalciferol (A11CC01) in medication list] AND symptoms of CKD such as mineral and bone disorders persist (AICP) AND eGFR < 30 ml/min/1.73 m^2] THEN [*Recommend clinician to prescribe calcitriol* (A11CC04) *(1-25 dihydroxycholecalciferol).*

Monitor serum calcium and phosphate concentrations in patients receiving calcitriol supplements [21].	] IF [calcitriol (A11CC04) (1-25 dihydroxycholecalciferol) in medication list] THEN [*Recommend adding labworks 'Monitor serum calcium and phosphate concentrations in patients receiving calcitriol supplements every 6 month'.*]

9.2.10 Chronic Obstructive Pulmonary Disease

Guideline	Rules after revision
Suspect a diagnosis of COPD in people over 35 who have a risk factor (generally smoking or a history of smoking) and who present with 1 or more of the symptoms: - exertional breathlessness, chronic cough, regular sputum production, frequent winter 'bronchitis', or wheeze.	IF the patient does not have [COPD] diagnosis and [Smoking] and [age>35] and has one of the following symptoms [exertional breathlessness] OR [chronic cough] OR[regular sputum production] OR[frequent winter 'bronchitis'] OR[wheeze] AND does not have a Spirometry in the past year THEN *Recommend Lab Test(Spirometry) and* *Recommend Lab Test(Chest Radiograph) and* *Recommend Lab Test(full blood count) to identify anaemia or polycythaemia*
	IF the patient does not have [COPD] diagnosis and [Smoking] and [age>35] and has one of the following symptoms [exertional breathlessness] OR [chronic cough] OR[regular sputum production] OR[frequent winter 'bronchitis'] OR[wheeze] AND has a Spirometry in the last year AND **[FEV1/FVC ratio] <70 percent of the predicted value** THEN *Recommend diagnosis (COPD)* *AND* *IF [FEV1]>=80% THEN* *Recommend setting [COPD Severity] as 'Stage 1'* *ELSE* *IF [FEV1] is between 50-79%THEN* *Recommend setting [COPD Severity] as 'Stage 2'* *ELSE* *IF [FEV1] is between 30-49% THEN* *Recommend setting [COPD Severity] as 'Stage 3'* *ELSE* *IF [FEV1]<=30% THEN* *Recommend setting [COPD Severity] as 'Stage 4'*
Ask the patient if they have: weight loss, reduced exercise tolerance, waking at night with breathlessness, ankle swelling, fatigue, occupational hazards, chest pain, haemoptysis (coughing up blood).	The following should be assessed and recorded via AICP: • weight loss, • reduced exercise tolerance (via mMRC) • waking at night with breathlessness, • ankle swelling, • fatigue, • occupational hazards • chest pain, • haemoptysis (coughing up blood).

Dyspnoea scale of grading • Grade 0 - I only get breathless with strenuous exercise • Grade 1 - I get short of breath when hurrying on level ground or walking up a slight hill • Grade 2 - On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level • Grade 3 - I stop for breath after walking about 100 metres or after a few minutes on level ground Grade 4 - I am too breathless to leave the house or I am breathless when dressing or undressing	We will enable filling in Dyspnoea scale in AICP IF Patient has [COPD] diagnosis THEN *Recommend Completing mMRC questonnaire via AICP*
Severity of COPD should either using the below classification, or using the GOLD-Classification, as outlined in the COPD guideline. classified as follows: ○ Mild: Breathless on moderate exertion, Cough and sputum production, Little or no effect on daily activities and FEV1 ≈ 60-80% predicted ○ Moderate: Breathless walking on level ground, Increasing limitation of daily activities, Recurrent chest infections, Exacerbations requiring oral corticosteroids and/or antibiotics and FEV1 ≈ 40-59% predicted	If the patient has [COPD] diagnosis AND (*IF [FEV1]>=80% THEN* *Recommend setting [COPD Severity] as 'Stage 1'* *ELSE* *IF [FEV1] is between 50-79%THEN* *Recommend setting [COPD Severity] as 'Stage 2'* *ELSE* *IF [FEV1] is between 30-49% THEN* *Recommend setting [COPD Severity] as 'Stage 3'* *ELSE* *IF [FEV1]<=30% THEN* *Recommend setting [COPD Severity] as 'Stage 4'*

○ Severe: Breathless on minimal exertion, Daily activities severely curtailed, Exacerbations of increasing frequency and severity and FEV1 < 40% predicted.	
Spirometry Perform spirometry: • At diagnosis. • To reconsider the diagnosis, for patients who show an exceptionally good response to treatment. • To monitor disease progression. Post-bronchodilator spirometry must be realized to confirm the diagnosis of COPD. However, in multimorbid older adults with cognitive impairment, spirometry may be difficult to be realized, and results may not be accurate.	IF the patient does not have [COPD] diagnosis and [Smoking] and [age>35] and has one of the following symptoms [exertional breathlessness] OR [chronic cough] OR[regular sputum production] OR[frequent winter 'bronchitis'] OR[wheeze] AND does not have a Spirometry in the last year THEN *Recommend Lab Test(Spirometry) and* *Recommend Lab Test(Chest Radiograph) and* *Recommend Lab Test(*full blood count) to identify anaemia or polycythaemia AND N*otify the Clinician that* 'Perform spirometry: • At diagnosis. • To reconsider the diagnosis, for patients who show an exceptionally good response to treatment. • To monitor disease progression. Post-bronchodilator spirometry must be realized to confirm the diagnosis of COPD. However, in multimorbid older adults with cognitive impairment, spirometry may be difficult to be realized, and results may not be accurate In addition to spirometry, at the time of the initial diagnosis, all patients should have a chest radiograph to exclude other pathologies, a full blood count to identify anaemia or polycythaemia, and a Body Mass Index calculated.'
In addition to spirometry, at the time of the initial diagnosis, all patients should have a chest radiograph to exclude other pathologies, a full blood count to identify anaemia or polycythaemia, and a Body Mass Index calculated.	
From diagnosis onwards, when discussing prognosis and treatment decisions with older adults with stable COPD, think about the following factors that are individually associated with prognosis: FEV, smoking status,	These will be recorded and reviewed in AICP: FEV, smoking status, breathlessness (MRC scale), chronic hypoxia and/or cor-pulmonale, low BMI, severity and frequency of exacerbations, hospital admissions, symptom burden (for example, COPD Assessment Test score), exercise capacity (for example, 6-minute walk test), whether the person meets the criteria for long-term oxygen therapy and/or home non-invasive ventilation, multimorbidity, and frailty (via Fried frailty phenotype) Multimorbidity is defined as: 'Co-existing chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension,

breathlessness (MRC scale), chronic hypoxia and/or cor-pulmonale, low BMI, severity and frequency of exacerbations, hospital admissions, symptom burden (for example, COPD Assessment Test score), exercise capacity (for example, 6-minute walk test), TLCO, whether the person meets the criteria for long-term oxygen therapy and/or home non-invasive ventilation, multimorbidity, and frailty.	incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. “Multiple” means at least three’

Refer older adults for specialist advice when there is diagnostic uncertainty, for diagnosis confirmation and therapy optimization, when suspected severe COPD or onset of cor-pulmonale, for assessment for oxygen therapy, or long-term nebuliser therapy, or need for continued treatment or supervise withdrawal.	IF the patient does not have [COPD] diagnosis AND [Smoking] and [age>35] AND ((has one of the following symptoms ([exertional breathlessness] OR [chronic cough] OR[regular sputum production] OR[frequent winter 'bronchitis'] OR[wheeze]) AND has a recent Spirometry AND [FEV1/FVC ratio] is above 0.7) THEN *Recommend Referral (Neumologist) for confirming diagnosis and therapy optimization* IF the patient has [COPD] AND [COPD severity] is >=3 THEN *Recommend Referral for therapy optimization* IF the patient has [COPD] AND [cor-pulmonale] THEN *Recommend Referral (Cargiologist) for therapy optimization* IF the patient has [COPD] THEN *Recommend Referral for 'assessment for oxygen therapy, or long-term nebuliser therapy, or need for continued treatment or supervise withdrawal.'*

○ Consider hospitalisation when: a. Marked increase in intensity of symptoms. b. Patient has acute exacerbation characterised by increased dyspnoea, cough or sputum production, plus one or more of the following: Inadequate response to ambulatory management, inability to walk between rooms when previously mobile, inability to eat or sleep because of dyspnoea. c. Cannot manage at home even with home-care resources. d. High risk comorbidity condition, pulmonary (e.g., pneumonia) or non-pulmonary. e. Altered mental status suggestive of hypercapnia. f. Worsening hypoxaemia or cor-pulmonale. g. Severe dyspnoea that responds inadequately to initial emergency therapy. h. Confusion, lethargy or evidence of hypoventilation. i. Persistent or worsening hypoxaemia despite supplemental oxygen, worsening hypercapnia (PaCO2 > 70 mmHg), or severe or worsening respiratory acidosis (blood pH < 7.3).	IF the patient has [COPD] AND [Marked increase in intensity of symptoms] OR([Patient has acute exacerbation characterised by increased dyspnoea, cough or sputum production] AND ([Inadequate response to ambulatory management] OR [Inability to walk between rooms when previously mobile] OR [Inability to eat or sleep because of dyspnoea] OR [Cannot manage at home even with home-care resources] OR [High risk co-morbidity condition — pulmonary (e.g., pneumonia) or non-pulmonary] OR [Altered mental status suggestive of hypercapnia] OR [Worsening hypoxaemia or cor pulmonale] OR [Severe dyspnoea that responds inadequately to initial emergency therapy] OR [Confusion, lethargy, or evidence of hypoventilation]OR [Persistent or worsening hypoxaemia despite supplemental oxygen, worsening hypercapnia (PaCO2 >70 mmHg), or severe or worsening respiratory acidosis (blood pH <7.3).]) THEN *Recommend Consider Hospitilisation*

At each step assess the ability to use and the correct use of the device, consider an alternative device, if handling is not correct and cannot be taught. ○ In patients with stable COPD, offer inhaled therapy with LAMA (long-acting muscarinic antagonists) + LABA (long-acting β-2 agonists) if they do not have asthmatic features or features suggesting steroid responsiveness, and remain breathless or have exacerbations despite optimized non-pharmacological management and using a short-acting bronchodilator. ○ Consider LABA + ICS (inhaled corticosteroids) for people who have asthmatic features or features suggesting steroid responsiveness and remain breathless or have exacerbations	See Figure 20

despite optimized non-pharmacological management and using a short-acting bronchodilator. ○ Before starting LAMA + LABA + ICS, conduct a clinical review to ensure that the person's non-pharmacological COPD management is optimized, and the person's day-to-day symptoms that are adversely impacting their quality of life are caused by COPD and not by another physical or mental health condition. ○ For people with COPD who are taking LABA + ICS, offer LAMA + LABA + ICS if their day-to-day symptoms continue to adversely impact their quality of life, or they have a severe exacerbation	

(requiring hospitalization), or they have 2 moderate exacerbations within a year. ○ For people with COPD who are taking LAMA + LABA, consider LAMA + LABA + ICS if they have a severe exacerbation (requiring hospitalization) or have 2 moderate exacerbations within a year. ○ For people with COPD who are taking LAMA + LABA and whose day-to-day symptoms adversely impact their quality of life, consider a trial of LAMA + LABA + ICS, lasting for 3 months only after 3 months, conduct a clinical review to establish whether or not LAMA + LABA + ICS has	

improved their symptoms: if symptoms have not improved, stop LAMA + LABA + ICS and switch back to LAMA + LABA; if symptoms have improved, continue with LAMA + LABA + ICS.	
Long-term use of oral corticosteroid therapy in COPD is not normally recommended. Some patients with advanced COPD may need long-term oral corticosteroids when these cannot be withdrawn following an exacerbation. In these cases, the dose of oral corticosteroids should be kept as low as possible.	See Figure 20
Do not continue nebulised therapy without assessing and confirming that 1 or more of the following occurs: a reduction in symptoms, an increase in the ability to undertake activities of daily living, an increase in exercise capacity, or an improvement in lung function.	IF the patient has [COPD] AND is on [nebulizers] THEN *Notify the clinician that* 'Do not continue nebulised therapy without assessing and confirming that 1 or more of the following occurs: a reduction in symptoms, an increase in the ability to undertake activities of daily living, an increase in exercise capacity, or an improvement in lung function.'
○ Assess the need for oxygen therapy in people with very severe airflow obstruction (FEV1 below 30% predicted), cyanosis, polycythaemia,	IF the patient has [COPD] AND one of the following ([Cyanosis] OR [Polycythaemia] OR[A raised jugular venous pressure] OR[SaO2]>=92%) THEN *Recommend a Referral for assesing the need for oxygen therapy* AND *Notify the clinician that 'Be aware that inappropriate oxygen therapy in people with COPD may cause respiratory depression.'*

peripheral oedema (swelling), a raised jugular venous pressure, pulmonary hypertension, or an oxygen saturations of 92% or less breathing air.	
Be aware that inappropriate oxygen therapy in people with COPD may cause respiratory depression.	
Consider Non-invasive mechanical ventilation when: a. Respiratory acidosis (pH ≤ 7.35 or partial pressure of carbon dioxide ≥45 mm Hg) b. Severe dyspnoea with signs of respiratory muscle fatigue such as use of accessory muscle, paradoxical motion of abdomen, or retraction of the intercostal spaces, especially in the presence of thoracical deformation. c. Persistent hypoxemia despite adequate oxygen supply	IF the pati,ent has [COPD] an done of the following ([Respiratory acidosis] OR [Persistent hypoxemia despite adequate oxygen supply] OR [Severe dyspnoea]) THEN *Recommend a Referral for Assessing the need for Non-invasive mechanical ventilation*
Symptom Management • Opioids (oral or parenteral) are effective therapy for the management of refractory dyspnoea and should be considered on an individual basis. • Anxiety and depression accompany dyspnoea and should	If the patient has [COPD] AND [refractory dyspnoea] THEN *Notify the clinician that* *'*Opioids (oral or parenteral) are effective therapy for the management of refractory dyspnoea and should be considered on an individual basis.*'* *Recommend starting Medication [Opioids]*
	If the patient has [COPD] AND ([Anxiety] OR [Depression] THEN *Notify the clinician that '*Anxiety and depression accompany dyspnoea and should be evaluated and treated accordingly.

be evaluated and treated accordingly. Benzodiazepines, tricyclic anti-depressants, and major tranquilisers may be useful in this context.	Benzodiazepines, tricyclic anti-depressants, and major tranquilisers may be useful in this context.' AND *(Recommend starting Medication [Benzodiazepines] OR Recommend starting Medication [tricyclic anti-depressants] OR Recommend starting Medication [major tranquilisers])*
• Oxygen and fans blowing air onto the face can relieve breathlessness.	If the patient has [COPD] AND [Breathlessness] THEN *Notify the clinician that '*Oxygen and fans blowing air onto the face can relieve breathlessness'
• Fatigue can be improved by self-management education, pulmonary rehabilitation, and mind-body interventions.	If the patient has [COPD] AND [Fatigue] THEN *Notify the clinician that '*Fatigue can be improved by self-management education, pulmonary rehabilitation, and mind-body interventions.' *AND* *Recommend assigning Education Material (COPD Self Management Education Material) to the patient* *AND* *Recommend assigning Mind-Body Interventions to the patient*

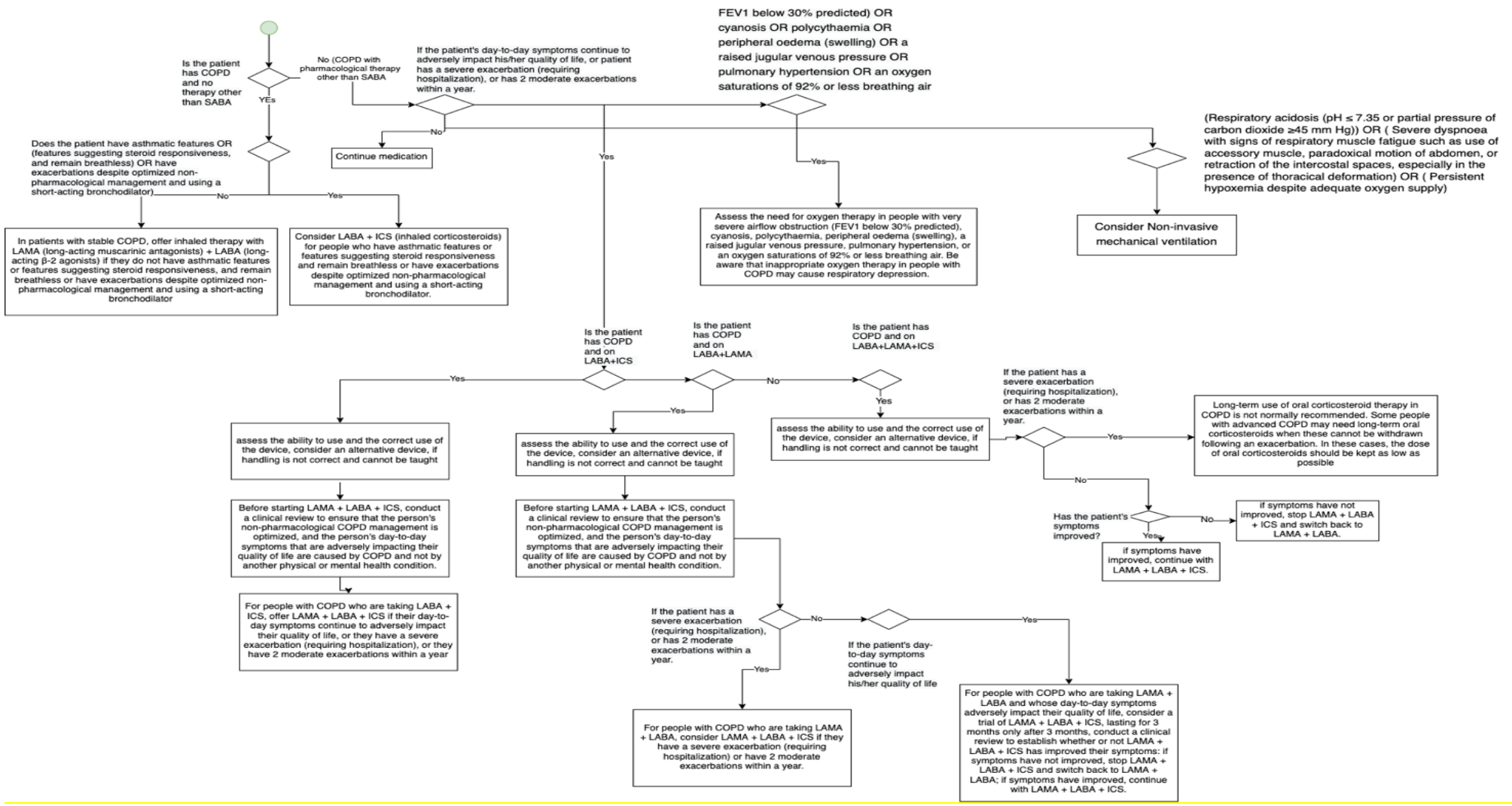

Figure 20- COPD pharmacological therapy algori

9.2.11 Stroke

Guideline	Rules after revision
Multimorbid older adults at risk of stroke and who have had a stroke or transient ischemic attack (TIA) should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking) (24).	IF [Patient at risk of stroke (AICP) OR With (history of [STROKE] (AICP) OR History of [transient ischemic attack] ICD-10-CM: G45)] THEN [*Clinician should Perform the assessment for* *‘* *vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, and smoking*) *‘*]
In patients suspected of having a stroke or TIA, Computed Tomography or Magnetic Resonance Imaging of the brain is recommended to confirm the diagnosis of symptomatic ischaemic cerebral vascular disease (23).	IF [Patient at risk of stroke (AICP)] THEN [*Recommend a Referral to Neurologist or A&E department to confirm the diagnosis of symptomatic ischemic cerebral vascular disease*]
In older adults with cryptogenic stroke, echocardiography with or without contrast is reasonable to evaluate for possible cardiac sources of or trans cardiac pathways for cerebral embolism (23). If there is not a contraindication to anticoagulation, long-term rhythm monitoring with mobile cardiac outpatient telemetry, implantable loop recorder, or other approach is reasonable to detect intermittent arrhythmia (23).	

Consider referral to a rehabilitation specialist when having new neurological impairments and functional limitations, for in-depth assessment and management (24).	IF [Patient has [(new neurological impairments) (AICP) OR (new functional limitations) (AICP)] THEN [*Recommend a Referral to rehabilitation specialist for in-depth assessment and management.*]
In older adults with an ischaemic stroke or TIA and obstructive sleep apnea, treatment with positive airway pressure (e.g., continuous positive airway pressure) can be beneficial for improved sleep apnoea, BP, sleepiness, and other apnoea related outcomes (23).	IF [Patient has [((Ischemic Stroke) (AICP) OR (TIA) (ICD-10-CM: G45.8 or G45.9)) AND (obstructive sleep apnea) (ICD-10-CM: G47.3)] THEN [*Recommend clinician treatment with positive airway pressure (e.g., continuous positive airway pressure for improved sleep apnea, BP, sleepiness, and other apnoea related outcomes*]

In multimorbid older adults with cognitive impairment, and with a TIA or non-disabling ischaemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, carotid endarterectomy should be considered, and risk-benefit evaluated, to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%. It is reasonable to select carotid endarterectomy over carotid artery stenting to reduce the periprocedural stroke rate (23).	IF [Patient has [((Ischemic Stroke) (AICP) OR (TIA) (ICD-10-CM: G45.8 or G45.9)) AND Occurred within 6 month (AICP) AND ipsilateral severe (70%–99%) carotid artery stenosis (AICP)] THEN [*Recommend clinician that Refer to Specialist* *'carotid endarterectomy should be considered, and risk-benefit evaluated, to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%. It is reasonable to select carotid endarterectomy over carotid artery stenting to reduce the periprocedural stroke rate* *'*]
Antiplatelet Therapy for Secondary Stroke Prevention: For patients with ischaemic stroke or TIA, antiplatelet therapy is recommended for long-term secondary stroke prevention to reduce the risk of recurrent stroke and other vascular events unless there is an indication for anticoagulant therapy (24). Antiplatelet therapy should be started as soon as possible after brain imaging has excluded haemorrhage, within 24 hours of symptom onset (ideally within 12 hours) (24). For long-term secondary stroke prevention, either acetylsalicylic acid (80-325 mg daily), or clopidogrel (75 mg daily), or combined acetylsalicylic acid and extended-release dipyridamole (25 mg/200 mg twice a day), are all appropriate treatment options and selection depends on patient factors or clinical circumstances (24).	IF [Patient has [((Ischemic Stroke) (AICP) OR (TIA) (ICD-10-CM: G45.8 or G45.9))] THEN [*Recommend clinician that* *antiplatelet therapy is recommended for long-term secondary stroke prevention to reduce the risk of recurrent stroke and other vascular events unless there is an indication for anticoagulant therapy).* *Antiplatelet therapy should be started as soon as possible after brain imaging has excluded haemorrhage, within 24 hours of symptom onset (ideally within 12 hours).* *For long-term secondary stroke prevention, either acetylsalicylic acid (80-325 mg daily), or clopidogrel (75 mg daily), or combined acetylsalicylic acid and extended-release dipyridamole (25 mg/200 mg twice a day), are all appropriate treatment options and selection depends on patient factors or clinical circumstances.*

	]
For patients with an acute high-risk transient ischemic attack or minor ischemic stroke of non-cardioembolic origin (National Institutes of Health Stroke Scale 0-3), who are not at high bleeding risk, dual antiplatelet therapy is recommended with clopidogrel 75 mg daily plus acetylsalicylic acid 81 mg daily for a duration of 21 days after the event, followed by antiplatelet monotherapy thereafter (acetylsalicylic acid or clopidogrel alone) (24). A single loading dose of clopidogrel (either 300 mg (CHANCE trial) or 600 mg (POINT trial)) and acetylsalicylic acid (160 mg – 325 mg) should be administered at the start of treatment (24).	IF [Patients (0=<[National Institutes of Health Stroke Scale<=3] AND NOT (Risk of high bleeding) (AICP) [THEN [*Recommend clinician that* *dual antiplatelet therapy is recommended with clopidogrel 75 mg daily plus acetylsalicylic acid 81 mg daily for a duration of 21 days after the event, followed by antiplatelet monotherapy thereafter (acetylsalicylic acid or clopidogrel alone) (24). A single loading dose of clopidogrel (either 300 mg (CHANCE trial) or 600 mg (POINT trial)) and acetylsalicylic acid (160 mg – 325 mg) should be administered at the start of treatment.*]
In patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%-99%) of a major intracranial artery, the addition of clopidogrel 75 mg/day to aspirin for up to 90 days is reasonable to further reduce recurrent stroke risk (23).	IF [Patient has [((Ischemic Stroke) (AICP) OR (TIA) (ICD-10-CM: G45.8 or G45.9)) AND (Occurred within 30 days (AICP) AND attributable to severe stenosis (70%-99%) of a major intracranial artery (AICP)] THEN [*Recommend clinician that* *the addition of clopidogrel 75 mg/day to aspirin for up to 90 days is reasonable to further reduce recurrent stroke risk*]

In patients with stroke at high risk of haemorrhagic conversion in the setting of atrial fibrillation, it is reasonable to delay initiation of oral anticoagulation beyond 14 days to reduce the risk of intracerebral haemorrhage (23).	IF [Patient has [(Stroke) (ICD-10-CM: I63) AND at high risk of haemorrhagic conversion in the setting of atrial fibrillation (AICP)] THEN [*Recommend clinician that* *it is reasonable to delay initiation of oral anticoagulation beyond 14 days to reduce the risk of intracerebral hemorrhage*]
In patients with ischaemic stroke or TIA with no known coronary heart disease, no major cardiac sources of embolism, and LDL cholesterol (LDL-C) > 100 mg/dL, atorvastatin 80 mg daily is indicated to a goal LDL-C of < 70 mg/dL, to reduce risk of stroke recurrence and cardiovascular events. In selected older adults, ezetimibe may be considered for additional LDL-C lowering (24). In patients with ischaemic stroke who are very high risk (defined as stroke plus another major atherosclerotic cardiovascular disease or stroke plus multiple high-risk conditions), are taking maximally tolerated statin and ezetimibe therapy and still have an LDL-C >70 mg/dL, it is reasonable to treat with PCSK9 inhibitor therapy (23).	IF [Patient has [((Ischemic Stroke) (AICP) OR (TIA) (ICD-10-CM: G45.8 or G45.9)) AND (NOT ((ICD-10-CM: I25) OR cardiac sources of embolism (AICP))) AND LDL cholesterol (LOINC: 2089-1) > 100 ? mg/dl] THEN [*Recommend clinician that* *Atorvastatin* (C10AA05) *80 mg daily is indicated to a goal LDL-C of < 70 mg/dL, to reduce risk of stroke recurrence and cardiovascular events.* *In selected older adults, ezetimibe* (C10AX09) *may be considered for additional LDL-C lowering.* *In patients with ischemic stroke who are very high risk (defined as stroke plus another major atherosclerotic cardiovascular disease or stroke plus multiple high-risk conditions), are taking maximally tolerated statin and ezetimibe therapy and still have an LDL-C >70 mg/dL, it is reasonable to treat with PCSK9 inhibitor therapy like Evolocumab* (C10AX13).]

In patients with ischaemic stroke or TIA, with fasting triglycerides 135 to 499 mg/dL and LDL-C of 41 to 100 mg/dL, on moderate or high-intensity statin therapy, with HbA1c <10%, and with no history of pancreatitis, AF, or severe heart failure, treatment with icosapent ethyl 2 g twice a day is reasonable to reduce risk of recurrent stroke (23).	IF [Patient has [((Ischemic Stroke) (AICP) OR (TIA) (ICD-10-CM: G45.8 or G45.9)) AND (135 < fasting triglycerides < 499 AND 41 < LDL cholesterol (LOINC: 86911-5) < 100 mg/dl AND on moderate or high-intensity statin therapy (AICP) AND HbA1c (LOINC: 86910-7) <10% AND NOT (history of [pancreatitis] (ICD-10-CM: K85,86) OR [Atrial Fibrillation] (ICD-10-CM: I48) OR severe [heart failure] (ICD-10-CM: I50)))] THEN [*Recommend clinician that* *treatment with icosapent ethyl* [C10AX06] *2 g twice a day is reasonable to reduce risk of recurrent stroke.*]
In patients with severe hypertriglyceridemia (i.e., fasting triglycerides ≥500 mg/dL [≥5.7 mmol/L]), it is reasonable to identify and address causes of hypertriglyceridemia and, if triglycerides are persistently elevated or increasing, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy should be considered (23).	IF [Patient has [severe hypertriglyceridemia (i.e., fasting triglycerides ≥500 mg/dL (LOINC: 3043-7) [≥5.7 mmol/L (LOINC: 70218-3)])] THEN [*Recommend clinician that* *it is reasonable to identify and address causes of hypertriglyceridemia and, if triglycerides are persistently elevated or increasing, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy should be considered.*]

9.2.12 Caregiver support

Guideline	Rules after revision
Psychological intervention, training, and support should be offered to family members and other informal caregivers of care-dependent older people, particularly, but not exclusively, when the need for care is complex and extensive and/or there is significant caregiver strain.	• Notify the clinician that 'Psychological intervention, training, and support should be offered to family members and other informal caregivers of care-dependent older people, particularly, but not exclusively, when the need for care is complex and extensive and/or there is significant caregiver strain.' • Assign Zarit Scale to Caregivers Clinicians will see Zarit result in AICP if filled in via PEP by Caregivers. In addition to this, it will be possible to fill in Zarit Scale via AICP.

10. Annex A: Deliverable 3.1 Release 1 (M8) version 1.10

An Integrated Solution for Sustainable Care for Multimorbid Elderly Patients with Dementia

CAREPATH

WP3: Foundation of the Clinical Decision Support Services for the Management of Multimorbid Elderly Patients with Dementia

D3.1: A Computer Interpretable Guidelines Specification of the Complete CAREPATH Decision Support Logic

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Executive Summary

The report identifies the process followed by T3.1 that will contribute to the “Foundations of the Clinical Decision Support Services for the management of multimorbid elderly patients with dementia”. Task 3.1 defines the “Patient-oriented Computer Interpretable Clinical guideline modelling”. The main objective of WP3 is to establish the foundations of the Clinical Decision Support tools to be employed in CAREPATH, based on the consolidated guidelines recommended by WP6. This first release of D3.1 covers the methodology for modelling clinical practice guidelines, an overview of the clinical decision support service architecture, and how the clinical decision support services will be specified.

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Abbreviations

CAREPATH	An Integrated Solution for Sustainable Care for Multimorbid Elderly Patients with Dementia
CDS	Clinical Decision Support
CIG	Computer Interpretable Guideline
CPG	Clinical Practice Guideline
CRG	Clinical Reference Group
EHR	Electronic Health Record
FHIR	Role Based Access Control
HTTP	Hyper Text Transfer Protocol
ICD	International Classification of Diseases
M1/M12	Project Month 1 / Month 12
PEP	Patient Empowerment Platform
RBAC	Role Based Access Control
UML	Unified Modelling Language
WP	Work Package

A.1. Introduction

A.1.1. Document Scope

The goal of Task 3.1 'Patient-oriented Computer Interpretable Clinical guideline modelling (M1-M12)' is to model clinical practice guidelines so they can be executed as computer interpretable guidelines, to guide clinical decision-making based on evidence-based guidelines. Figure 1 shows the overview for Task 3.1 and its dependencies on other work packages in the CAREPATH project.

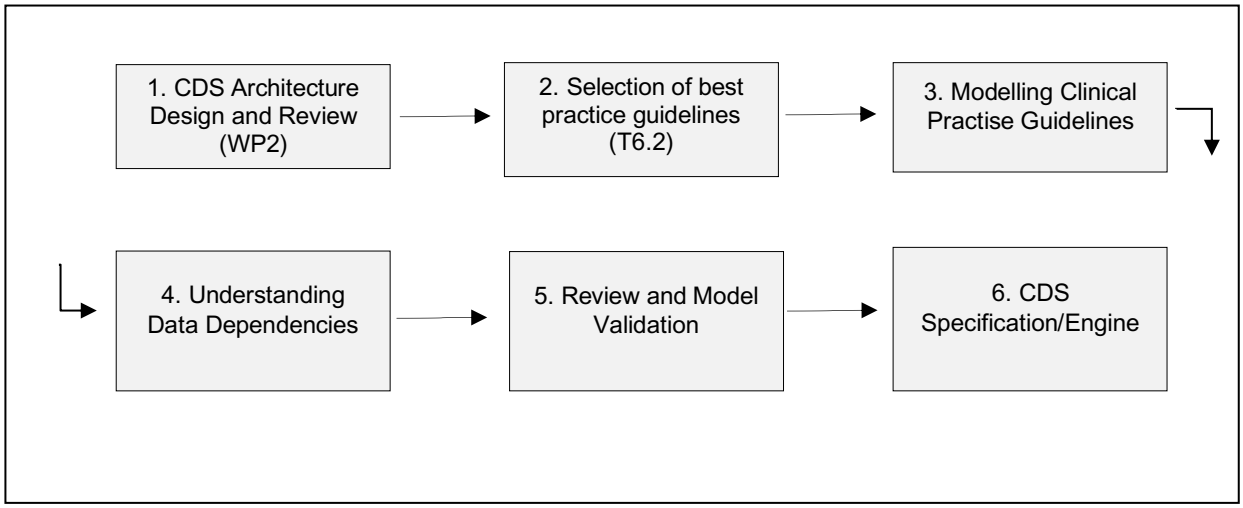

Figure 21: Overview of Task 3.1 and Dependencies

WP2 focuses on specification of the overall architecture, including the Clinical Decision Support (CDS) module, and how it will interact with the rest of the CAREPATH infrastructure (see D2.1, D2.2 and D2.3). This includes specification of the module level functionality, test cases, input, outputs, as well as the technical interfaces. The latter includes the standards and technology used, as well as how it will be configured specifically for CAREPATH.

In the case of computer interpretable guidelines (CIG), this includes how the CIGs will be communicated with the rest of the modules (output), including the API for data that CIG will need (input). This affects the work in T3.1 as the task will annotate the guideline models with elements of these specifications. For example, the modelled guidelines will be annotated using semantic interoperability standards (e.g., ICD-10 codes) to avoid ambiguity on clinical terms. Examples of other such standards include the FHIR resources from which information will be retrieved, and the CDS-hooks cards [1] that will be produced at each step of the guideline algorithm.

Task 6.2 is the task that will identify the best practice guidelines that will be adapted and modelled into the CAREPATH guidelines, from the review of relevant guidelines identified in D6.1. The task will integrate relevant guidelines, reconciling potential conflicts, resulting in the CAREPATH integrated guidelines. Task 3.1 will then unpack the decision making in the CAREPATH integrated guidelines and will model them as algorithms using flowcharts and activity diagrams. This will explicitly model every decision and path a patient may follow during their care. Where the guidelines are not clear, input will be elicited from the CAREPATH Clinical Reference Group (CRG) in WP6. If the pilot sites have identified aspects that will need to be implemented differently in their local setting, these will be recorded as localizations. Use of the model-based approaches will enable clear and traceable documentation of these variations.

Following specification of the decision-making logic, the task will annotate parts of the models with terminological codes for medical concepts, medications, as well as the FHIR resources [2] from which the data will be taken. This will allow unambiguous specification of what concepts the guidelines refer to, and which data elements correspond to each decision. This is a key step, as the models created will be in a form that is appropriate for review and validation by the CRG. Additionally, by identifying the data elements that will be needed from the FHIR repository, the task will also provide early specification of the requirements on pilot sites, with regards to integrating their Electronic Health Records with the CAREPATH FHIR repository, de-risking the deployment task (Task 4.8).

The guideline models will be reviewed and validated by the CRG and clinicians at the pilot sites (according to the integration protocol of each site).

Finally, the annotated CAREPATH guideline models will be used by Task 3.4 for definition with CDS Hooks specification and by Task 4.5 for implementation as executables in the CDSS engine. Task 3.1 is crucial to the verification and validation of the CDSS, as the models that will be produced will be the link between the validation offered by the CRG, and the requirements provided to the CDS technical team. All rules, decisions, and algorithms in the models should be fully traceable to the code in the implementation. The model specification can therefore act as the requirements for the CDSS. Hence, the technical teams can verify that their implementation is what was specified in the models to a very high degree of confidence. Furthermore, the models are to be reviewed and approved by the CRG, hence, offering high degree of confidence in its validity. This is enabled by the increased comprehensibility of models, as they break down and visualize information that may be difficult to review as text, which could result in ambiguities.

A.1.2. Document Structure

The deliverable is organised as follows:

- Section 1 describes the scope of the task and document.
- Section 2 describes how the best practice guidelines and consolidated guidelines are selected and developed in CAREPATH.
- Section 3 describes the methodology for modelling clinical practice guidelines.
- Section 4 describes how the clinical guidelines are specified as CDS Hooks.
- Section 5 describes the process of review and validation of the models developed.
- Section 6 concludes the first release of the deliverable.

A.1.3. Clinical Decision Support System (CDSS)

Clinical Decision Support Systems (CDSS) provide decision support aids offering treatment suggestions, carry out risk assessments and provide guidance about polypharmacy management as well as being utilized by AICP during the creation and update of care plans. The CDSS also includes an Early Warning System (EWS), utilising algorithms built using machine learning techniques to identify potentially preventable situations.

- **Suggestion for Clinical Guidelines:** In CAREPATH, we will build clinical decision support services to deliver personalized guidance to healthcare professionals about the goals and interventions (treatment actions, patient monitoring activities and lifestyle management activities) that can be put into the active care plan of the patient. These suggestions will be built upon the recommendations of the clinical guidelines to achieve patient-centred and customised care. The exact content of Clinical Decision Support Systems (CDSS) to be implemented in CAREPATH depends on the output of Task 6.2 in which a holistic patient centred CAREPATH best practice guideline will be established. Task 3.1 will deliver the rules that will be implemented as clinical decision support services based on the holistic clinical guideline flow. The architectural design of the CDSS for clinical guideline suggestions, from a technical perspective is defined in D2.3 Section 3.3.4.

A.2. Definition of CAREPATH Guideline

Candidate guidelines have been identified in D6.1, such as guidelines for frailty, which will be reviewed and cross referenced against current practice at pilot sites. Additional guidelines will also be considered for example, the guidance using concept of intrinsic capacity. Task 6.2 is assessing the guidelines identified in D6.1 to create a consensus guideline for the project, also taking into account local variations at the sites. The second release of this deliverable (M12) will model these guidelines after these have been defined in Task 6.2.

Review of the formalised guidelines will be carried by the CRG, liaising with local clinicians where applicable. Identification of variation in terms of process, clinical decision making, as well as representation and use of semantic interoperability concepts will be modelled. The task will receive the consolidated guidelines from WP6, which will represent best practice. Task 3.1 will transform the clinical guidelines into models amenable to ICT software execution. The task will employ state of the art Computer Interpretable Guideline practice, to model the flow, information dependencies, as well as decisions that need to be made by the software. The logic of the guidelines will also identify the information, which when implemented will result in patient-centred and customised care. The task will also enrich the decision-making based on clinical guidelines, with information that will be collected by the Patient Empowerment Platform as well as the Home Monitoring Platform. With input from WP6 the task will develop a specification of how passively collected data can satisfy the various conditions of decision-making, allowing the pathways to automatically progress using the collected data, and offer recommendations. The task will also identify the data types missing to make decisions in line with the guidelines, and review with WP6 how actively collected data such as patient reported outcomes can be used to fill the gap and result in decisions. As part of this, Task 3.1 will liaise with the Clinical Reference Group (CRG) and WP2 to evaluate whether data collection is compliant with the project data handling objectives. These specifications will be implemented within the scope of Task 4.5.

A.3. Modelling Clinical Practice Guidelines

This deliverable will be updated with Flow Charts and Activity Diagram from the Interim M8 Release through to the M12 Final release. Semantic interoperability (coding) allocation, and review by clinicians' disambiguation of concepts and assignments of codes will be considered. This will be performed by the clinical reference group. Rules are to be documented with a constrained language based prepositional logic e.g., "blood pressure (SNOMED code) AND higher than previous 3 measurements" will trigger an action.

A.3.1. What is a UML Activity Diagram?

The Unified Modelling Language (UML) is general-purpose modelling language [3]. UML Diagrams can be grouped into two main types, structural and behavioural, as seen in Figure 3.

An activity diagram visually presents a series of actions or flow of control in a system like a flowchart or a data flow diagram. Activity diagrams are often used in business process modelling. They can also describe the steps in a use case diagram. Activities modelled can be sequential and concurrent [3].

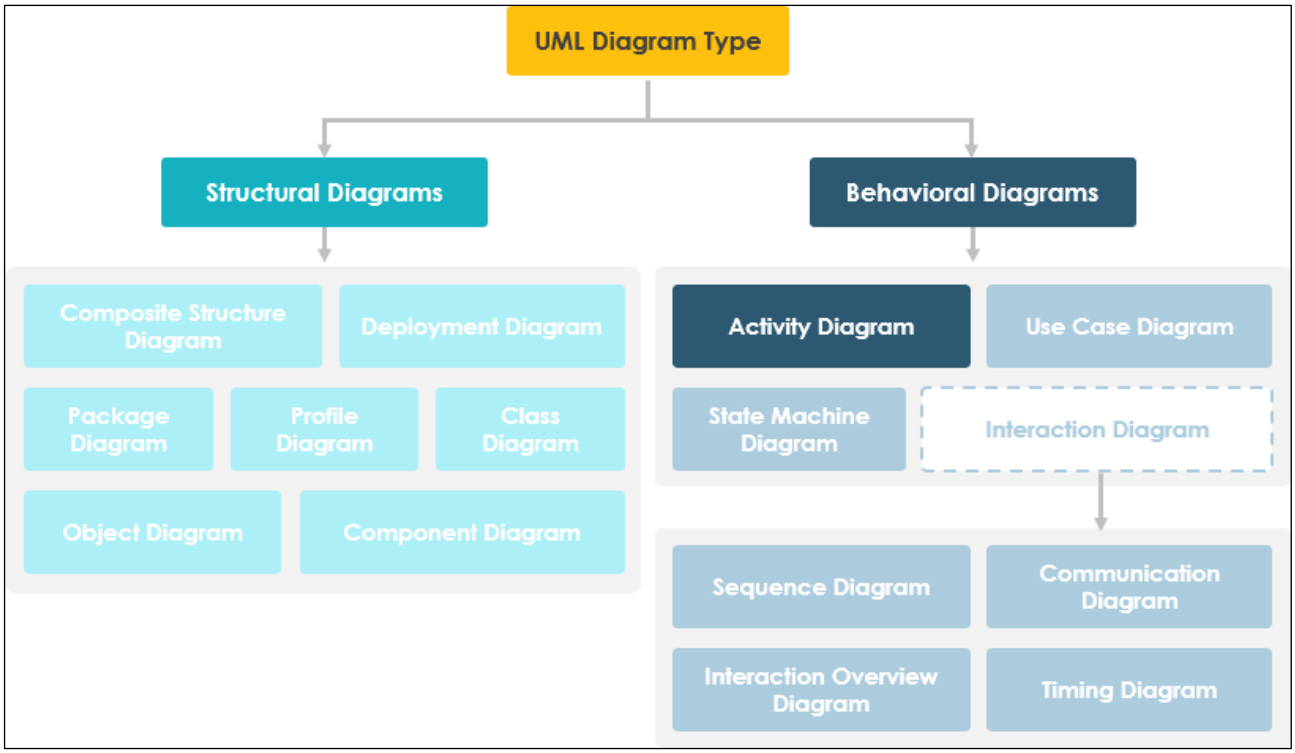

Figure 22: UML Activity Diagram Classification

A.3.2. When to Use Activity Diagrams

Activity Diagrams describe how activities are coordinated to provide a service which can be at various levels of abstraction. Typically, an event needs to be achieved by some operations, particularly where the operation is intended to achieve several different things that require coordination, or how the events in an individual use case relate to one another where activities may overlap and require coordination. It is also suitable for modelling how a collection of use cases coordinates to represent business workflows, an example of how an activity diagram for this might be developed is given below:

1. Identify candidate use cases, through the examination of business workflows
2. Identify pre- and post-conditions (the context) for use cases
3. Model workflows between/within use cases

4. Model complex workflows in operations on objects
5. Model in detail complex activities in a high-level activity Diagram

An activity diagram is an important behavioural diagram in UML, used to describe dynamic aspects of the system. Activity diagrams are an advanced version of flow charts that model the flow from one activity to another.

Below in **Figure 23**, we show an example flowchart of a Blood Pressure (BP) Management Module for a Diabetes CDS service, which encodes the decision support logic presented in the NICE diabetes guideline – blood pressure management (2015 version, chapter 1.4) [4].

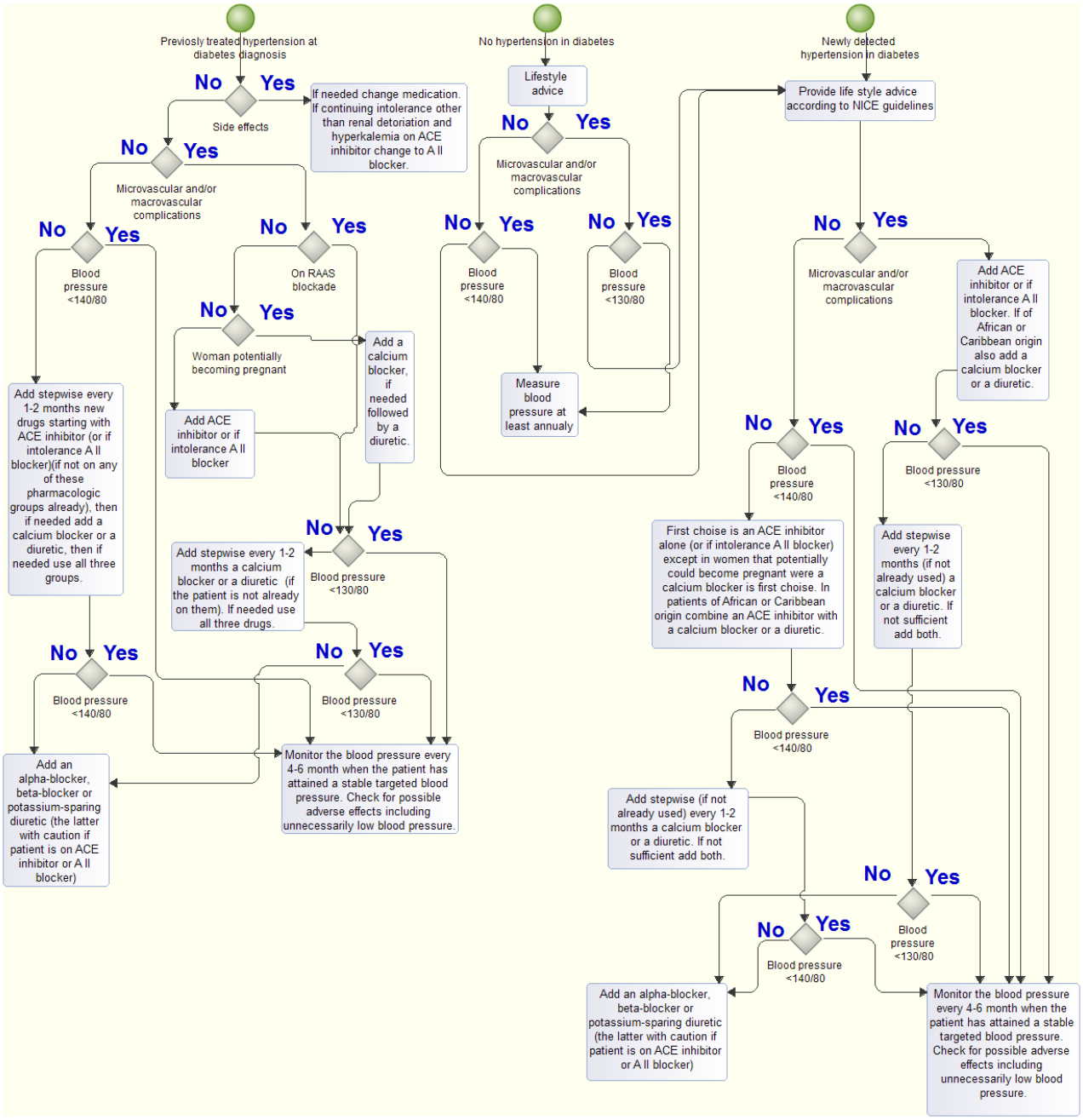

Figure 23: Diabetes - Blood Pressure Management [5, Figure 3]

A.4. CDS Hooks

The CDS Hooks specification describes the RESTful APIs and interactions to integrate Clinical Decision Support (CDS) between CDS Clients (typically Electronic Health Record Systems (EHRs) or other health information systems) and CDS Services. All data exchanged through the RESTful APIs must be sent and received as JSON structures and must be transmitted over channels secured using the Hypertext Transfer Protocol (HTTP) over Transport Layer Security (TLS), also known as HTTPS and defined in RFC2818 [1].

The CDS Hooks application programming interface (API) is a specification that builds on the FHIR core specification to describe how an electronic health record (EHR) can automatically invoke external decision support service based on events that occur during normal application use. The output that is produced by this system will be in the forms of cards that are required to be actioned by the user. The user action will be in the form of advice, or a request for user input as proposed by the system in relation to the patient's holistic care plan [1].

Using the same example of blood pressure management in diabetes, the flowchart (**Figure 23**) has been adapted into an implementable one with executable conditions, CDS hooks information and suggestion cards (Figure 24, Figure 25) [6]. The details of the decision points of the flowchart are explained in **Table 2**. The ICD (International Code of Diseases) INC and ATC codes in the table are used to unambiguously define the conditions within the guideline. These codes are assessed and mapped local codes when necessary, during the implementation phase. The flowcharts in Figure 24 and Figure 25 are not an exact match of the flowchart in **Figure 23**. In **Figure 23**, 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 24 and Figure 25 show the changed control flow [6].

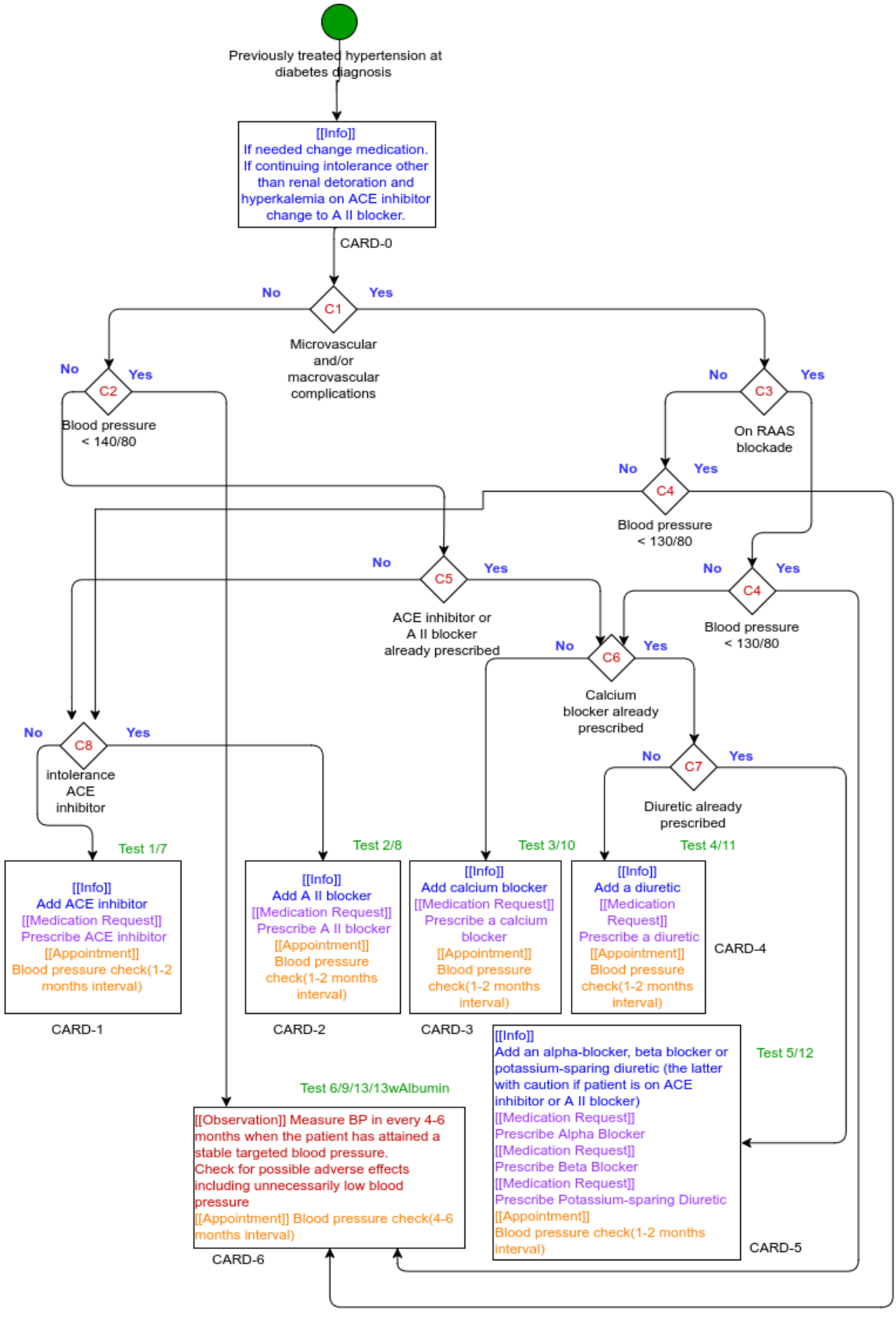

Figure 24: First half of the BP management flowchart [6, Figure 2]

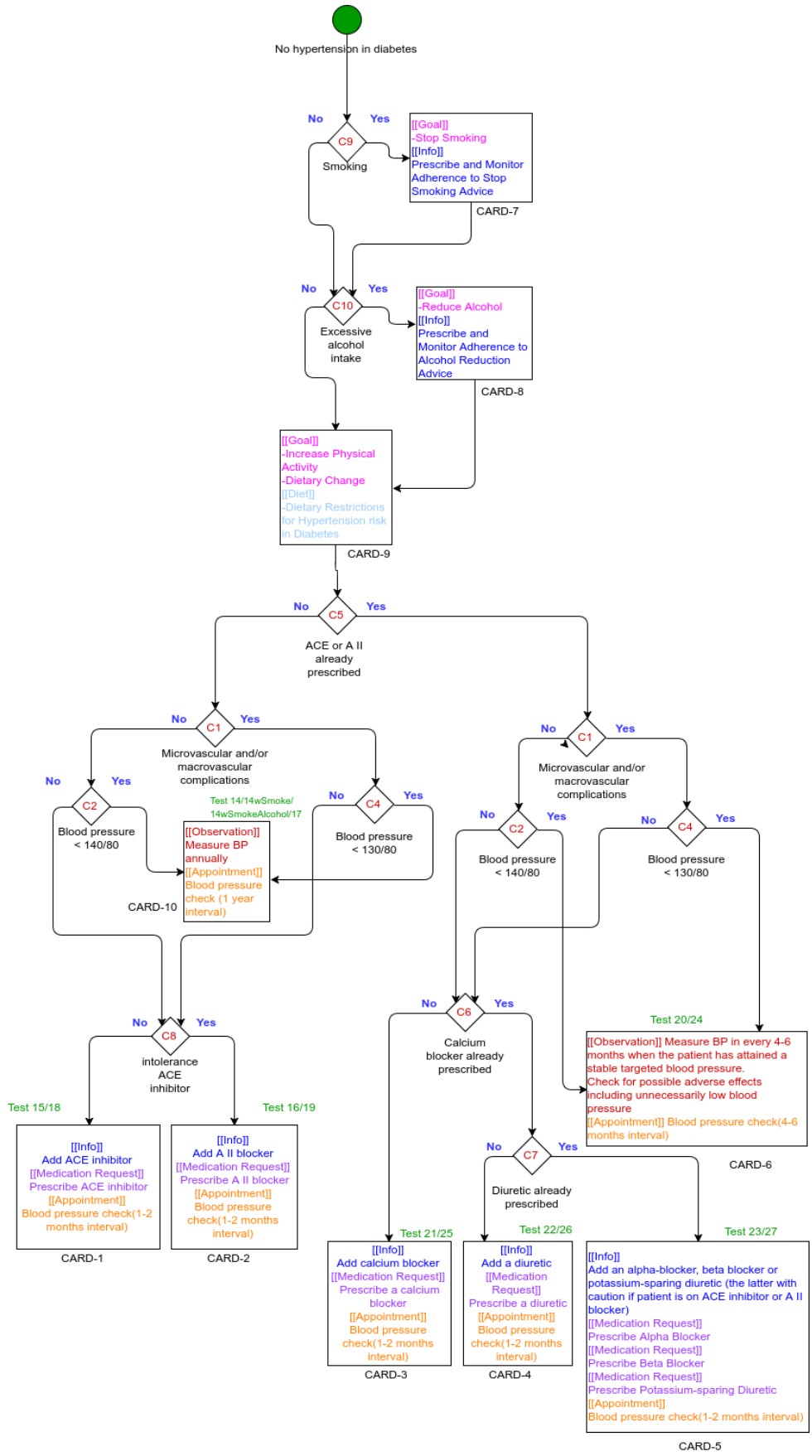

Figure 25: Second half of the BP management flowchart [6, Figure 3]

Table 2: Blood pressure management module condition table [6, Table 4]

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

A.4.1. Understanding Data Dependencies

To successfully implement CDS services, we need to identify the data sources for the CIG logic. This is done by the technical partners by using a list of FHIR resources that are expected to be implemented by the system. This is then checked (in the deployment package) against technical interoperability and what the pilot sites offer. For CAREPATH we also need to identify data sources from the home-based devices. Nevertheless, all these sources will interact with the FHIR repository, hence becoming a data interoperability exercise.

Data that will be provided from pilot sites will consist of different categories and will follow international health standards e.g., CDA, FHIR, HL7v2. This data will be stored in HIS consisting of structured and unstructured data. Data from these pilots' sites will be categorised based on their class, e.g., demographics, lab results, medical images, medication, procedures, allergies, vital signs, medical conditions based on problem and symptoms. There is a dependency on WP4 to identify the relevant data sources.

The output from this deliverable (Release 2) will describe the input to Task 3.4 and Task 4.5 for CAREPATH project.

A.5. Review and Validation of Models

The clinical reference group, primarily supported by the local sites, will examine the guidelines and the scenarios of use to identify where the guidelines may fall short of information. Clinicians will need to understand the gaps and conflicts between single disease guidelines and offer an integrated guideline covering the main conditions being investigated within CAREPATH. This involves another subprocess including identification of care plan, and medication conflicts which will need to be reconciled. Reconciliation happens at various levels: a) guideline, static and documented reconciliation, b) CDS based dynamic reconciliation e.g., drug to drug interactions and c) clinical expertise and judgment reconciliation when the professional will need to assess the plan and discuss it with other experts to find consensus. The project does a and b (to an extent) and we offer the tools for c). Task 3.1 does not provide any clinical content but will facilitate validation of the consolidated guidelines through providing the guideline models for review by the CRG.

A.5.1. Reference Guidelines

CAREPATH includes the implementation of a polypharmacy module as part of its CDS. Task 3.2 will implement the polypharmacy CDS services, such as drug-drug interactions and others as identified in Task 6.2. Polypharmacy is defined as the concurrent use of multiple (usually more than four) medications or, sometimes, as the unnecessary use of multiple and/or redundant medications. As described in [7], polypharmacy is common in adults older than 65 years, which shows that generally more than half of all patients older than 65 years take more than 5 prescription drugs. The situation is complicated further by over-the-counter medications. Studies regarding such medications show that, especially in certain communities, 90% of the patients take more than 1 and almost 50% take 2 to 4 of these freely available medications. Additionally, because of incomplete case histories and cases of low patient compliance, the medical professionals treating the patient often have incomplete knowledge on which substances the patient is actually using. Patient safety is a problem area and topic of active research in general, as adverse drug events are a serious problem in modern health care. Multiple studies brought this to attention, notably the report" To Err is Human" in the US, however, adverse events are preventable in many cases. Multiple clinical guidelines and screening tools have been developed to check for Potentially Inappropriate Prescribing (PIPs). Mark Beers et al. created a list of medications that can be considered inappropriate for older patients in long-term care in 1991. Beers' criteria were updated regularly and are the basis for other criteria sets, most notably" Screening Tool of Older Persons potentially inappropriate Prescriptions" (STOPP) and" Screening Tool to Alert doctors to the Right Treatment" (START). Both are evidence-based lists of criteria, first published in 2008 and developed in Ireland by a round of experts using the Delphi consensus method. Version 2 of these criteria was published in 2014. STOPP/START resulted in much research interest, many countries and institutions support the tools and consider them appropriate for evaluating prescriptions. Here is an example of the STOPP criteria: The following prescriptions are potentially inappropriate to use in patients aged 65 years and older for cardiovascular system:

1) Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit).

2) Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).

3) Beta-blocker in combination with verapamil or diltiazem (risk of heart block).

And here is an example of the START criteria for the respiratory system:

1) Regular inhaled 2 agonist or antimuscarinic bronchodilator (e.g., ipratropium, tiotropium) for mild to moderate asthma or COPD (Chronic Obstructive Pulmonary Disease).

2) Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50

3) Home continuous oxygen with documented chronic hypoxaemia (i.e., pO2 <8.0 kPa or 60 mmHg or SaO2 <89

None of these guidelines are available in a machine-readable format, they were intended to be used manually by medical professionals, which can create a considerable workload. The usage of the paper-based guidelines is likely unrealistic due to time restrictions on medical staff. There is an urgent need to translate such rules into machine readable form and integrate them into decision support systems as part of the medication prescription process making them available in almost real time for medical doctors. CAREPATH will build in this regard on previous efforts by consortium members [7] in Task 3.2.

A.5.2. Role of CRG

The analysis work of the guidelines identified in D6.1 is being done in Task 6.2. By detailed analysis of the texts the CRG will study the assigned guidelines from D6.1 and select what is relevant to be included in the CAREPATH CDSS. They will also support the development of flowcharts for the CAREPATH guidelines. The CRG/sites will also undertake the following activities (steps to be confirmed):

5. Summarize the result of the reviewed guidelines with reference to the original clinical guideline/chapter for validation.
6. The CRG will make a joint agreement of what recommendations should be used and note any local variations to be considered.
7. The CRG will review and confirm the annotations used in the models, disambiguating potential medical concepts covered by the same term. Code annotation will also contribute to accurate translation of content for deployment in each pilot site.
8. The representatives of each pilot site on the CRG, will distribute the guideline models to appropriate stakeholders in their pilot site, approving the guidelines for deployment, or suggesting customizations, which will be negotiated with the project.

Develop Flowchart Diagrams

The clinical partners will develop if-else-then programming flows structured in decision trees for the clinical guidelines, with help and feedback from technical partners. The flowcharts will represent all the decision making of the collated guidelines.

Review of Formalised Guidelines

The CRG will review the formalised guidelines produced by technical partners to assure their validity/interpretation.

A.6. Conclusions

This deliverable describes the process and technologies used for modelling clinical guidelines as computer interpretable guidelines and is related to Task 3.1 which defines “Patient-Oriented Computer Interpretable Clinical Guideline Modelling”. Flowcharts can be used to model guidelines, then transformed into implementable guidelines with annotations, CDS Hook information and card suggestions. Steps to validate and verify the modelling approaches are also defined. It should be noted that although this initial Clinical Guideline modelling approach has been defined, the formalization and implementation of Clinical Guidelines in CAREPATH is an ongoing task as this is also dependent on other Work Packages which are still in progress. The final version of the guideline specification will be presented in the next release of deliverable D3.1 “Computer Interpretable Guidelines specification of the complete CAREPATH decision support logic” that will be delivered in M12, after the CAREPATH guidelines have been defined in Task 6.2.

A.7. References

[1] CDS Hooks Specification, https://cds-hooks.org/

[2] FHIR HL7 Fast Healthcare Interoperability Resources (FHIR), http://hl7.org/fhir/

[3] Unified Modelling Language and Activity Diagram, https://www.visual-paradigm.com/guide/uml-unified-modeling-language/what-is-activity-diagram/

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A.8. Document History

Date	Changes	Version	Authors
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14-02-2022	Updates to descriptions, references	1v5	Sarah Lim Choi Keung
14-02-2022	Updated Technical Information Reviewers Comments	1v6	George Despotou, Bilal Ahamad
15-02-2022	Corrections and proof reading before review. Document sent for review	1v7	Theo Arvanitis
20-02-2022	Corrections and proof reading by reviewers.	1v8	Yehya Mohamad, Gokce Laleci Erturkmen
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- End of Document -

11. Review status

Deliverable leader:	Warwick
Contributors:	Warwick, SRDC
Reviewers:	Jaouhar Ayadi , Yehya Mohamad
Approved by:	Sarah Lim Choi Keung, Theo Arvanitis

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24-02-2022	Updated with reviewer comments	1v9	Bilal Ahmad
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