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D6.1 ADLIFE Decision Support Modules Scope and Content

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Abstract

The objective of the deliverable D6.1 “ADLIFE Decision Support Modules Scope and Content” is to summarise and present the medical content of the three Clinical Decision Support Services (CDSS) to be used in ADLIFE; evidence-based clinical guidelines, Potentially Preventable Situations (PPS), and assessment scales and Patient Reported Outcome Measures (PROMs).

For the work, clinical reference groups (CRGs) were formed at all seven pilot sites: Osakidetza (Spain), Odense University Hospital (Denmark), Werra-Meißner-Kreis (Germany), Assuta Ashdod hospital and Maccabi Healthcare Services Southern Region (Israel), FALKHOSP Lower Silesia (Poland), Lanarkshire NHS (United Kingdom), and Region Jämtland Härjedalen in Sweden. These CRGs split the work with all three CDSS among them and, thereafter decisions were taken by a project-wide CRG.

The target patients in ADLIFE are chronic patients with severe chronic obstructive pulmonary disease (COPD) and/or congestive heart failure (CHF). As multimorbidity is frequent in this patient group, guidelines for relevant co-morbidities, namely diabetes type 2, chronic kidney disease (CKD), hypertension, hyperlipidaemia, hepatopathy, depression, stroke, and mild cognitive disorder (MCI) have also been reviewed.

In the work with evidence-based guidelines, CRGs have firstly identified the guidelines currently in use in their regions and nations for COPD, CHF, co-morbidities, but also for more generic and organisational guidelines on terminal care, social care, and supporting adult carers. In accordance with the Description of Action (DoA), the UK National Institute for Health and Care Excellence (NICE) guidelines have been the reference guideline for this work. All countries share the same science and interpretations and in general there were minor local deviations amongst guidelines at different pilot sites. For COPD, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) is used in all pilot sites. For diabetes, NICE guidelines were not considered fully up to date regarding diabetes treatment in concomitant CHF and therefore the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) joint statement was used instead. Recommendations for multimorbid patients were derived reconciling single diseases guidelines, identifying potential interactions in the recommendations (disease to disease; disease to drug; drug to drug). The next step for the CRGs was to develop logical flowcharts for the clinical guidelines to be used for the entire project by technical partners. A major part of this deliverable consists of flowcharts that model the clinical recommendations from the guidelines for deployment. In the few cases, where local deviations were identified these have been noted as comments to the flowcharts and will also be deployed in the coming technical implementations.

The second task for the CRGs was to identify care needs and deterioration that can potentially be avoided. These Potentially Preventable Situations (PPS) are presented together with data and electronic health record (EHR) sources and other input that with the use of artificial intelligence (AI) on real life EHR, could result in predictive algorithms alarming if the risk for a PPS increase.

The work, with scales and PROMs by the CRGs, has already been presented in D11.1 “Research protocol, Appendix D” and in D7.1 “Patient reported outcome measures” and is thus only briefly covered in this deliverable.

Statement of originality

This deliverable contains original unpublished work, except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation, or both.

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Definitions and acronyms

Table 1 List of abbreviations/acronyms and their descriptions

Abbreviation/Acronym	Definition
A&E	Accident and emergency
AI	Artificial intelligence
ACCF	American College of Cardiology Foundation
ACE	Angiotensin Converting Enzyme
ACEi	Angiotensin Converting Enzyme Inhibitor
ACR	Albumin Creatinine Ratio
ADA	The American Diabetes Association
ALF	Advanced liver fibrosis
AHA	American Heart Association
AMCA	Assuta Ashdod LTD
ARB	Angiotensin Receptor Blocker
ASCVD	Atherosclerotic cardiovascular disease
ATC	Anatomical Therapeutic Chemical
BB	Beta Blocker
BMI	Body Mass Index
BP	Blood Pressure
BPMN	Business Process Model and Notation
CAT	COPD assessment test
CBC	Complete blood count
CBT	Cognitive Behavioural Therapy
CCBT	Computerised cognitive behavioural therapy
CCB	Calcium Channel Blocker
CDSS	Clinical Decision Support Services
CG	Clinical guidelines
CHF	Congestive heart failure
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease

CRG	Clinical reference group
CVD	Cardiovascular Disease
Dexa	Dual energy x-ray absorptiometry
DoA	Description of Action
DPP-4i	Dipeptidylpeptidase-4 inhibitor
EASD	The European Association for The Study of Diabetes
EF	Ejection fraction
eGFR	Estimated Glomerular Filtration Rate
EHR	Electronic Health Records
ELF	Enhanced liver fibrosis
eos	Eosinophilic
ER	Emergency room
EQ-5D-5L	European quality of life 5-dimension 5-level
everis	Everis Spain SL
EWS	Early warning signs
FALKIEWICZ	Szpital specjalistyczny im a Falkiewicza we Wroclawiu
FEV	Forced expiratory volume
Fib	Fibrosis
FP	Family physician
GESUNDER	Gesunder Werra-Meissner-Kreis GMBH
GFR	Glomerular filtration rate
GI	Gastrointestinal
GLP-1 RA	Glucagon-like peptide-1 receptor agonist
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GP	General Practitioner
HADS	Hospital anxiety and depression scale
HbA1c	Glycated haemoglobin A1c
HCC	Hepatocellular carcinoma
HDL	High-density lipoprotein
HF	Heart failure

HFrEF	Heart failure reduced ejection fraction
ICD	International Classification of Diseases
ICS	Inhaled corticosteroid
ICU	Intensive care unit
IPT	Interpersonal Therapy
IQCODE	Informant questionnaire on cognitive decline in the elderly
IT	Information technology
JTAI	Just in time interventions
KRONIKGUNE	Asociación instituto de investigación en servicios de SALUD-KRONIKGUNE
kPa	Kilopascal
LABA	Long-acting beta agonist
LAMA	Long-acting muscarinic antagonist
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVRS	Lung volume reduction surgery
MACCABI	Maccabi Sheirutei Bruit Foundation
MCI	Mild cognitive impairment
MELD	Model for end stage liver disease
mini-Cog	Mini cognition
mmHg	Millimetre mercury
mMRC	Modified Medical Research Council dyspnoea scale
MMSE	Mini mental state examination
MRA	Mineralocorticoid receptor antagonists
NAFLD	Non-alcoholic fatty liver disease
NASH-CRN	Non-alcoholic steatohepatitis- clinical research network
NG	NICE guidelines
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIV	Non-invasive positive pressure ventilation
NPH	Neutral Protamine Hagedorn

NYHA	New York Heart Association Classification (Class I-IV)
OM	OPTIMEDIS AG
OSAKIDETZA	Servicio Vasco de Salud Osakidetza
OUH	Odense University Hospital
PaO2	Partial pressure of oxygen
PEP	Patient empowerment platform
PHQ	Patient health questionnaire
PPS	Potentially preventable situations
PROM	Patient reported outcome measures
QRISK2	Cardiovascular Disease Risk Calculator 2
R&D	Research and development
RASA	Renin-angiotensin system antagonist (ARB or ACEi)
RJH	Region Jämtland Härjedalen
SABD	Short-acting bronchodilator
SAF	Steatosis, activity, fibrosis
SaO2	Oxygen saturation
SGLT-2	Sodium-glucose cotransporter 2
SGLT-2i	Sodium-glucose cotransporter 2 inhibitor
SR	Slow release
SRDC	SRDC Yazilim arastirma ve gelistirme ve danismanlik ticaret anonim sirketi
SU	Sulfonylurea
TSH	Thyroid stimulating hormone
T2DM	Type 2 diabetes mellitus
UML	Unified Modeling Language
USTRATH	University of Strathclyde
Warwick	The University of Warwick
ZBI	Zarit burden interview

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1.1 Introduction

The purpose of T6.2 is to provide best practice from national and international guidelines, medical science, and clinical knowledge into the ADLIFE Clinical Decision Support Services (CDSS). The work has been divided into three themes; evidence-based clinical guidelines, Potentially Preventable Situations (PPS), and assessment scales and Patient Reported Outcome Measures (PROMs). D6.1 will focus on the two first themes as the last theme assessment scales and PROMS have already been presented in D11.1 "*Research protocol*, *Appendix D Evaluation essential data and variables for quantitative, qualitative and socioeconomic impact assessment"* and in section 7 of D7.1 "*Patient reported outcome measures*".

Clinical reference groups (CRGs) at all seven pilot sites; Osakidetza (Spain), Odense University Hospital (Denmark), Gesunder (Germany), Assuta Ashdod hospital and Maccabi Healthcare Services Southern Region (Israel), FALKHOSP Lower Silesia (Poland), Lanarkshire NHS (United Kingdom), and Region Jämtland Härjedalen in Sweden have had a key role in the work. The deliverable will describe the processes from search of the field for best knowledge to the final results.

A major part of the deliverable consists of 50 flowcharts of guidelines, modelled in a formal way using Unified Modelling Language (UML), an established modelling language used in development of IT systems, for technical partners to implement as executables along with local customisations. Secondly the Task has selected a number of potentially preventable situations (PPS) for ADLIFE patients. PPS refers to what initially was named early warning signs (EWS). CRGs have also chosen relevant assessment scales, clinical, and other relevant input to be used by artificial intelligence (AI) in building prediction algorithms to potentially avoid these situations.

D6.1 has received input and material from T7.1, T9.1, and T11.1. Other work tasks that depend on the outcomes of D6.1 are found in WP5: Task 5.1 *Clinical decision support system design and implementation*, Task 5.2 *Integration of the scales and heuristic risk algorithms*, Task 5.3 *Integration of the clinical guidelines*, and Task 5.4 *Risk prediction model design and implementation*.

1.2 Patients in the scope of ADLIFE

Inclusion criteria in ADLIFE are patients over 55 years of age having COPD and/or CHF at more advanced or sever stages corresponding to a GOLD stage >2 and a New York Heart Association (NYHA) stages III or IV, respectively. Further inclusion criteria definitions for COPD and CHF are presented in **Table 2.** Most patients, in the scope of ADLIFE, have other diseases and many have a complex care situation with e.g., social care need or terminal care. Guiding documents for the most frequently co-existing and/or causative diseases to COPD and CHF namely diabetes type 2, chronic kidney disease (CKD), hypertension, hyperlipidaemia, hepatopathy, depression, stroke, and mild cognitive disorder (MCI) together with guidelines for complex care situations are also included in the deliverable when appropriate. **Table 3** present these other included diseases/situations together with limitations in the performance of guideline reconciliation analysis and if these diseases represent an exclusion criterion to participance in ADLIFE.

Table 2 Inclusion criteria

Diagnosis/Topic	Inclusion criterions	
Overall	Patients over 55 years	AND
COPD	FEV1<50, >2 GOLD scale	AND/OR
CHF	Heart failure in functional stage NYHA III-IV and stages C and D of the ACCF/AHA classification in a stable phase for at least two months.	

Abbreviations: ACCF= American College of Cardiology Foundation AHA= American Heart Association, CHF= Congestive heart failure, COPD= Chronic obstructive pulmonary disease, FEV= Forced expiratory volume, GOLD= Global Initiative for Chronic Obstructive Lung Disease, NYHA= New York Heart Association Classification (Class I-IV), PPS Potentially preventable situations.

Table 3 Other included guidelines for diseases/complex situations with restrictions in mapping and reconciliation analysis and potential cause for exclusion

Diagnosis/Topic	Limitations in inclusion	Limitations in mappings and reconciliations	Exclusion criterions
Diabetes	Diabetes type 2 only.		
Hypertension			
Hyperlipidaemia	Restricted to patients with diabetes type 2 and/or CKD.	Restricted to patients with diabetes type 2 and/or CKD	
Chronic renal failure		Severe CKD with GFR <15 ml/min is not included in the mapping.	
Chronic hepatopathy	Mild/moderate stages.	Mild/moderate stages. Reconciliation analysis with CHF only. Focus on medications, nutrition, and alcohol.	
Stroke	Analysed regarding PPS. Focus on how post stroke symptoms impact care of COPD/CHF: nutrition, depression, and physical activity.	Analysed regarding PPS and reconciled with COPD/CHF only. Focus on how post stroke symptoms impact care of COPD/CHF: nutrition, depression, and physical activity.	
Cognitive disorder	Only MCI is included.	Only MCI is included and analysed as a single guideline, not reconciled with other guidelines.	More severe cognitive impairment than MCI is an exclusion criterion.

Depression	Mild/moderate stages.	Only analysed as a single guideline, without reconciliations.	
Terminal care		Only analysed as a single guideline, without reconciliations.	
Social care/needs		Only analysed as a single guideline, without reconciliations.	
Supporting carers		Only analysed as a single guideline, without reconciliations.	

Abbreviations: CHF= Congestive heart failure, CKD= Chronic kidney disease, COPD= Chronic obstructive pulmonary disease, GFR= Glomerular filtration rate, MCI= MCI Mild cognitive impairment, PPS Potentially preventable situations.

1.3 Participating partners in the deliverable

Both clinical and technical partners, from the ADLIFE consortium, have participated in the work contributing to this deliverable. The clinical perspective was given by CRG from the pilot sites in the participating seven countries: Osakidetza (Spain), Odense University Hospital (Denmark), Werra-Meißner-Kreis (Germany), Assuta Ashdod hospital and Maccabi Healthcare Services Southern Region (Israel), FALKHOSP Lower Silesia (Poland), Lanarkshire NHS (United Kingdom), and Region Jämtland Härjedalen (RJH) in Sweden. All technical partners: SRDC from Turkey, everis from Spain, and Warwick from United Kingdom have participated in clarifications and analysis of results from the CRGs.

1.4 Methodology

1.4.1 Clinical Reference Groups (CRGs)

Local CRGs have been formed at the pilot sites with competences from different professionals: family physicians (FP), hospital specialist doctors, and nurses. Members of the local CRGs also participated in the ADLIFE (project-wide) CRG, which was responsible for all final decisions.

CRGs tasks relevant for D6.1 have been to

- Guide the process of defining and refining the CDSS;
- Review and select assessment scales and PROMs that will be computerized;
- Select the most adequate guidelines to provide evidence-based input to these CDSS;
- Review recommendations taking into account the Pilot sites´ reference guidelines;
- Systematically reconcile conflicting recommendations for multimorbid patients and adapt to local context and guides;
- Develop “If-else-then” programming flows and structure in decision trees;
- Agree an initial and basic list of the symptoms/signs to be used by PPS;

- Review the variables used for clinical prediction algorithms, including output (mortality, admissions, re-admissions, complications...);
- Review, assess and refine the reference predictive algorithms selected for COPD and CHF;
- Define the types of recommendations and alerts.

Local CRGs have done most of the practical work shared among them while decisions have been taken at monthly project-wide CRG meetings. A list of individual CRG members is attached in **Appendix A1** and a document describing the scope, governance, and activities for the CRGs in **Appendix A2**.

1.4.2 General methodology for CRGs work

The CDSS preparative work with evidence-based clinical guidelines, PPS, and assessment scales / PROMs have been performed in a similar way for all themes with the following consecutive steps.

- The scope with relevant co-morbidities and relevant other guidelines e.g., terminal care was presented for all ADLIFE partners at the project kick-of meeting;
- Project-wide CRG confirmed the scope;
- Local CRGs performed a search for relevant best practice documents at national and international level;
- A decision was taken in the central CRG on what guidelines, what PPS, etc. to include in the continuing work;
- The WP lead RJH split the initial work in all themes among the local CRGs e.g., what guidelines each local CRG should map;
- All flowcharts and other results from the local CRGs were reviewed by the other local CRGs and if needed refined and re-reviewed;
- All technical partners have worked closely with the CRGs analysing all output, requesting clarifications when needed;
- At their reviews all local CRGs listed existing needs for local customisations based on care traditions, local guidelines, or use of assessment scales/questionnaires;
- Project-wide CRG jointly approved the resulting flowcharts, PPS descriptions, chosen assessment scales/questionnaires, and PROMS to be deployed in ADLIFE together with local customisations.

An example of one of the steps, in the review work with one of the flowcharts, is presented in **Appendix A3**. Some of the material from the CRGs are complementary or describe improvements of the guidelines but outside the scope of ADLIFE. Such material is presented in **Appendix A4**.

1.4.3 Review and mapping of guidelines

In the Description of Action (DoA), it was stated that the task starts with the identification of the national and international clinical guidelines in use for the selected focus areas of the project: COPD and CHF at severe stages together with frequently associated diseases,

namely diabetes type 2, CKD, hypertension, hyperlipidaemia, hepatopathy, depression, stroke, and MCI. To this, the existence of guidelines on terminal care, on social care, and on supporting informal caregivers were included. In the first step, focus was on single disease or single topic guidelines. For this work CRGs with clinicians from relevant specialities from primary and secondary care were formed at each pilot site. In the DoA it was also stated that the UK National Institute for Health and Care Excellence (NICE) [1] guidelines would be the reference guidelines. This was since NICE guidelines are respected, based on best knowledge in a transparent way, well researched, and well known. NICE also includes guidelines covering broad aspects of care as patient involvement and social needs. ADLIFE is based on and expands the work in a previous Horizon 2020 project C3-Cloud where the NICE guidelines were found to be well in line with national and local guidelines in the participating pilot sites.

The second step was for all CRGs jointly to evaluate if the NICE guidelines were fully up to date and applicable. As all pilot sites had their COPD guidelines based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [2] guidelines, these were used instead of the NICE guidelines (NG115) [3]. For diabetes type 2 the NICE guidelines (NG 28) [4] were not updated in accordance with the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) guideline [5] regarding the use of in particular Sodium/Glucose Cotransporter 2 (SGLT-2) in patients with diabetes and CHF. As the ADA/EASD guidelines were fully in use in the pilot sites these latter guidelines were used for drug treatment instead of NICE guidelines. **Table 4** presents the chosen guidelines included for the further steps in the task.

Table 4 Guidelines included in the analysis

Included diseases/care topics	Included guidelines
Chronic obstructive pulmonary disease	GOLD
Congestive heart failure	NICE NG106
Depression	NICE CG90
Diabetes	NICE NG28, NG19, and CG173
Chronic kidney disease	NICE CG182
Lipid lowering	NICE NG181
Hypertension	NICE NG136
Chronic hepatopathy	NICE NG49
Stroke	NICE NG128
Mild cognitive disorder	NICE NG97
Terminal care, care of elderly	NICE NG142 and NG31
Supporting carers	NICE NG150
Social care needs	NICE NG22

Abbreviations: CG= Clinical guidelines, GOLD= Global Initiative for Chronic Obstructive Lung Disease, NG= NICE guidelines, NICE= National Institute for Health and Care Excellence.

The next step was to decide what parts of the guidelines were relevant to include in the CDSS regarding diagnostic and therapeutic recommendations, recommendations regarding monitoring and follow up. Simultaneously identification of potential EWS to be included in the PPS work was also made together with identification of potential areas for early adaptive interventions, “just in time interventions” (JTAI) for the up-coming work with the patient empowerment platform (PEP).

Following this, the fourth step was for all local CRGs to review and comment if there were any important deviations between the locally used guidelines and the finally chosen reference guidelines that called for local adaptations at implementation in the automatic decision support and care planning functionality in ADLIFE. The work did not include trying to rewrite or reshape existing guidelines beyond identifying local deviations. As previously noted in C3-Cloud all national and local guidelines used were highly aligned with each other and the reference guidelines. The few existing local deviations are mapped under corresponding flowcharts in section 1.5.

The fifth and main task has been to model the guidelines chosen into flowchart-based specifications that can guide technical implementation. This analysis carried out by local CRG clinicians from all sites resulted in a total of 50 flowcharts defining the major content of various aspects for all the included diseases and for generic care organisation and support. The flowcharts were then reviewed by all local CRGs and analysed by technical partners before being accepted by the project-wide CRG. The project decided, as a prime option, to use the Modelio® (www.modelio.org) freeware modelling tool and its Business Process Model and Notation (BPMN) for the notations of the process diagrams. A similar mapping and review process had previously been performed in the Horizon 2020 project C3-Cloud for some of the diseases in ADLIFE. When possible, i.e., when these mappings were in accordance with actual international guidelines used, that mapping was reused in ADLIFE after a similar validation, steps one to four described above was undertaken. Flowcharts reprinted from C3-Cloud are clearly marked as such.

The sixth step was the analysis undertaken of potential interactions between different single guidelines. All medical guidelines are based on an imaginary situation with just one disease present. Multi-morbidity in elderly though is more of a rule than an exception. Treatment modifications due to co-existing diseases are seldom included in guidelines but is expected to be undertaken by the skilled clinician reading the guidelines. In this section potential problems and/or interactions that call for a modified output when moving from a single disease perspective (guideline) to a multi-morbidity perspective with two, three, or four diseases involved, are listed. The types of interactions studied are Disease to Disease; Disease to drug; Drug to Drug interactions.

- Disease-Disease interaction: The presence of a second disease might be a risk factor for comorbidities to develop, or worsens the prognosis, or interfere with the diagnosis or treatment.
- Disease to Drug/ Drug to disease interactions: The presence of a second disease might call for modification in treatment. This is particularly relevant for nephropathy.
- Drug-drug interactions of prescribed drugs will be dealt with separately but should be noted here if drugs are explicitly mentioned in the guidelines.

When conflicts were identified**,** a modified output was suggested. The initial work was split among the local CRGs and then all results were reviewed by the other CRGs before being jointly accepted as ADLIFE guidelines. As no guidelines cover this complex situation, all work and resulting output was based on clinical experience and knowledge from the participating CRGs. The potential interactions/problems were studied for all key clinical diseases and guidelines and were problems, as judged by the project-wide CRG, could be expected. The reconciliation areas studied, and the reconciliation results are presented in **Table 5** and **Table**

6. Appendix A5 and **Appendix A6** include work descriptions for CRGs for single guidelines and guideline reconciliations, respectively. Lastly it´s important to be aware that creating new guidelines or re-writing existing guidelines beyond what local adaptations or clinical judgement regarding reconciliations required, is not within the scope of ADLIFE or this deliverable.

1.4.4 Potentially preventable situations (PPS)

A second major work task for the CRGs was a preparatory work for T5.4, where AI will use real patient data from electronic health records (EHRs) to create predict algorithms for the identification of potentially preventable situations for ADLIFE patients in a non-hospital setting. The work started with identification of situations (e.g., avoidable admission or malnutrition) that potentially are avoidable, taking into account that real-time and acute situations (that would need attention within a week) were outside of the scope.

The next step was to discretely identify the preventable situations of each of the proposed PPS (e.g., ICD-10 codes, drug prescription). This subset of clinical events defines each of the PPS and allows to train the AI to detect these events across patient´s longitudinal historical data. The next step was to identify, based on clinical experience and scientific search of the field, what input data (e.g., lab test, demographic information, relevant scales, or questionnaires) could be used by the AI to trace an evolving pattern indicating an increasing risk for PPS. In T5.4, the AI algorithms will confirm which are statistically significant for predicting each event. Also, a relevant time frame (early action window) for the AI search was suggested by the CRGs. This time frame is the chosen period of time for early action before the preventable situation occurs. There is another relevant time frame called “observation window” (since when AI considers historical data for the next prediction) that will be defined within T5.4 due to statistical parameters and performance output metrics. As with the guideline review and mapping, all CRGs worked separately at first and thereafter a decision was taken by the project-wide CRG. **Figure 1** presents a schematic diagram of the AI work with PPS with a preventable care need as a result that you wish to avoid. Before the unwanted outcome could occur, different patient data will be traced longitudinally during the observation window and with the use of different AI predictive algorithms an alert/warning will be notified before the early action window time frame is exceeded. An example of working material for this theme is presented in **Appendix A7**.

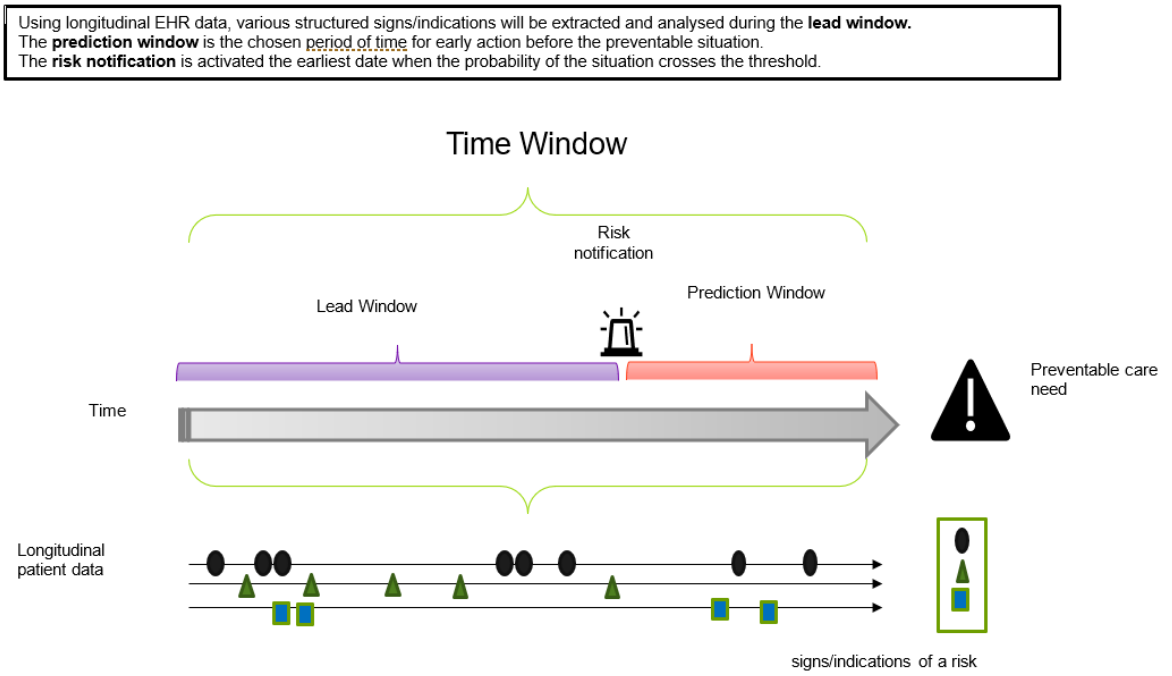
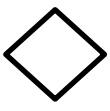


Figure 1 Schematic presentation of the work with PPS

1.5 Flowcharts of the guidelines

1.5.1 Flowchart symbols

The following symbols are used at the modelling process:

Name	Flowchart Symbol	Usage
Start point		Indicates the starting of a process.
End point		Indicates the ending of a process.
Process		Represents a process, action, or function.
Decision		Indicates a point where the outcome of a decision dictates the next step. There can be multiple outcomes.
Flow arrow		Indicates the flowcharting path.

1.5.2 Flowcharts for chronic obstructive pulmonary disease (COPD)

All flowcharts under this theme are based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) report 2021 [2].

1.5.2.1 Classification of exacerbation and pharmacological treatment

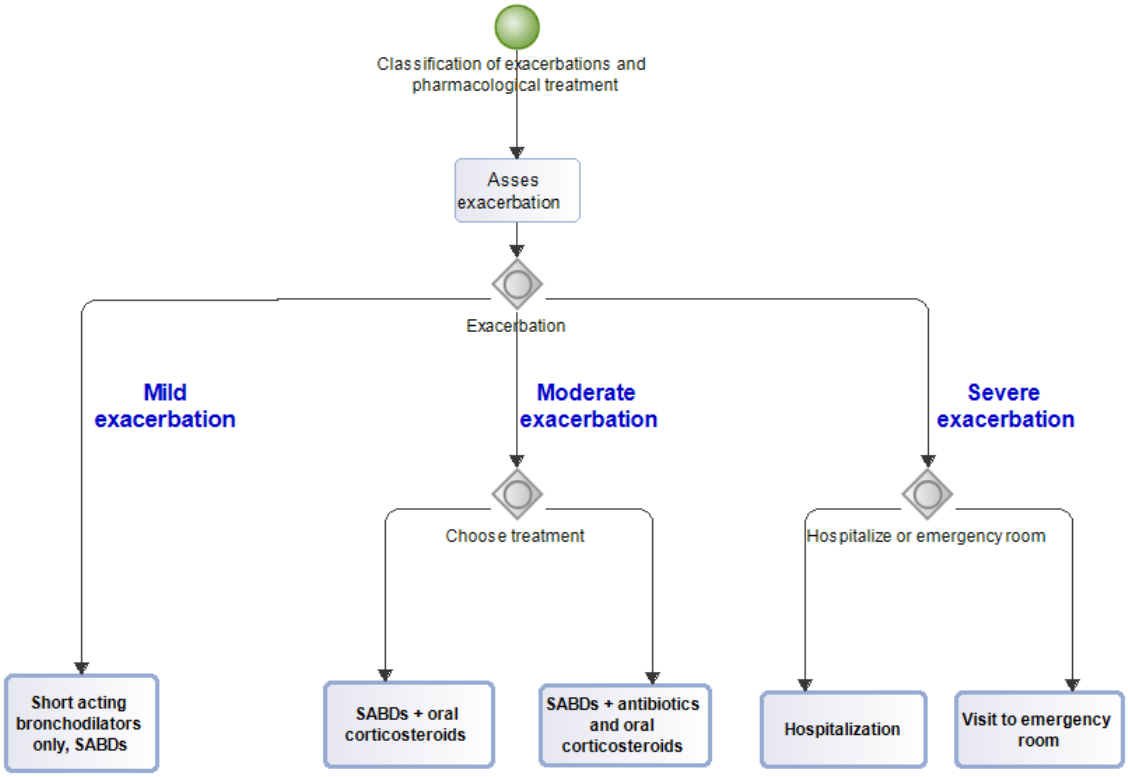


Figure 2: COPD – Classification of exacerbation and pharmacological treatment

Abbreviation: SABD= short-acting bronchodilator

1.5.2.2 Management of COPD

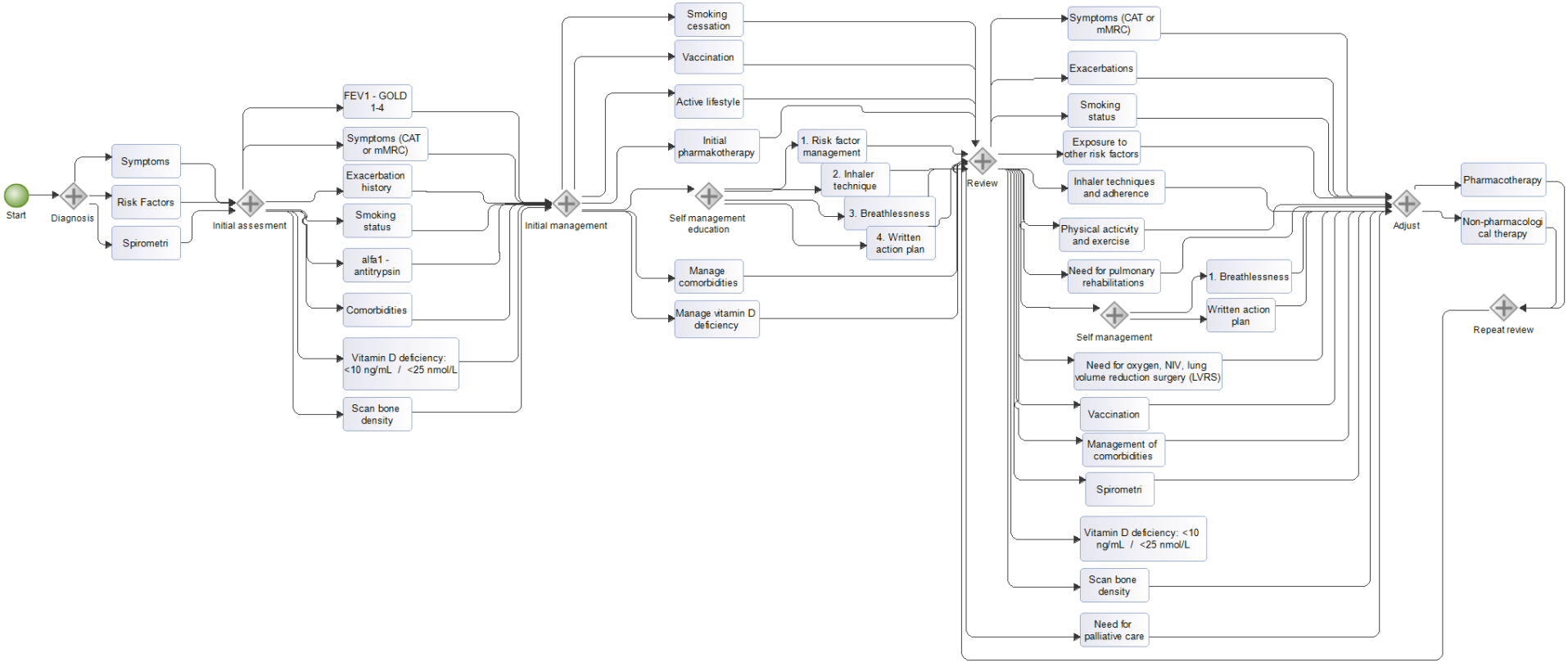


Figure 3: COPD - Management

Abbreviations: FEV= forced expiratory volume, CAT= COPD assessment test, mMRC= Modified Medical Research Council dyspnoea scale, NIV= non-invasive positive pressure ventilation, LVRS= lung volume reduction surgery.

Local deviations: USTRATH: Add evaluation of fracture risk, incl. DEXA scan evaluation/frequency and potentially bisphosphonate treatment. OSAKIDETZA and RJH: Add annual influenza vaccination. OSAKIDETZA: Not all centres have access to pulmonary rehabilitation.

1.5.2.3 Initial pharmacological treatment

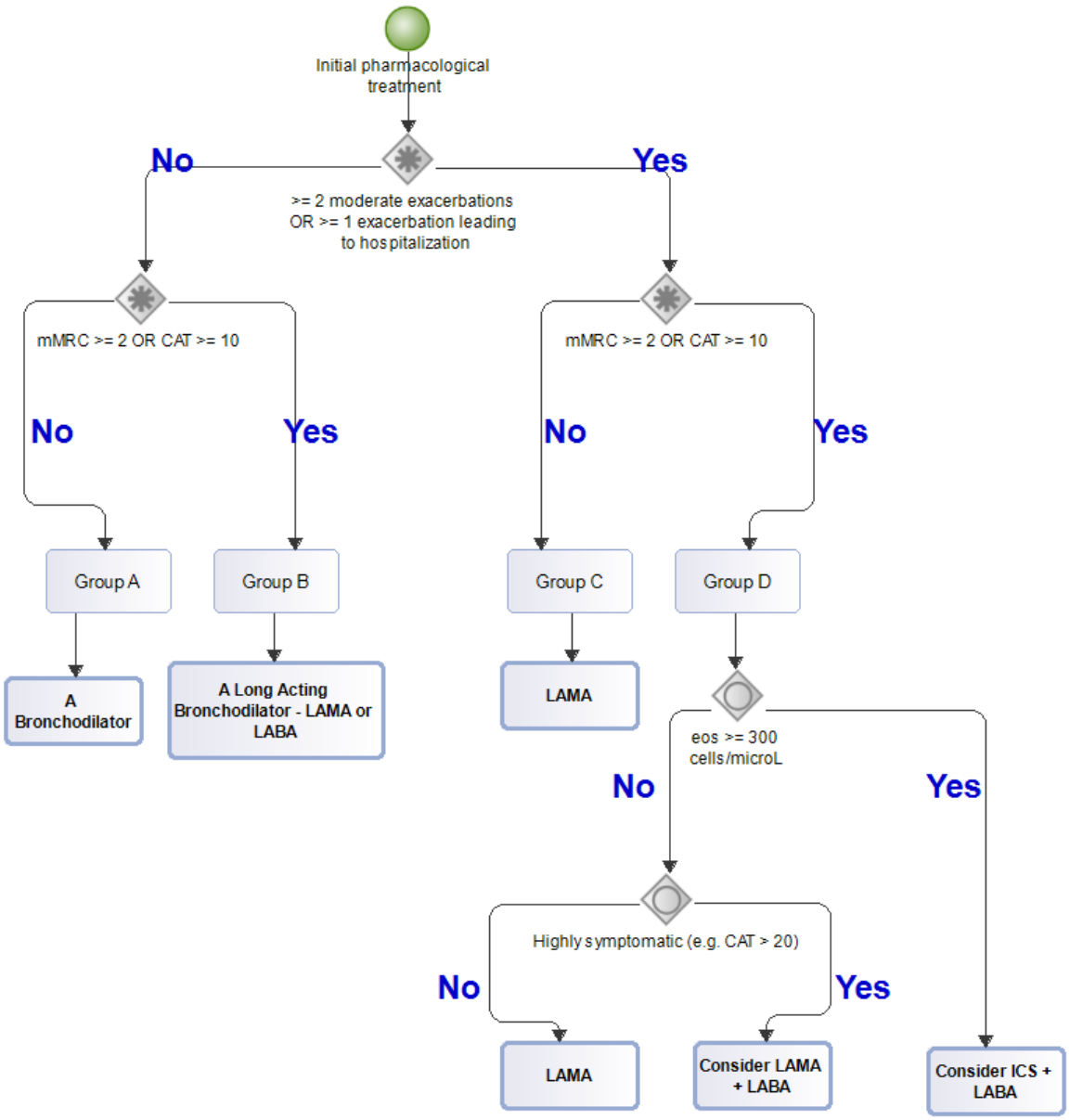


Figure 4: COPD - Initial pharmacological treatment

Abbreviations: CAT= COPD assessment test, mMRC= Modified Medical Research Council dyspnoea scale, LAMA= long-acting muscarinic antagonist, LABA= long-acting beta agonist, ICS= Inhaled corticosteroid

Local deviation: AMCA: For Group D subgroup (with an eos>=300) the decision tree and flow chart need to continue – if ICS+ LABA doesn't work then consider LABA+LABA+ICS, if that doesn't work add Roflumilast and if that doesn't work add azithromycin

1.5.2.4 Follow up pharmacological treatment

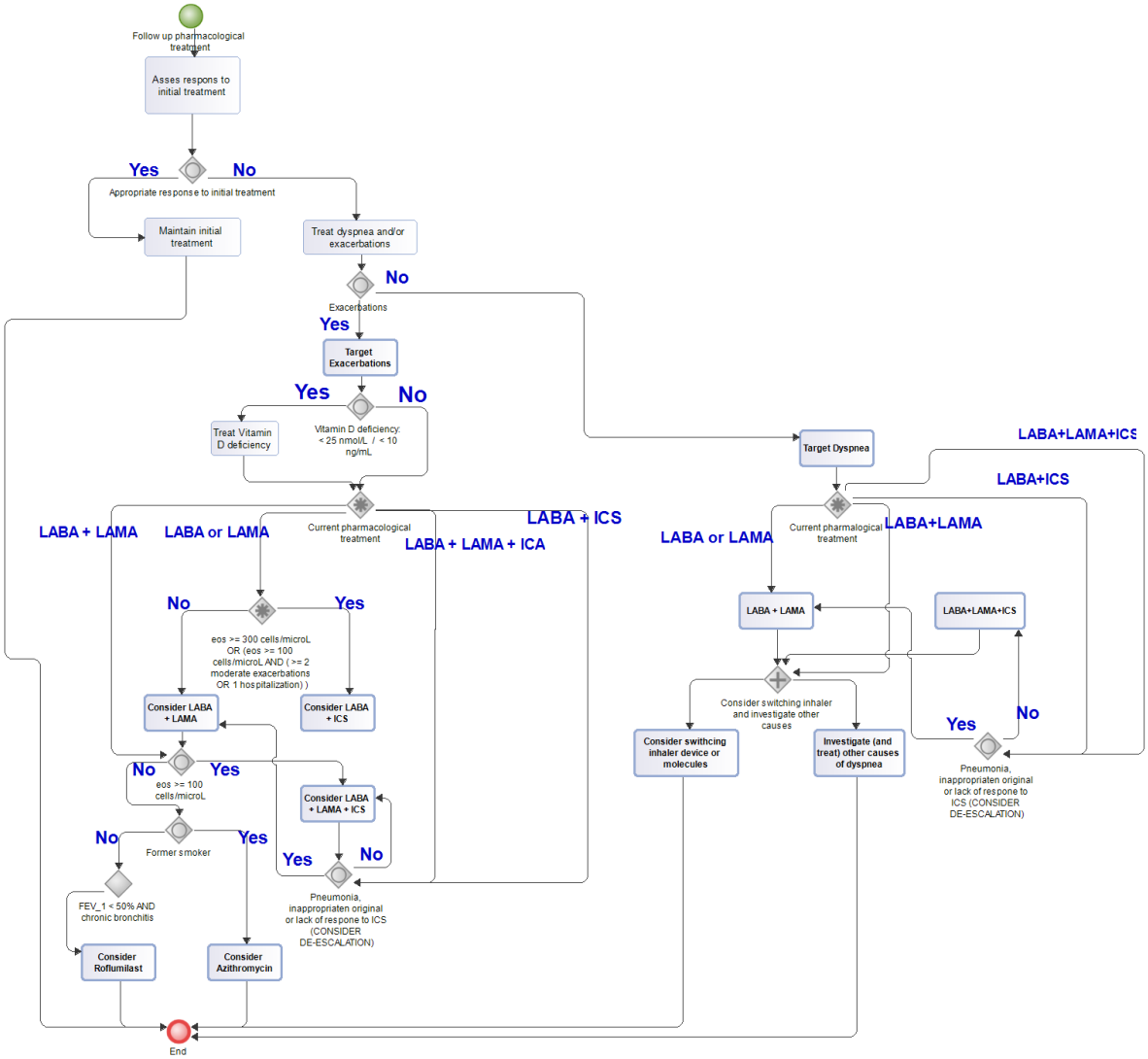


Figure 5:COPD - Treatment follow up

Abbreviations: FEV= forced expiratory volume, LAMA= long-acting muscarinic antagonist, LABA= long-acting beta agonist, ICS= Inhaled corticosteroid, eos= eosinophilic

Local adaptation: OSAKIDETZA: Not all centres have access to pulmonary rehabilitation.

1.5.2.5 Oxygen treatment

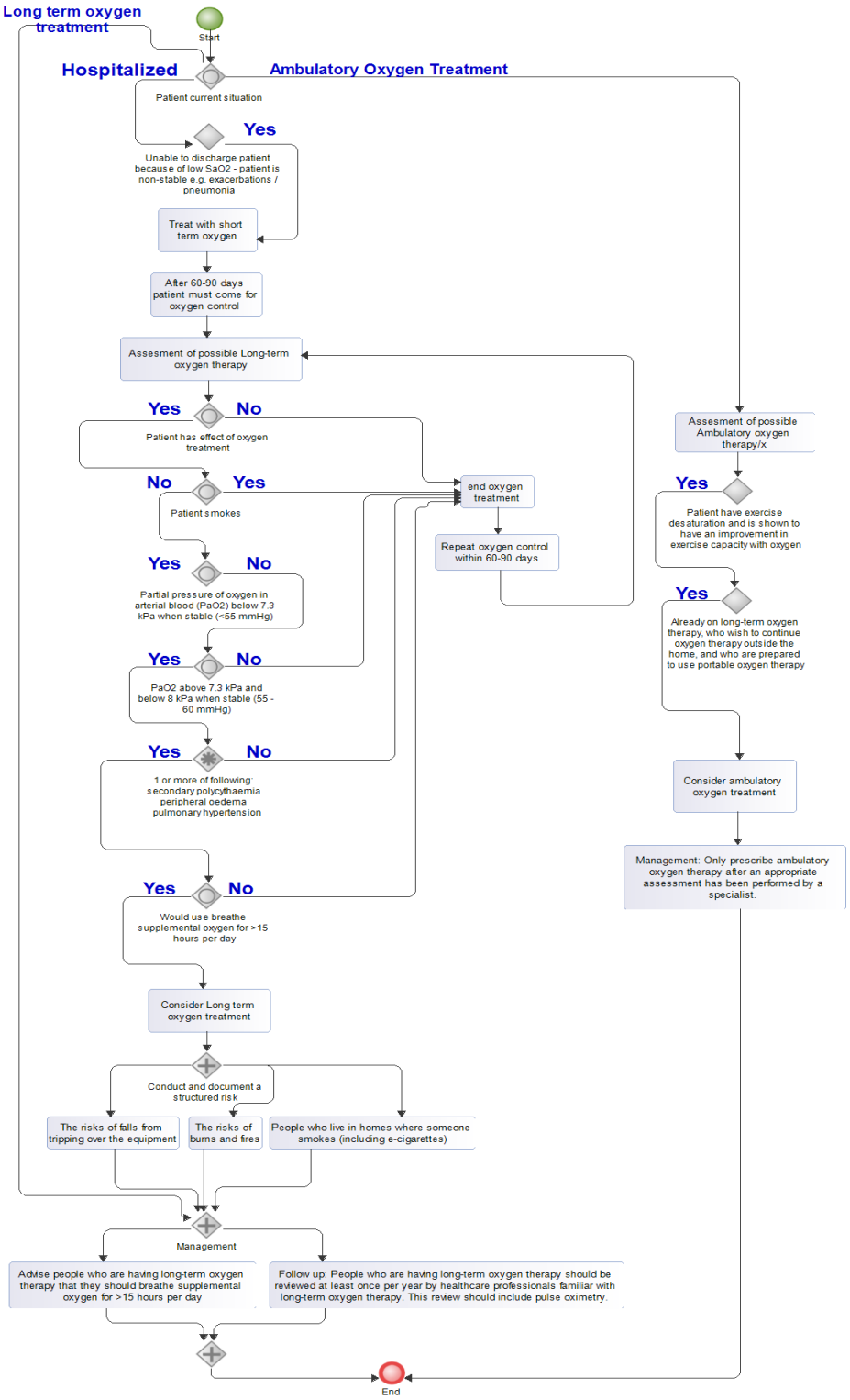


Figure 6: COPD - Oxygen treatment

Abbreviations: kPa= Kilopascal, mmHg= millimetre mercury, PaO2= Partial pressure of oxygen, SaO2= Oxygen saturation

Local deviation: OSAKIDETZA: Pa02 units are mmHg, not kPa.

1.5.2.6 Treat at home or in hospital

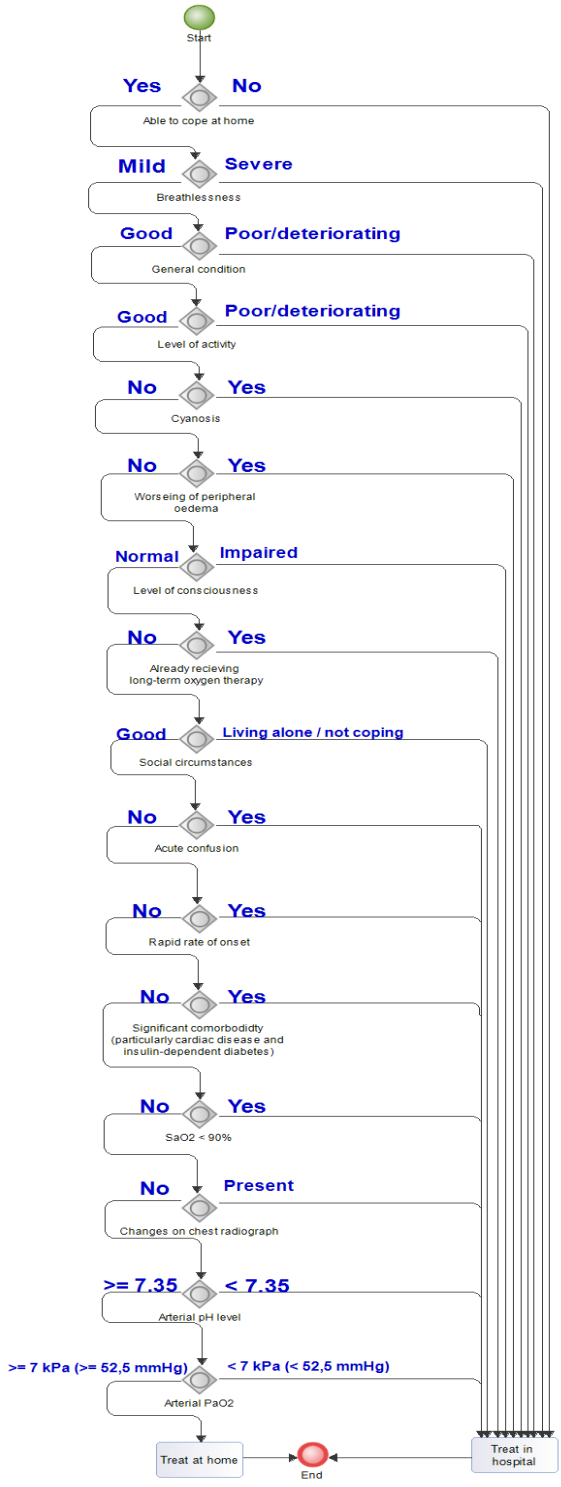


Figure 7: COPD - Treatment at home or at hospital

Abbreviations: kPa= Kilopascal, mmHg= millimetre mercury, PaO2= Partial pressure of oxygen, SaO2= oxygen saturation

Local adaptation: OSAKIDETZA: Local resources need to be considered.

1.5.2.7 Follow up in primary care

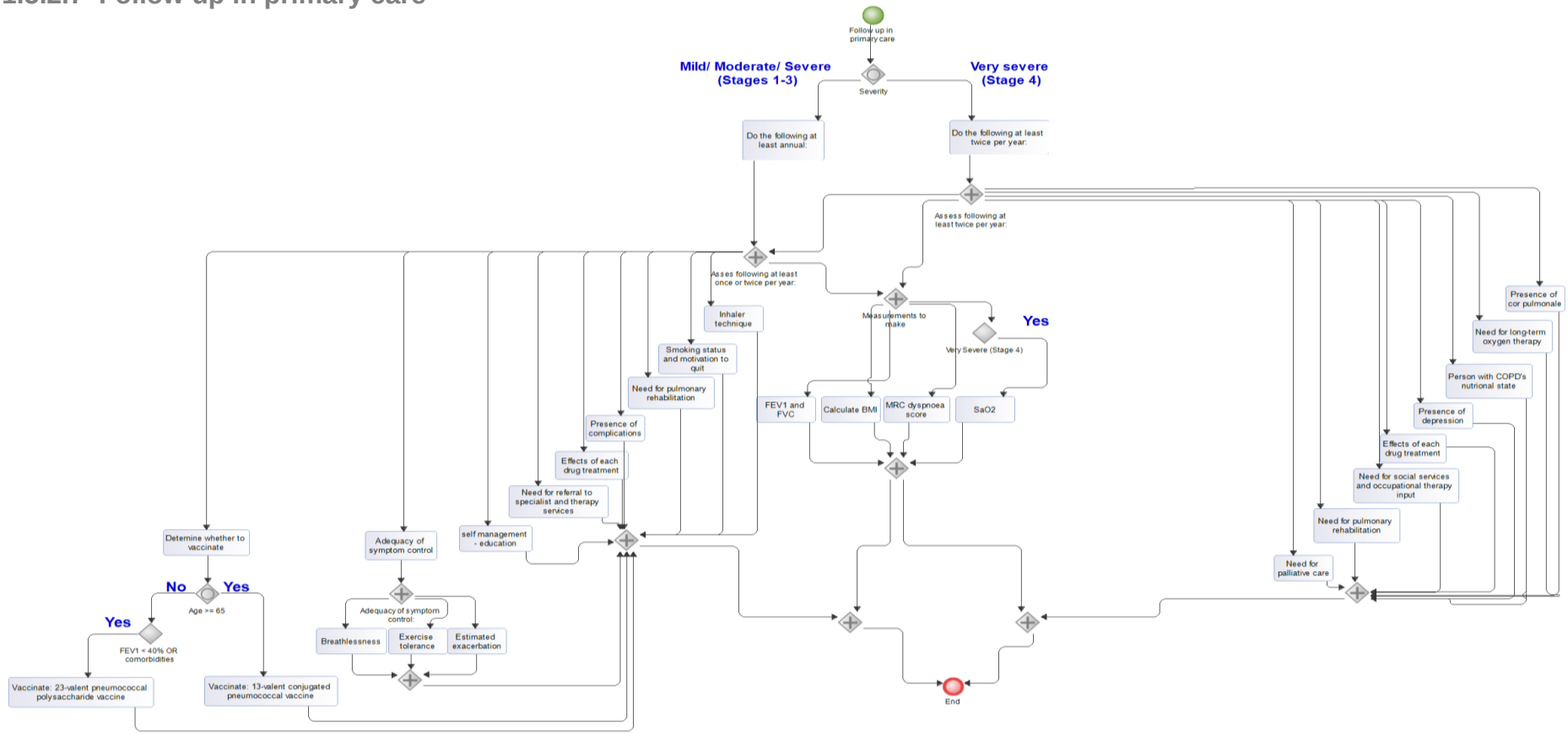


Figure 8: COPD - Primary care follow up

Abbreviations: BMI= body mass index, FEV= forced expiratory volume, FVC= forced vital capacity, MRC= Medical Research Council, SaO2= oxygen saturation **Local deviations**: OSAKIDETZA**:** not all centres have access to rehabilitation. AMCA: Pneumococcal conjugate vaccine (PCV13) - CDC recommends adults 65 years or older get a shot of PCV13 if they have never received a dose and have a condition that weakens the immune system, cerebrospinal fluid leak, or cochlear implant.

1.5.3 Flowcharts for congestive heart failure (CHF)

All flowcharts under this theme are based on NICE guideline NG106 [6] Chronic heart failure in adults: diagnosis and management.

1.5.3.1 Newly confirmed diagnosis

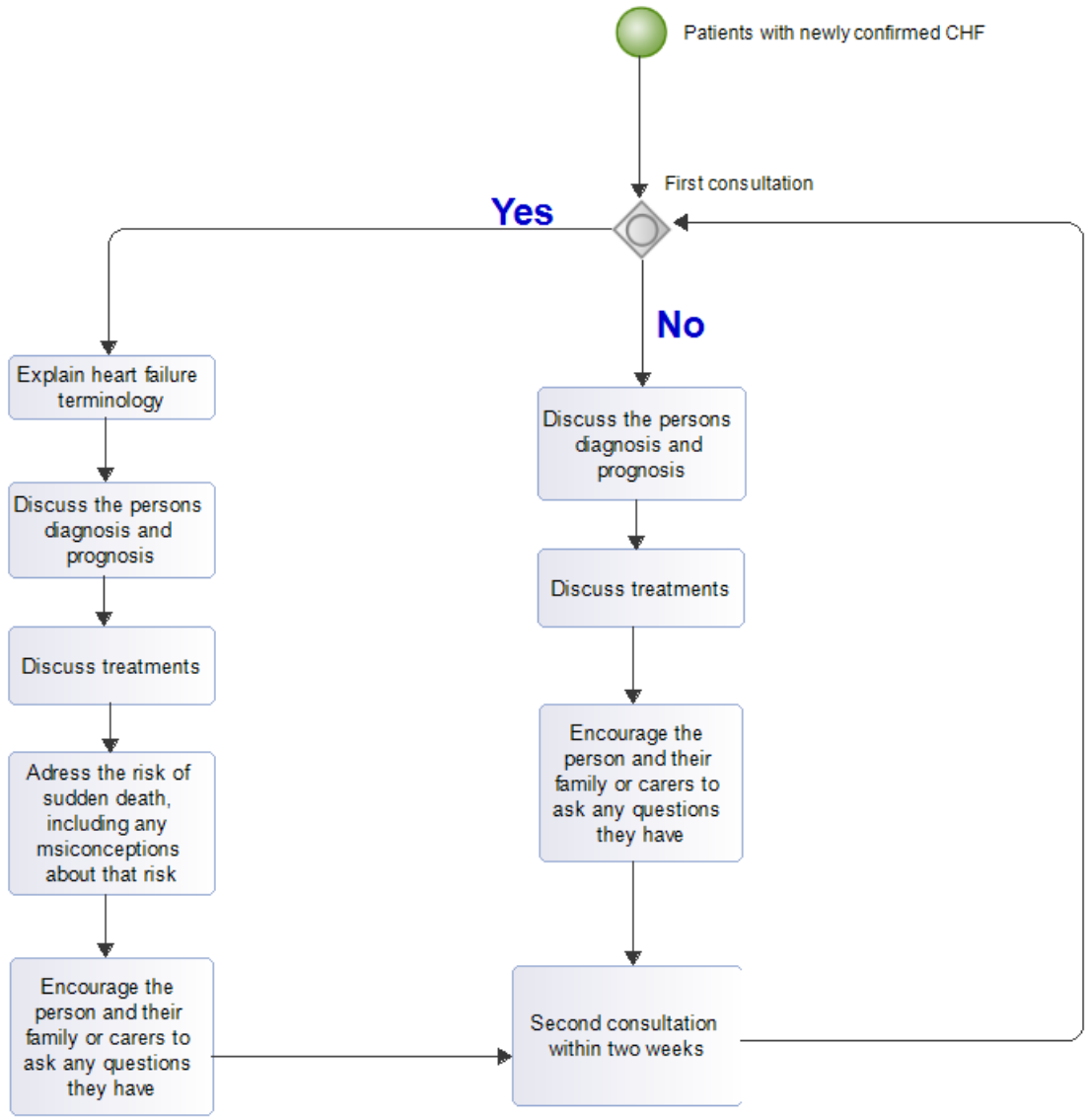


Figure 9: CHF – Newly confirmed diagnosis

1.5.3.2 Treatment confirmed diagnosis

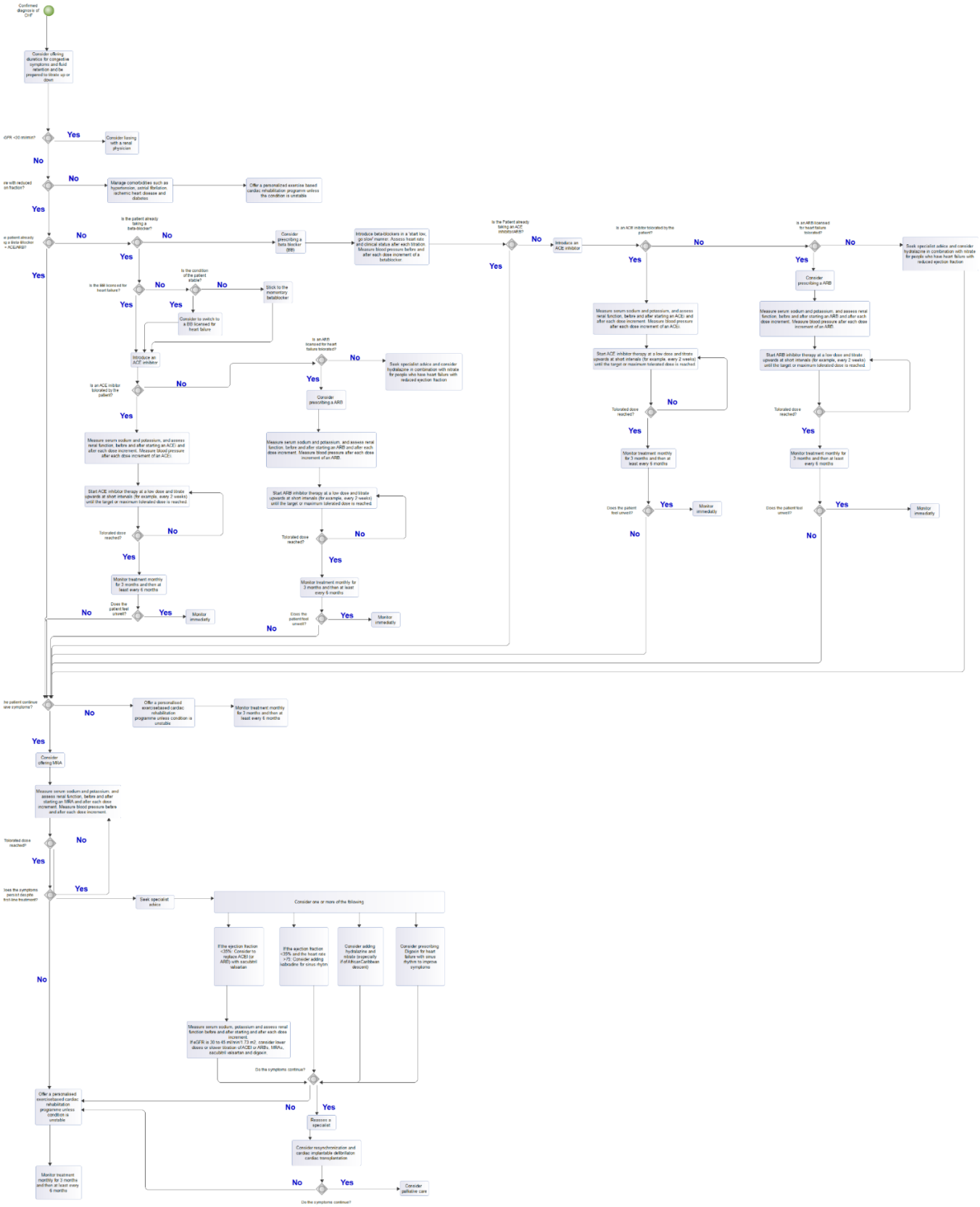


Figure 10: CHF treatment

Abbreviations: ACE= angiotensin converting enzyme, ACEi= angiotensin converting enzyme inhibitor, ARB= angiotensin receptor blocker, BB= beta blocker, eGFR= estimated glomerular filtration rate, MRA= Mineralocorticoid receptor antagonists

Local deviations: AMCA: For patients that don´t take beta blockers for any other co-morbidity and have eGFR>30 consider treatment with SGLT2i. Lanarkshire: Consider Dapagliflozin® in symptomatic patients with reduced EF.

1.5.3.3 CHF without reduced ejection fraction

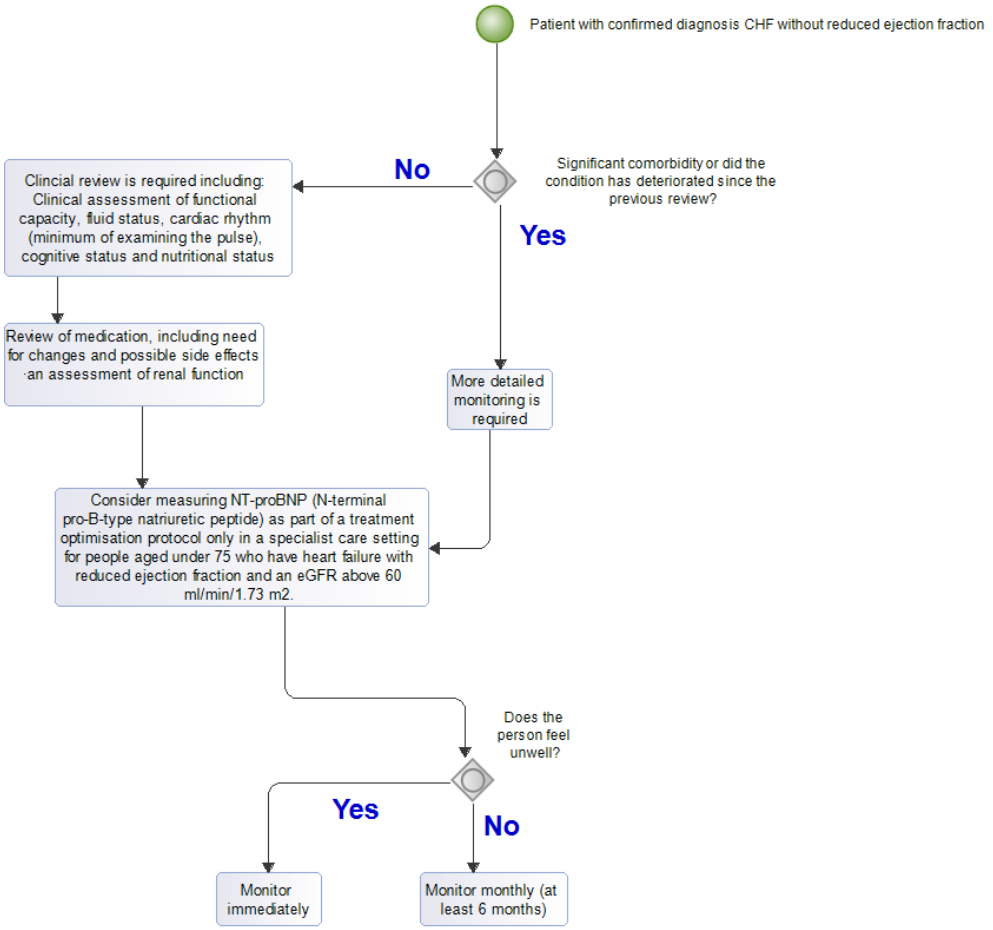


Figure 11: CHF - without reduced ejection fraction

Abbreviation: eGFR= estimated glomerular filtration rate

Local deviation: AMCA: Monitoring of these patients can also be done by a nurse.

1.5.4 Flowcharts for diabetes mellitus type 2

The starting point of this section assumes that the patient is already diagnosed with diabetes type 2, so the algorithms does not study the diagnostic criteria of diabetes.

The treatment flowchart is based on the ADA/EASD consensus statement [5] from 2018, the diabetic foot problem on NICE guideline NG19 [7] from 2015 and updated 2019, neuropathic pain is based on NICE clinical guideline CG173 [8] from 2013 and last updated in 2020, and remaining flowcharts under this theme on NICE diabetes guidelines NG28 [4] from 2015, partially updated in 2020.

1.5.4.1 Treatment

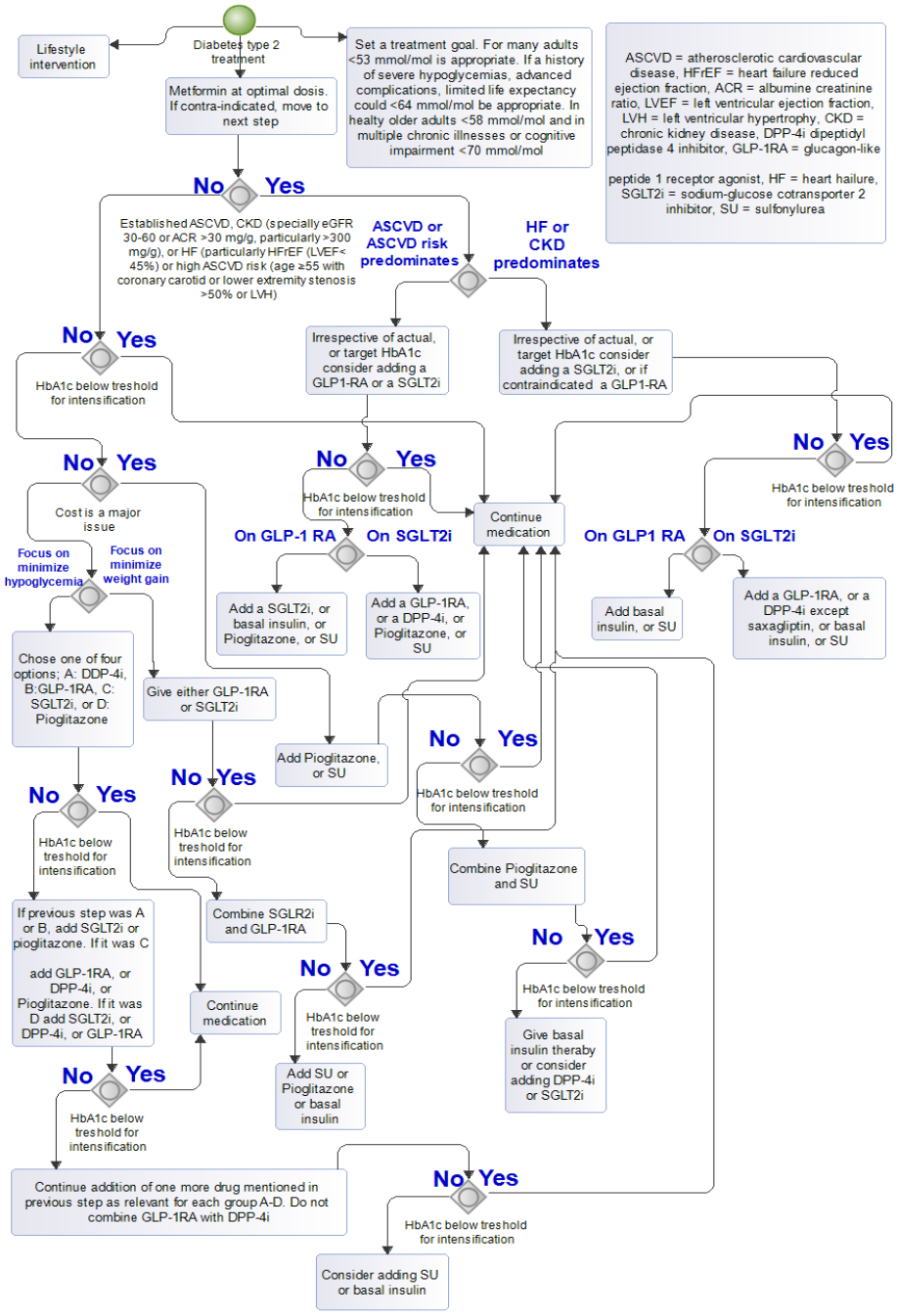


Figure 12: Diabetes – Treatment

Local deviations Lanarkshire: Switch Metformin to Metformin SR. GLP-1RA considered in people with BMI of ≥ 30 Km/m^2 (or ethnicity-adjusted equivalent) in combination with oral glucose-lowering drugs or basal insulin (or both) as third- or fourth-line treatment. OSAKIDETZA: Use of repaglinide is an alternative to sulfonylurea in the situations where this is recommended in the flowchart. AMCA: In case Metformin is contraindicated: DPP-4-Inhibitor is the preferred option for treatment, followed by SGLT2. Pioglitazone and Sulfonylurea would be the last option of treatment in Israel.
In case HbA1C below threshold for intensification- we disagree only patients with BMI>35 should receive GLP-1. All patients, regarding their BMI should be prescribed GLP-1, unless contra- indicated. RJH: A treatment goal of <48 mmol/mol should be considered in younger patients and in newly diagnosed patients without co-morbidities.

1.5.4.2 Autonomic neuropathy

Reprinted from C3-Cloud D7.1

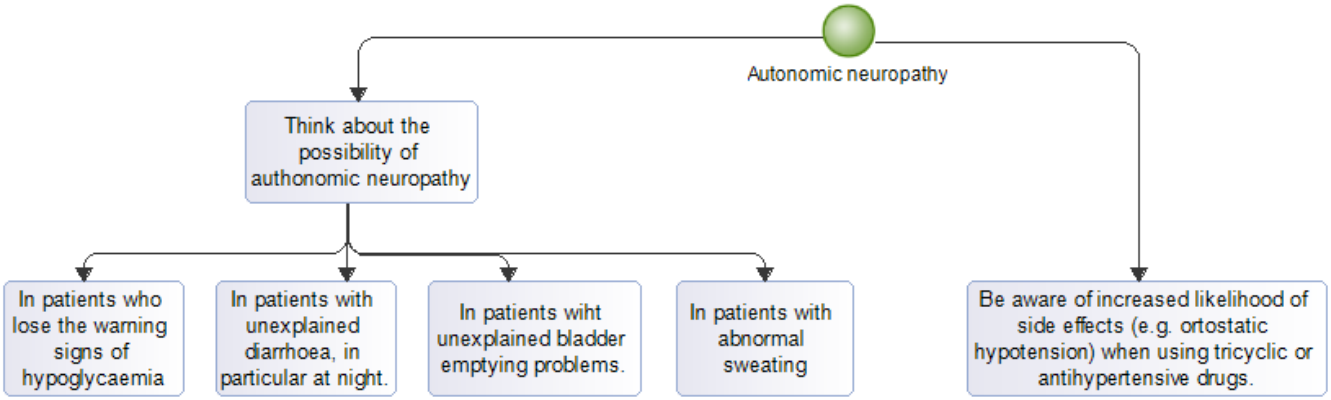


Figure 13: Diabetes - Autonomic neuropathy

Local deviation: Lanarkshire: Annual screening for autonomic neuropath.

1.5.4.3 Diabetic foot problems

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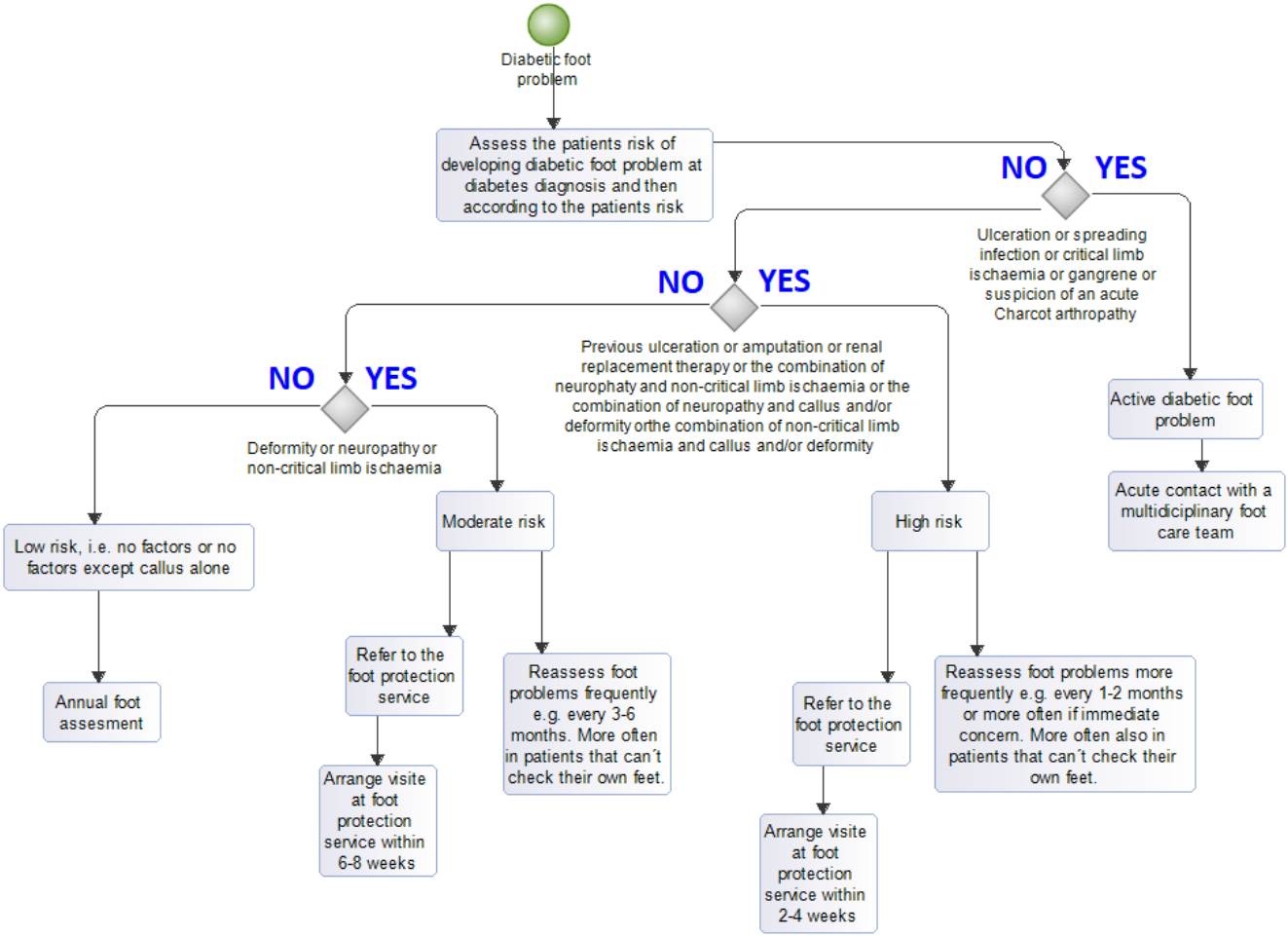

Figure 14: Diabetes - Foot problems

Local deviations: Lanarkshire: All wounds - local refer to community podiatry – assessment for shared care, pressure relief and specialist dressings/debridement
Wound assessment for infection – local – as per local policy, systemic – arrange admission
Ischaemia – refer for vascular opinion. OSAKIDETZA: Does not have the option sending patients to a multidisciplinary team. AMCA: Add diabetes nurse as an alternative to foot protection service.

1.5.4.4 Care organisation for diabetic foot problems

Reprinted from C3-Cloud D7.1

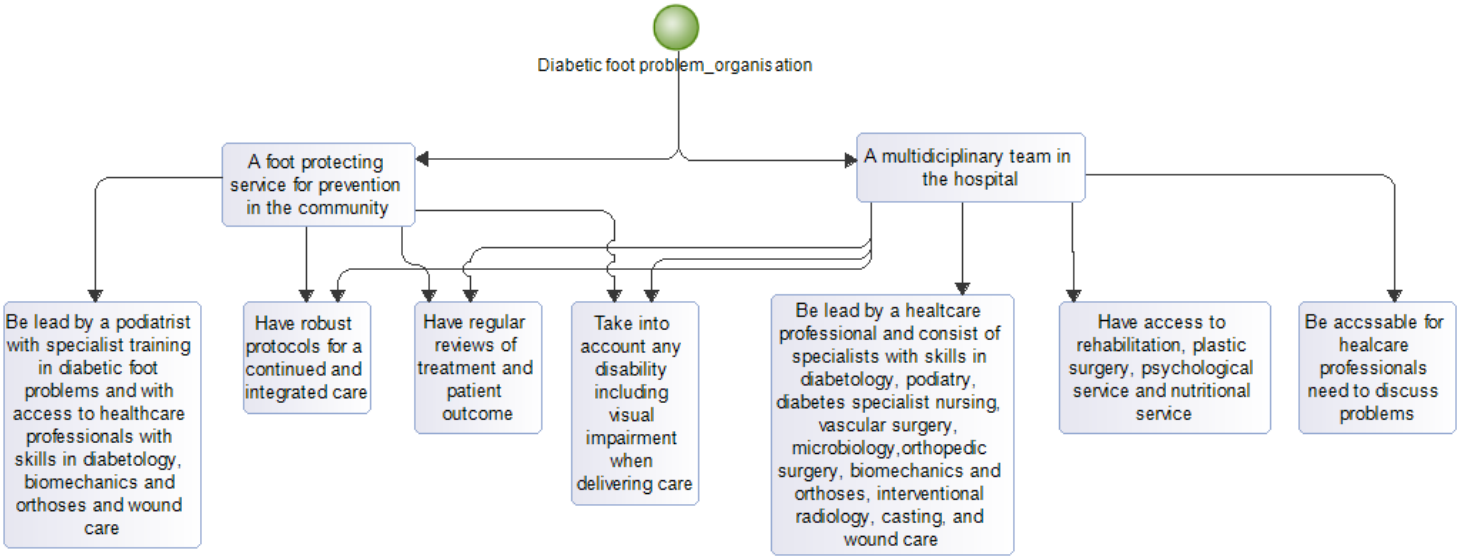

Figure 15: Diabetes - Organisation for foot problems

Local deviations OSAKIDETZA: Care is guaranteed but not through a multidisciplinary team or foot protection service. “Refer to foot protection service” - in the Basque Country, this should be “or to specialized care”.

1.5.4.5 Erectile dysfunction

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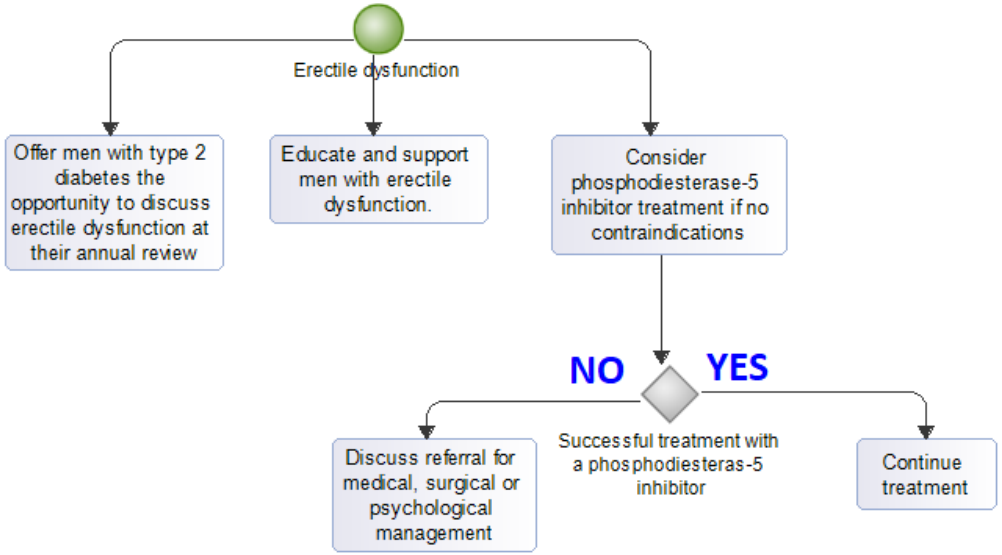

Figure 16: Diabetes - Erectile dysfunction

1.5.4.6 Eye disease

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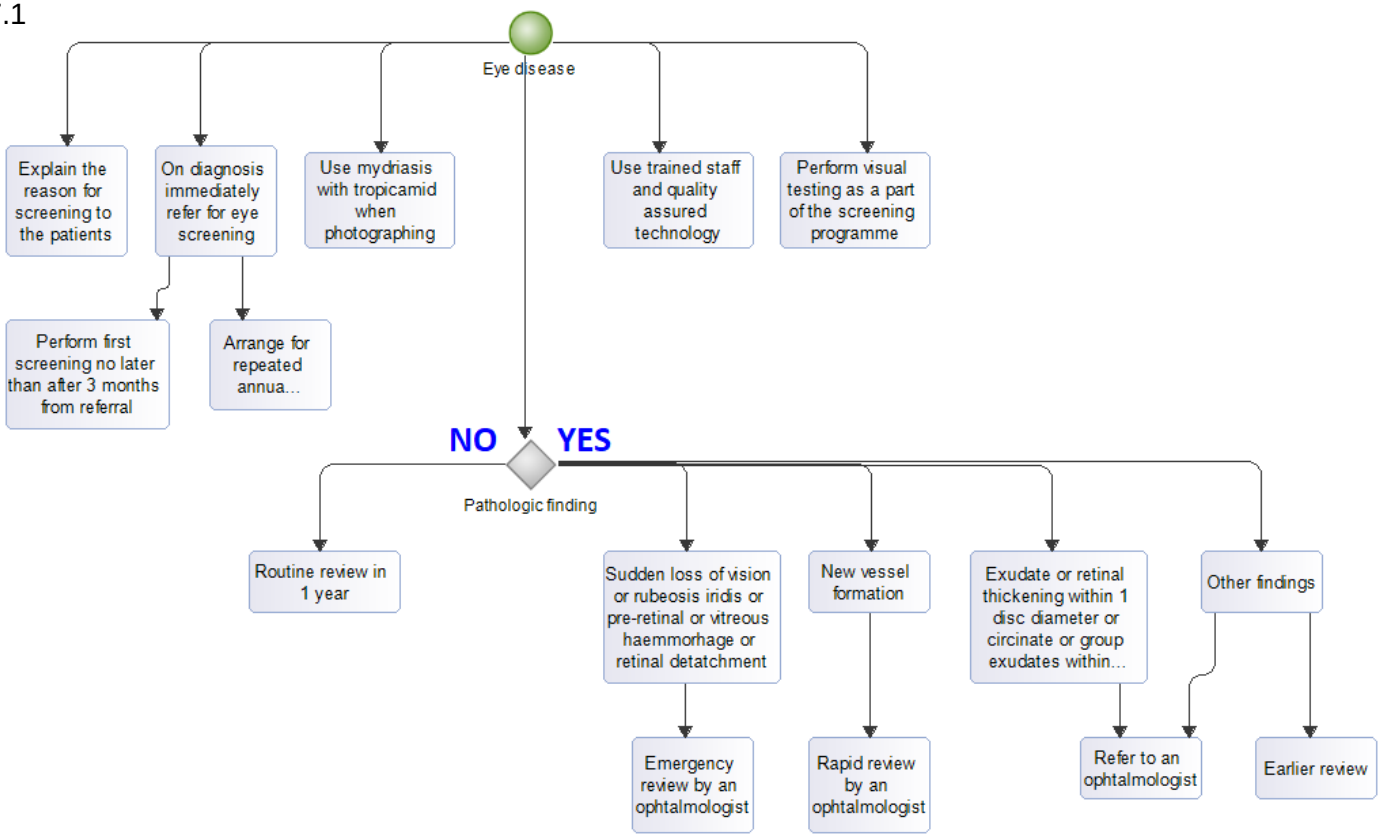

Figure 17: Diabetes - Eye diseases

Local deviations: RJH: All photos are taken and controlled at specialist care and there is thus no need for referral based on photo findings as the patient is taken care of automatically. Other options with longer time intervals than annual check-ups are used based on a normal eye photo in an older patient. Lanarkshire: Have automated screening through coding on IT platforms. OSAKIDETZA: There is a screening program with retinography and with the following screening frequency: every 3 years for type 2 diabetic patients without retinopathy, annual in which they suffer mild non-proliferative retinopathy with poor metabolic and biennial control in those with good control metabolic.

1.5.4.7 Gastroparesis

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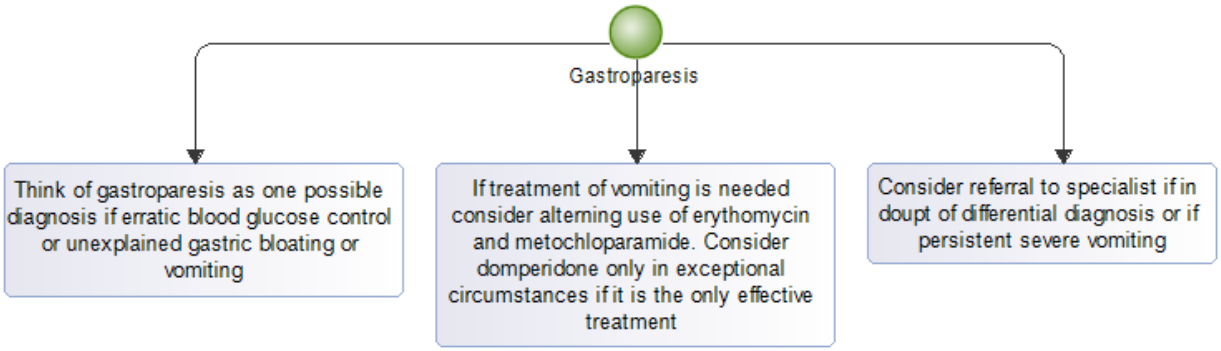

Figure 18: Diabetes – Gastroparesis

Local deviations: AMCA: After diagnosis of gastroparesis, we would add dietary consultation before necessarily prescribing. If treatment of vomiting is needed, consider use of metoclopramide. Second option would be domperidone. Erythromycin is the last option.

1.5.4.8 HbA1c measurements and targets

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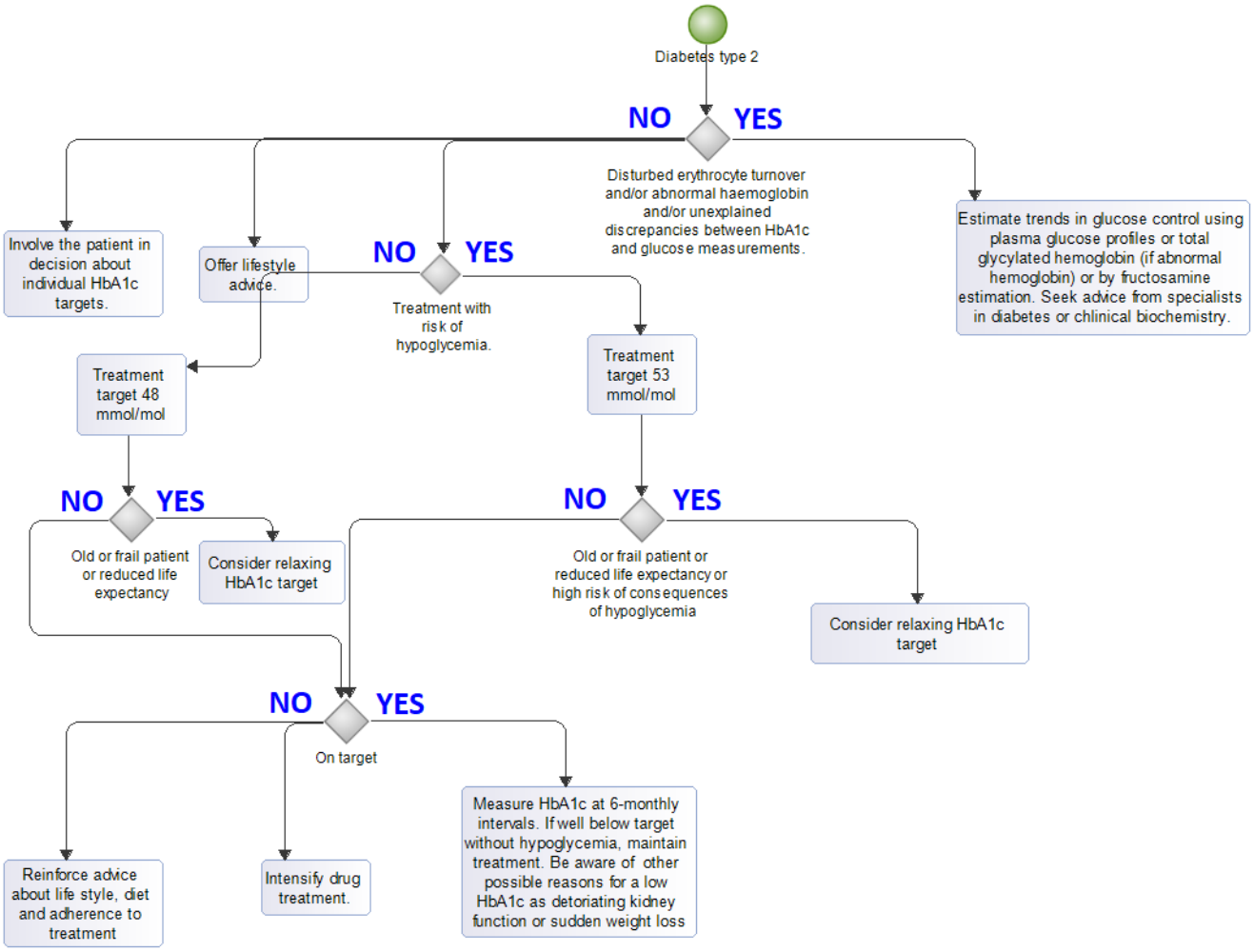


Figure 19: Diabetes - HbA1c measurements and targets

Abbreviation: HbA1c= Glycated haemoglobin A1c

Local deviations: AMCA: Present HbA1c as %, not only mmol/mol. OSAKIDETZA: The guideline of the Ministry is from 2013. 53 mmol/mol (HbA1c 7%) is a general objective if there is no risk of hypoglycemia. In young patients, and in recently diagnosed patients without comorbidity 48 mmol/mol (6.5%) can be considered as a goal. RJH: A treatment goal of <48 mmol/mol should be considered in younger patients and in newly diagnosed patients without co-morbidities.

1.5.4.9 Insulin based treatment

Reprinted from C3-Cloud D7.1

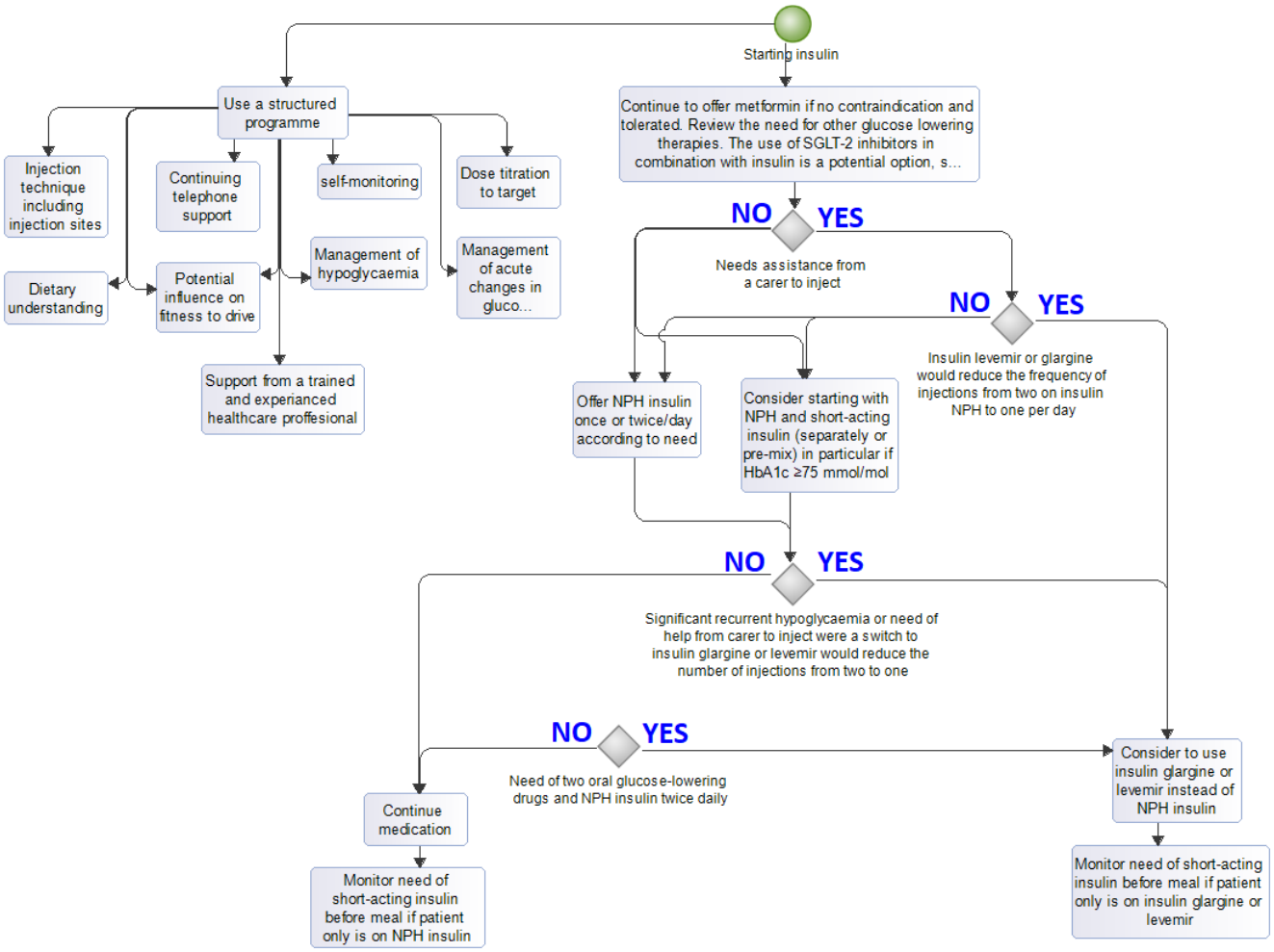


Figure 20: Diabetes - Insulin based treatment

Abbreviations: NPH= Neutral Protamine Hagedorn, SGLT-2=sodium-glucose cotransporter 2, NICE= National Institute for Health and Care Excellence, HbA1c= Glycated haemoglobin A1c

Local deviation: AMCA: Are not administrating NPH, only Insulin.

1.5.4.10 Insulin delivery

Reprinted from C3-Cloud D7.1

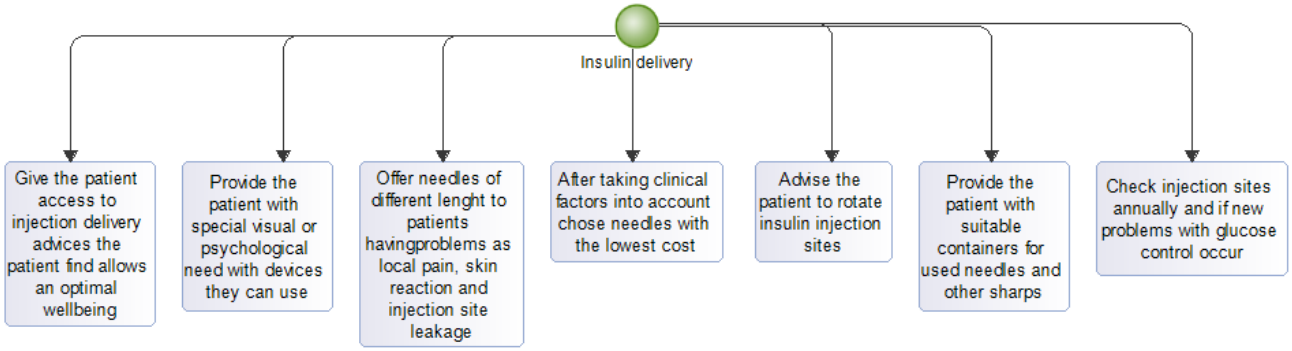


Figure 21: Diabetes - insulin delivery

Local deviation: Lanarkshire: Involve local services if patient is unable to self-care with insulin delivery.

1.5.4.11 Painful diabetic neuropathy

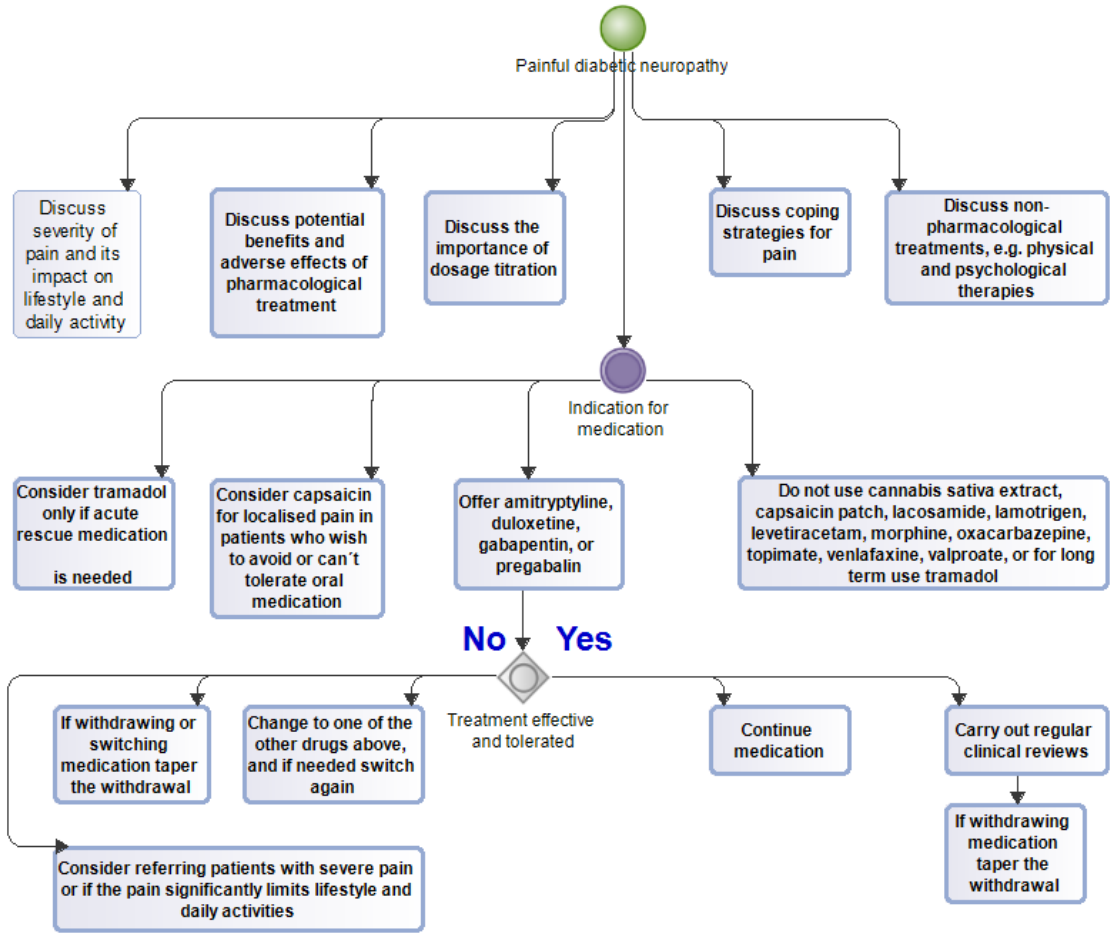


Figure 22: Diabetes - Painful neuropathy

Local deviations: Lanarkshire: Step one pharmacological treatment: Amitriptyline, Imipramine, Duloxetine, or Gabapentin. Step two: Pregabalin, or phenytoin. Step three: (and/or) Tramadol, Morphine, Oxycodone and/or topical lidocaine.

1.5.4.12 Patient education

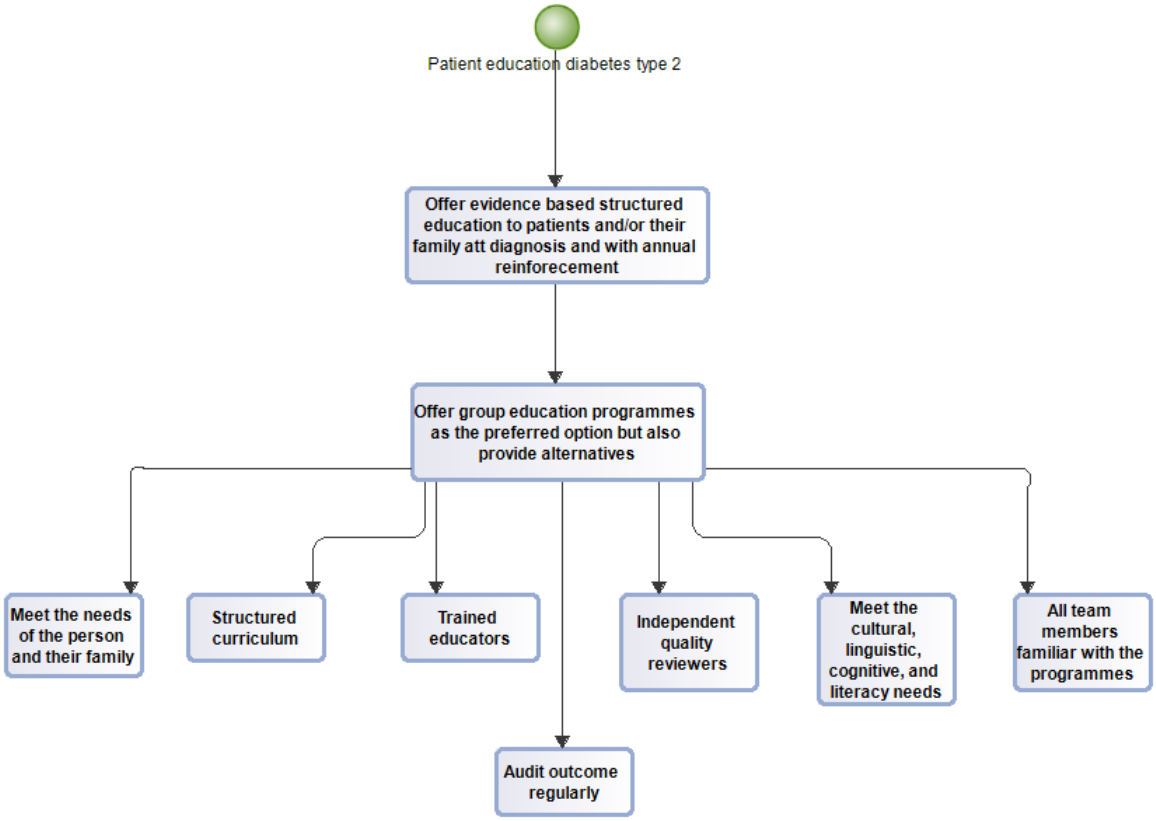


Figure 23: Diabetes - Patient education

1.5.4.13 Self-monitoring

Reprinted from C3-Cloud D7.1

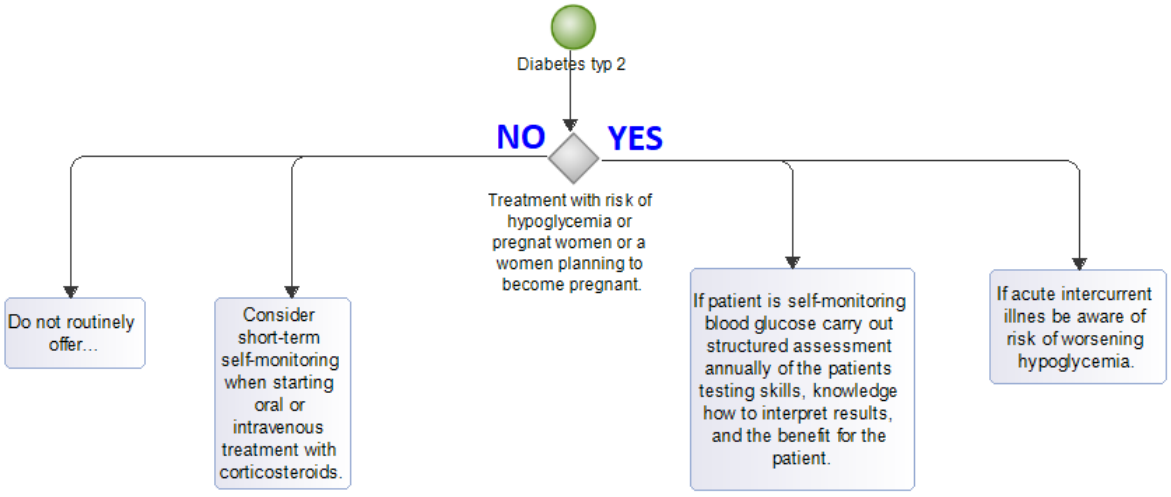


Figure 24: Diabetes - Patient education

1.5.5 Flowcharts for lipid lowering

Flowcharts for diagnosis and treatment with lipid lowering drugs, in familial hypercholesterolemia or in atherosclerotic macrovascular disease, are not included. The flowchart is based on NICE guidelines on cardiovascular disease NG181 [9] from 2014 and partially updated in 2016.

1.5.5.1 Treatment

Reprinted from C3-Cloud D7.1

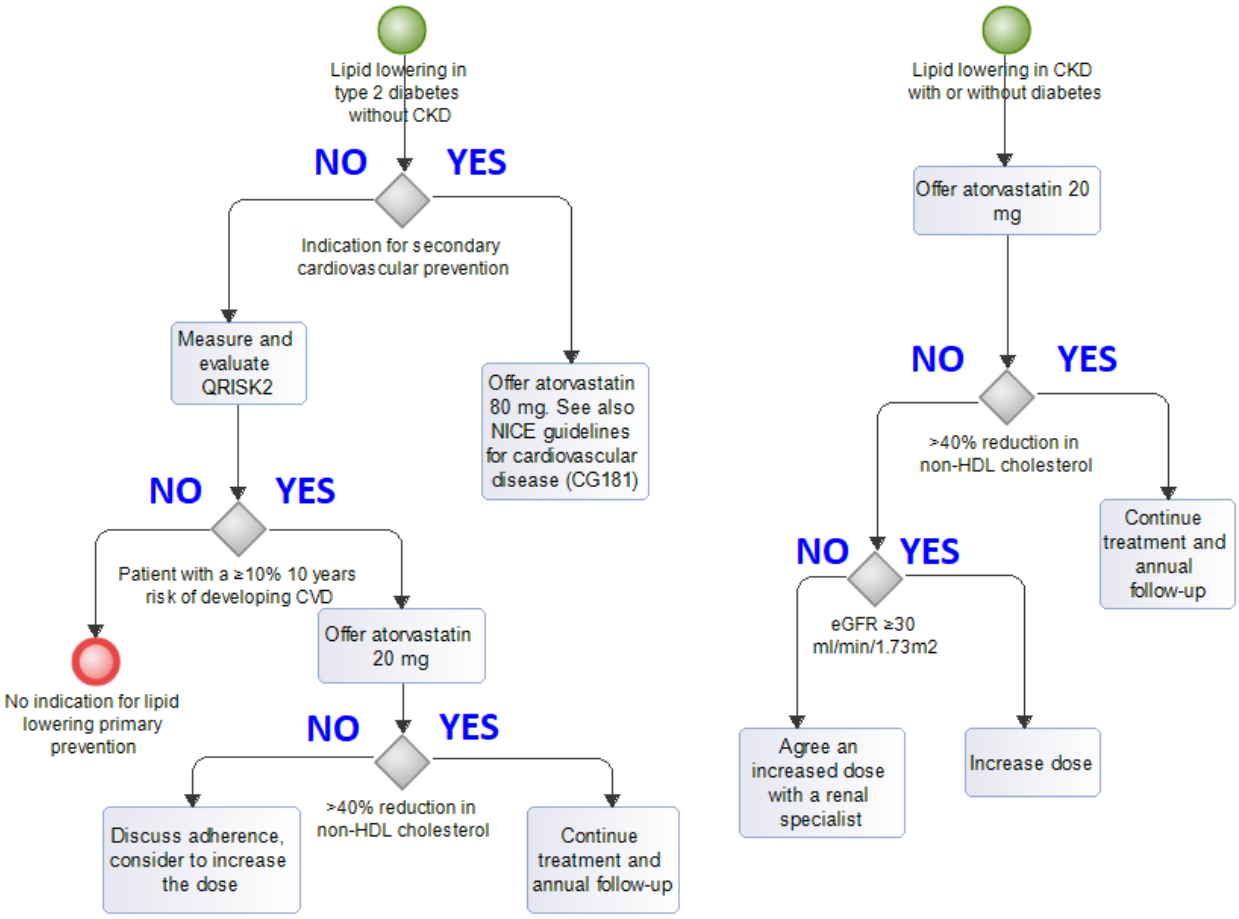


Figure 25: Lipid lowering - Treatment in diabetes and CKD

Abbreviations: CKD=chronic kidney disease, CG= clinical guidelines, CVD= cardiovascular disease, eGFR estimated glomerular filtration rate, HDL= high-density lipoprotein, NICE National Institute for Health and Care Excellence, QRISK2= cardiovascular disease risk calculator 2.

The cardiovascular risk score QRISK2 has been developed by the English National Health Service. Background and validation reports can be found on the QRISK website [10].

Local deviation: AMCA, RJH, Lanarkshire: Instead of QRISK write measure risk with locally recommended risk predictor algorithms. USTRATH: Offer as primary prevention simvastatin 40 mg or atorvastatin 10 mg to all patients with T2DM >40 years old irrespective of cholesterol levels. RJH: At a CVD risk >8% is statin treatment recommended. RJH does not use QRISK2. AMCA: uses HEARTSCORE, not QRISK2.

1.5.6 Flowcharts for hypertension

The flowcharts in this section are based on NICE guidelines NG136 [11] for hypertension from 2019.

1.5.6.1 Overview

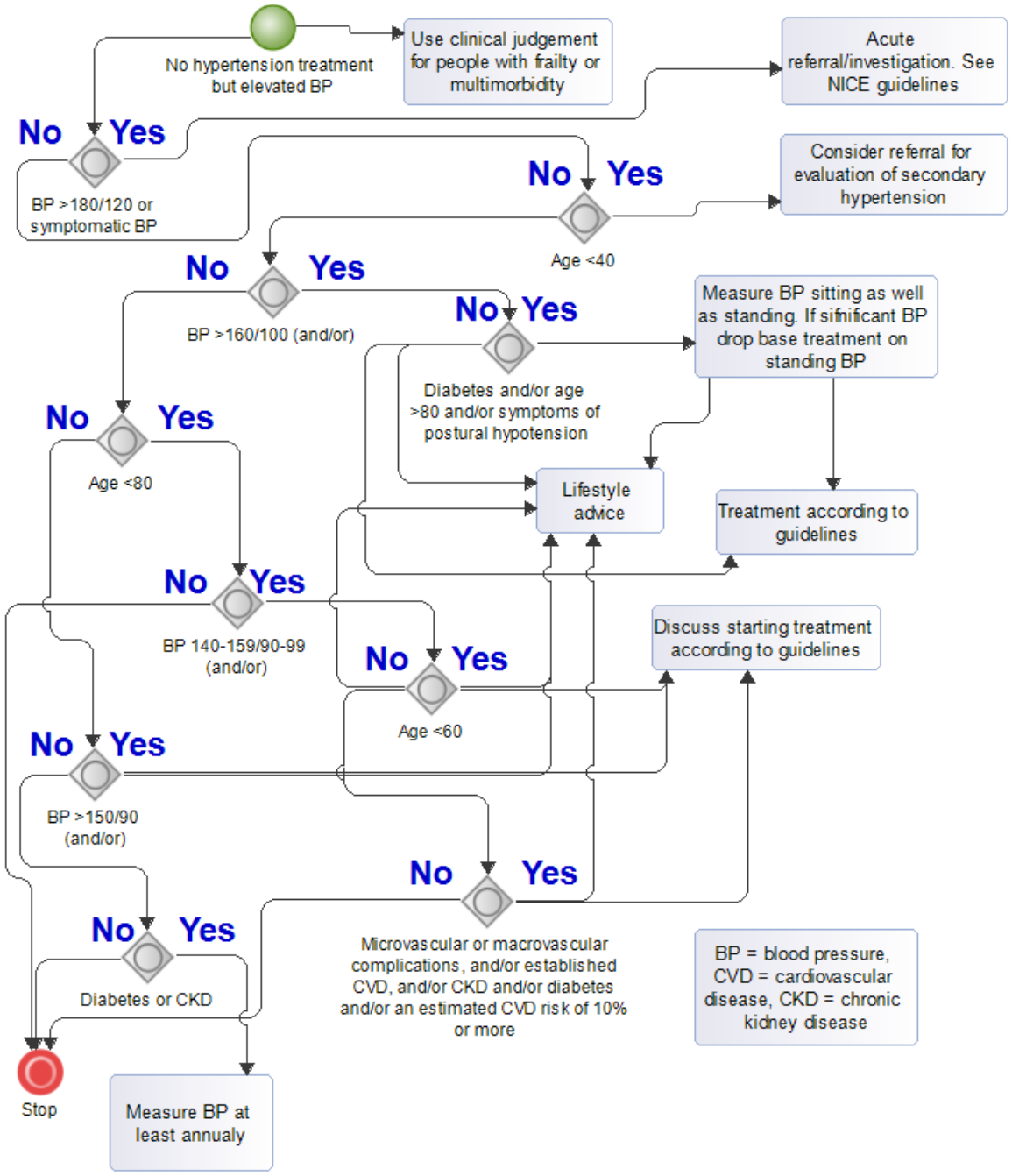


Figure 26: Hypertension - Treatment overview

Local deviation: Lanarkshire: Calculate ASSIGN/QRISK" at diagnosis to determine lipid lowering therapy.

1.5.6.2 Treatment step 1

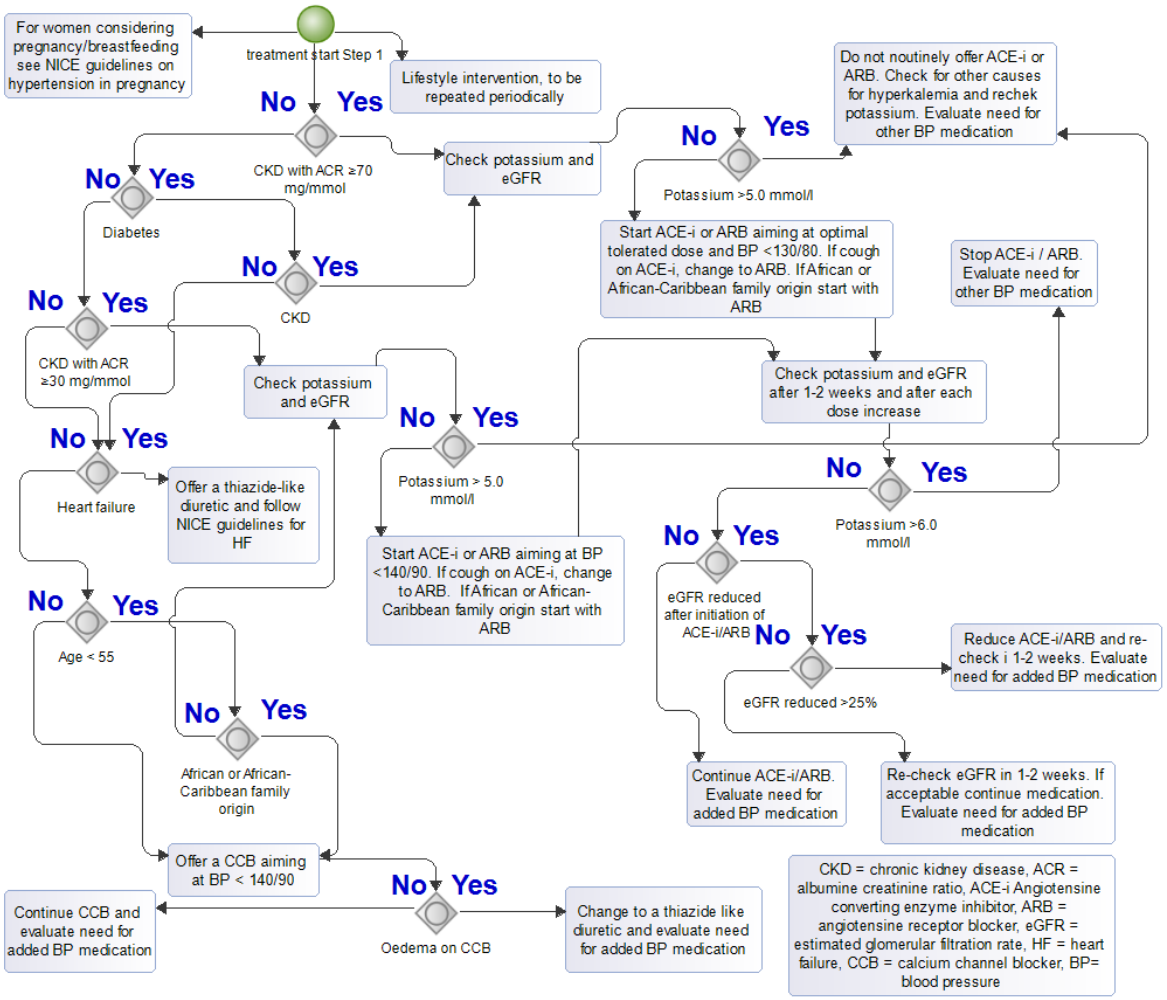


Figure 27: Hypertension - Treatment step 1

Local deviations: AMCA: If treatment with thiazides control potassium two weeks after treatment start. CCB is relevant only for people under age 55. Black African or African Caribbean origin is irrelevant in Israel. OSAKIDETZA and RJH: Thiazides are not recommended for CKD stages 4 and 5. OSAKIDETZA: The target figures are 140/90 in all cases.

1.5.6.3 Treatment step 2-4

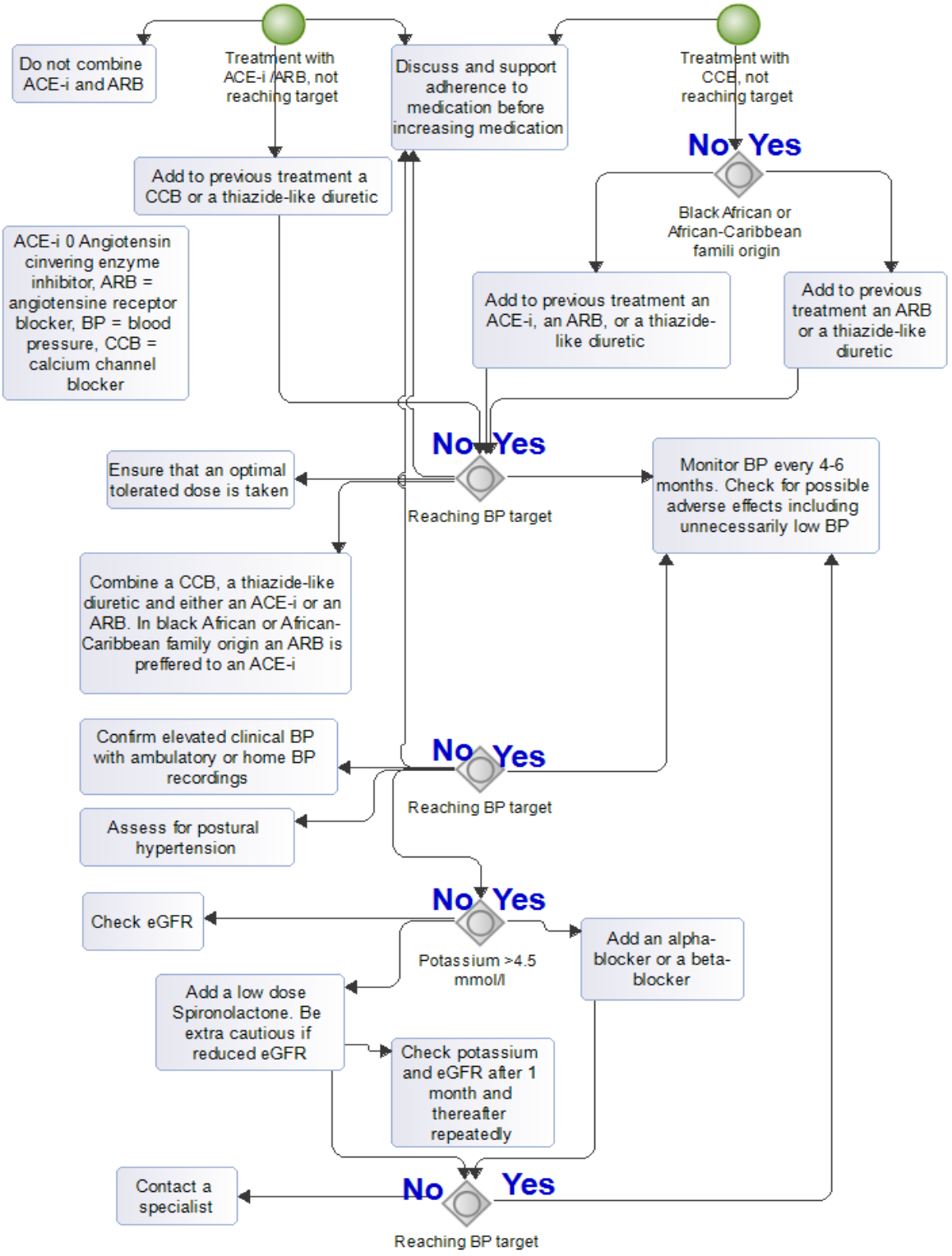


Figure 28: Hypertension - Treatment step 2-4

Local deviations: AMCA: If treatment with thiazides control potassium two weeks after treatment start. CCB is relevant only for people under age 55. Black African or African Caribbean origin is irrelevant in Israel. OSAKIDETZA and RJH: Thiazides are not recommended for CKD stages 4 and 5.

1.5.7 Flowcharts for chronic kidney disease (CKD)

All flowchart under this theme reprinted from C3-Cloud D7.1 and are based on NICE clinical guidelines for CKD CG182 [12] from 2014.

1.5.7.1 Self-management

Reprinted from C3-Cloud D7.1

This flowchart is based on NICE CKD guideline CG182, Chapter 1.4.10-1.4.11 [60, p. 30]

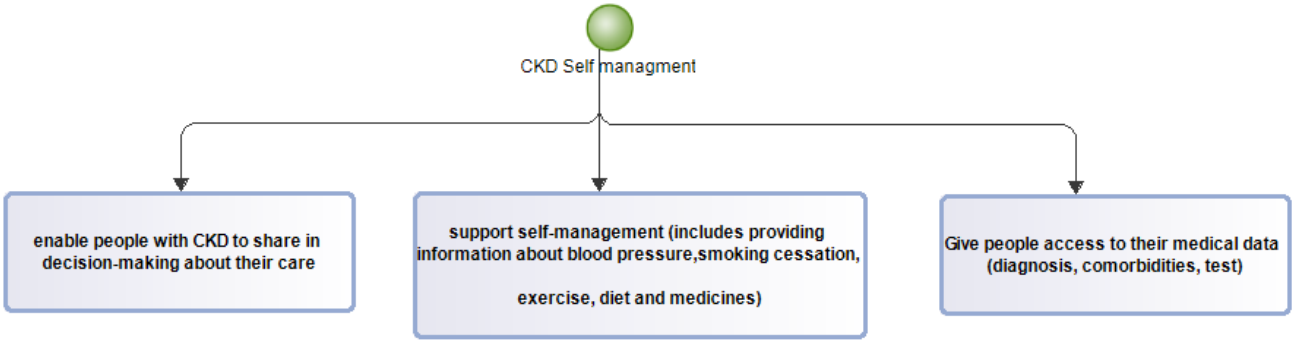


Figure 29: CKD - Self management

Abbreviation: CKD= chronic kidney disease.

1.5.7.2 Lifestyle and dietary advice

Reprinted from C3-Cloud D7.1

This flowchart is based on NICE CKD guideline CG182, Chapter 1.4.6-1.4.9 [60, pp. 29-30]

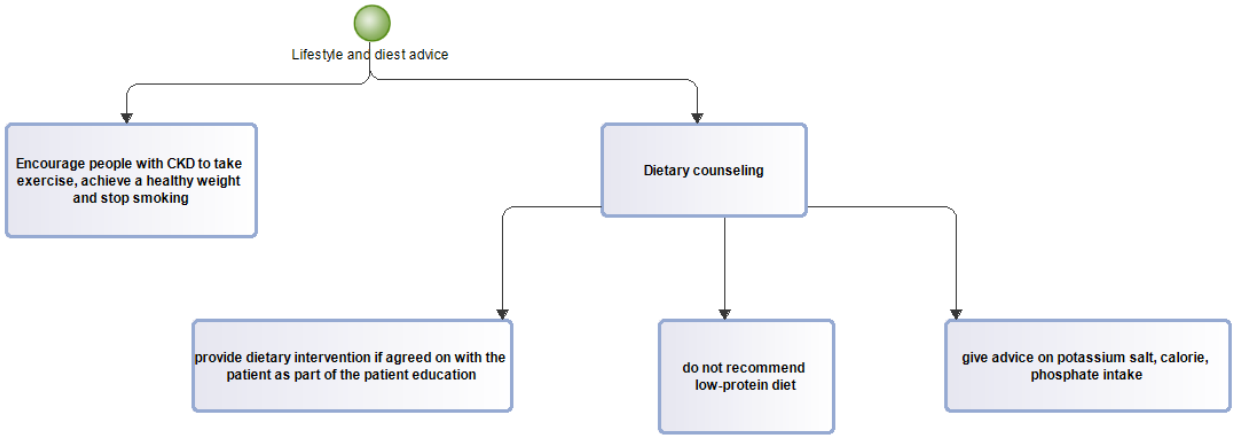


Figure 30: CKD - Dietary and lifestyle advise

Abbreviation: CKD= chronic kidney disease.
Local deviations: OSAKIDETZA and RJH: In stages 4 and 5 without diabetes protein restriction is recommended.

1.5.7.3 Information and education

Reprinted from C3-Cloud D7.1

This flowchart is based on NICE CKD guideline CG182, Chapter 1.4.1-1.4.5 [60, pp. 28-29]

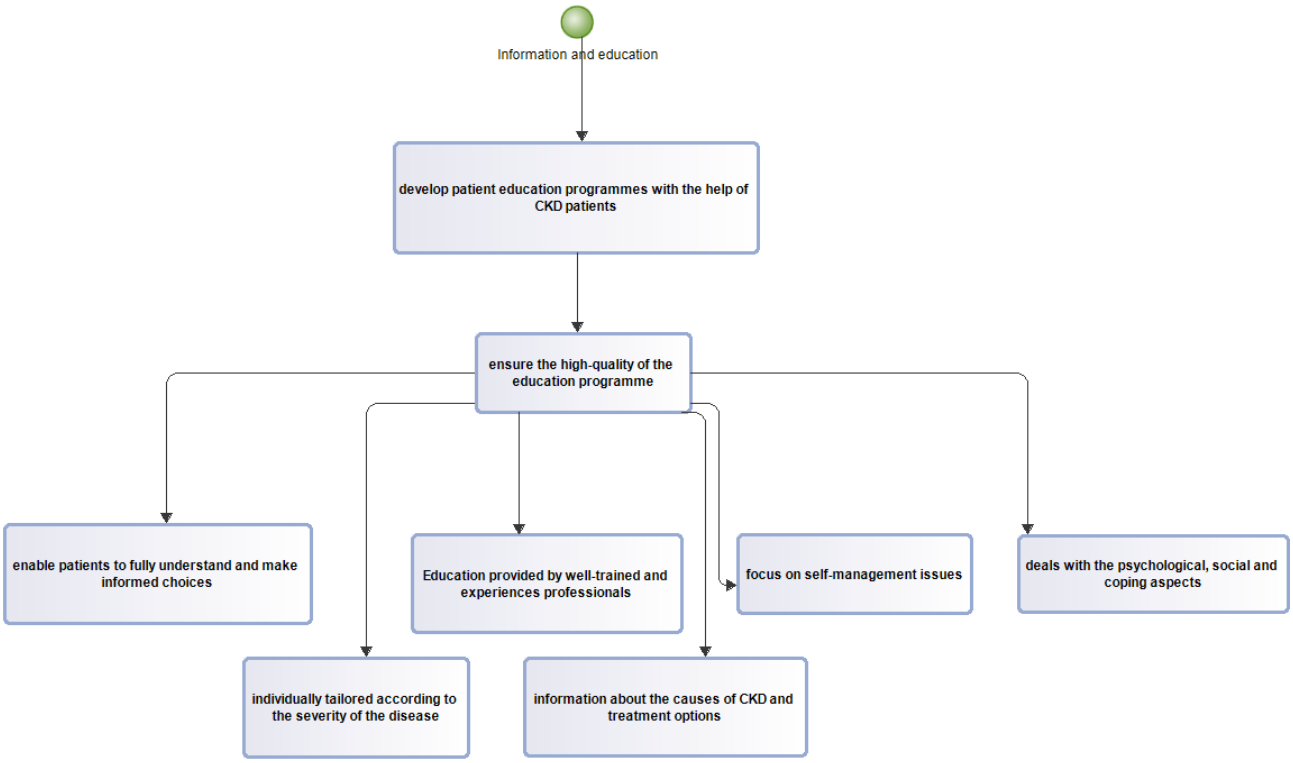


Figure 31: CKD - Patient information and education

Abbreviation: CKD= chronic kidney disease.

1.5.7.4 Referral criteria

Reprinted from C3-Cloud D7.1

This flowchart is based on NICE CKD guideline CG182, Chapter 1.3, Table 2 [60, p.26]. It describes the conditions for the referral. The patient should not be referred if they are not met.

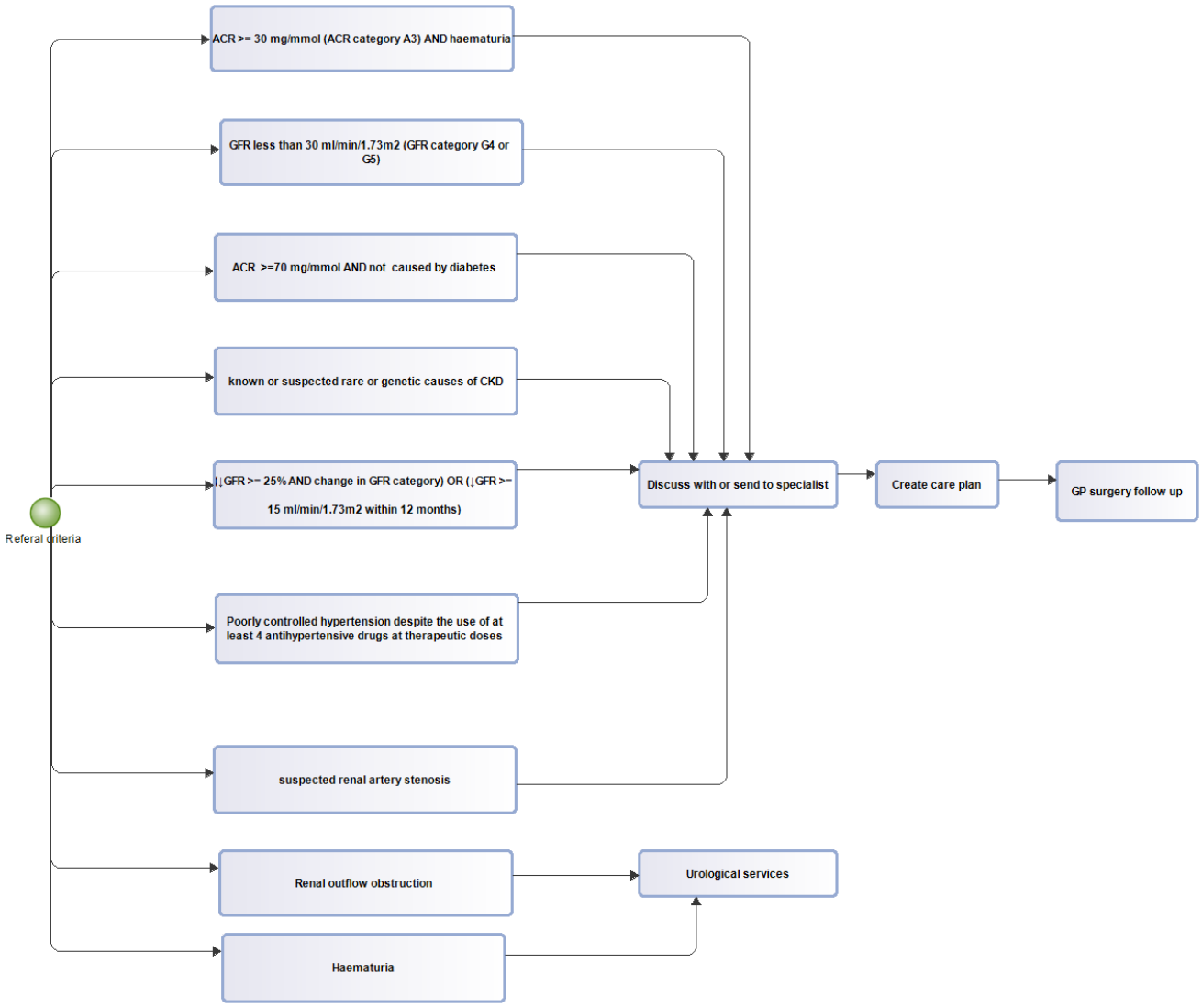


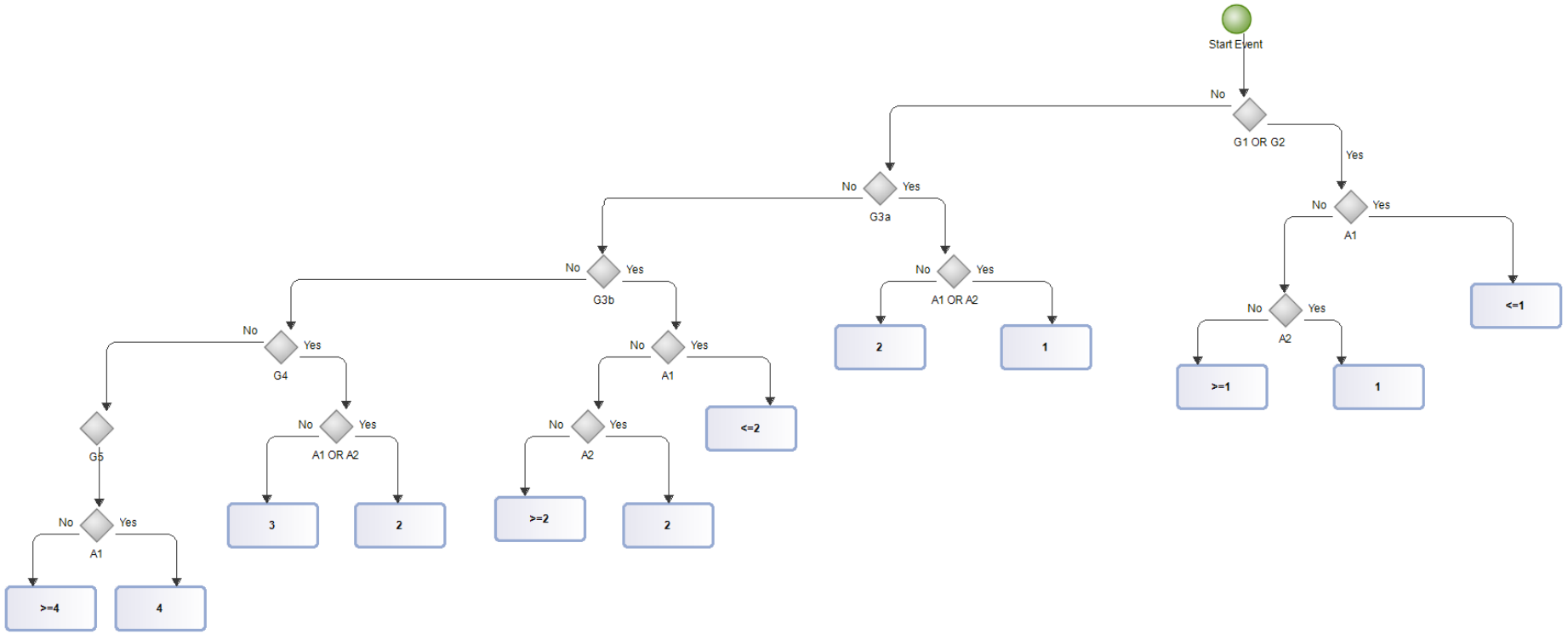
Figure 32: CKD - Referral criteria

Abbreviations: ACR= Albumin creatinine ratio GFR= Glomerular Filtration Rate GP= General Practitioner

1.5.7.5 Frequency of eGFR controls

Reprinted from C3-Cloud D7.1

This flowchart is based on NICE CKD guideline CG182, Chapter 1.3, Table 2 [60, p.26]. It represents the frequency of monitoring of GFR (number times per year, by GFR and ACR category) for people with, or risk of, CKD.



Glomerular filtration rate (GFR) Categories in Chronic Kidney Disease		
GFR Category	GFR (mL/min/1.73m^2)	Description
G1	>=90	Normal or High
G2	60-89	Mildly decreased*
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure
*Relative to young adult level		
Albumin: creatinine ratio (ACR) Categories		
ACR Category	ACR (mg/mmol)	Description
A1	<3	Normal to mildly increased
A2	3-30	Moderately increased
A3	>30	Severely increased

Figure 33: CKD – Annual frequency of eGFR controls

Abbreviations: ACR= albumin creatinine ratio, GFR= glomerular filtration rate.

1.5.7.6 Non-RASA treatment of blood pressure in CKD

Reprinted from C3-Cloud D7.1

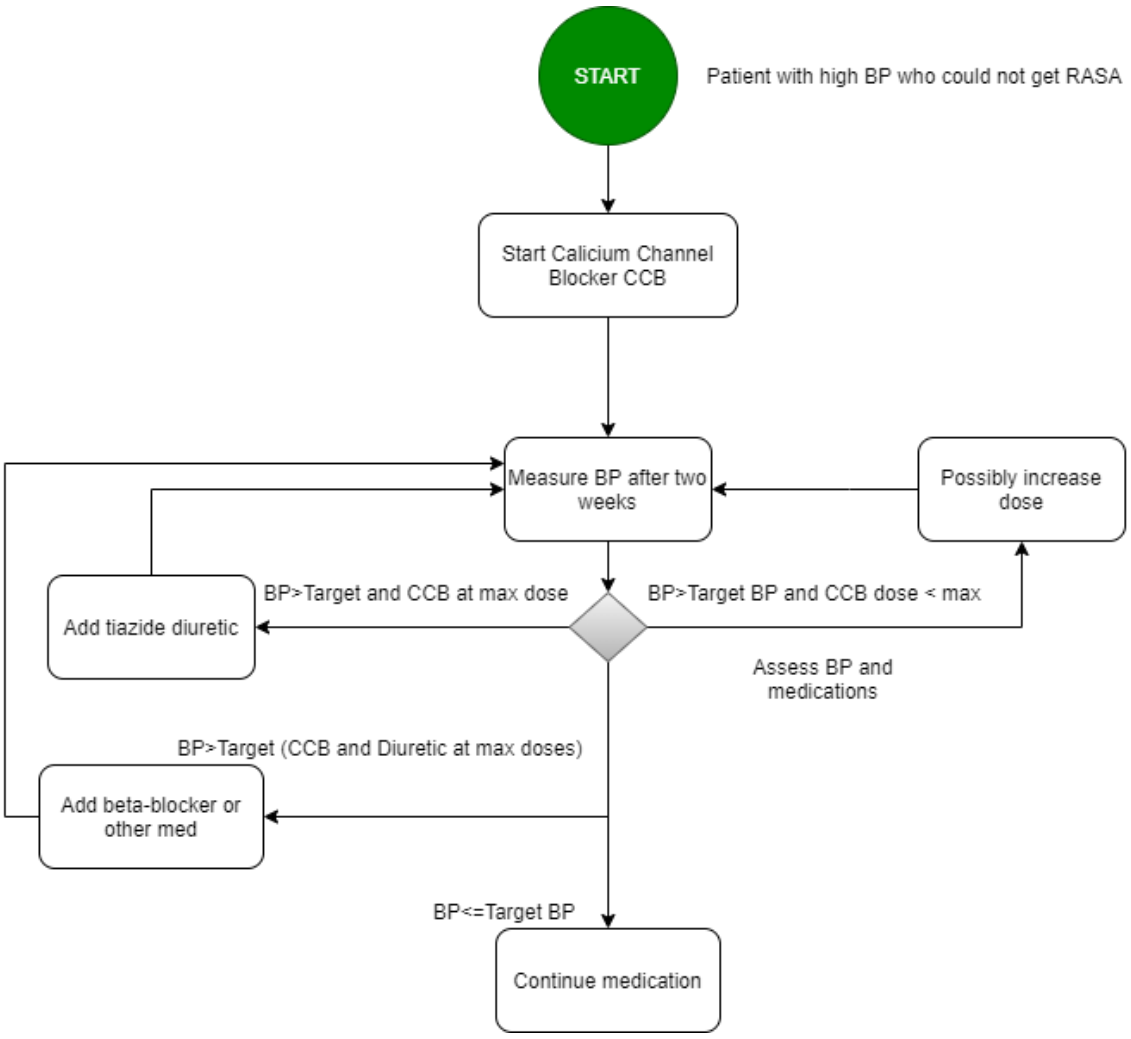


Figure 34: CKD - Non-RSAS treatment of hypertension

Abbreviations: BP= blood pressure, CCB= calcium channel blockers, RASA=renin-angiotensin-aldosterone system antagonists

1.5.7.7 Oral anti-platelet and anti-coagulant treatment

Reprinted from C3-Cloud D7.1

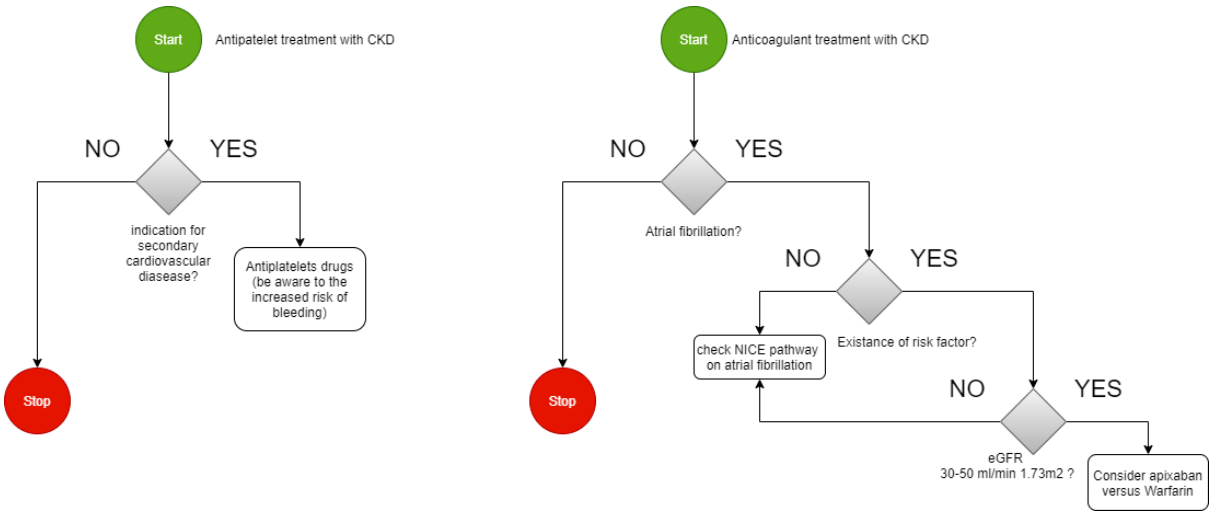


Figure 35: CKD – Anti-platelet and anti-coagulant treatment

Risk factor condition: if one or more risk factors exist:

- Prior stroke and/or transient ischaemic attack (TIA);
- Age 75 years or older;
- Hypertension;
- Diabetes mellitus;
- Symptomatic heart failure.

Abbreviation: eGFR= estimated glomerular filtration.

Local deviations: AMCA and RJH uses CHADSVASC as a risk factor scoring instrument.

1.5.8 Flowcharts for depression

The starting point of this section states that the patient is already diagnosed with depression, so the algorithm does not study the diagnostic criteria of depression. The antidepressant choice is also outside the ADLIFE scope and thus not mapped. The flowcharts in this section are based on the NICE clinical guideline for depression CG90 [13] from 2009.

1.5.8.1 Classification and treatment overview

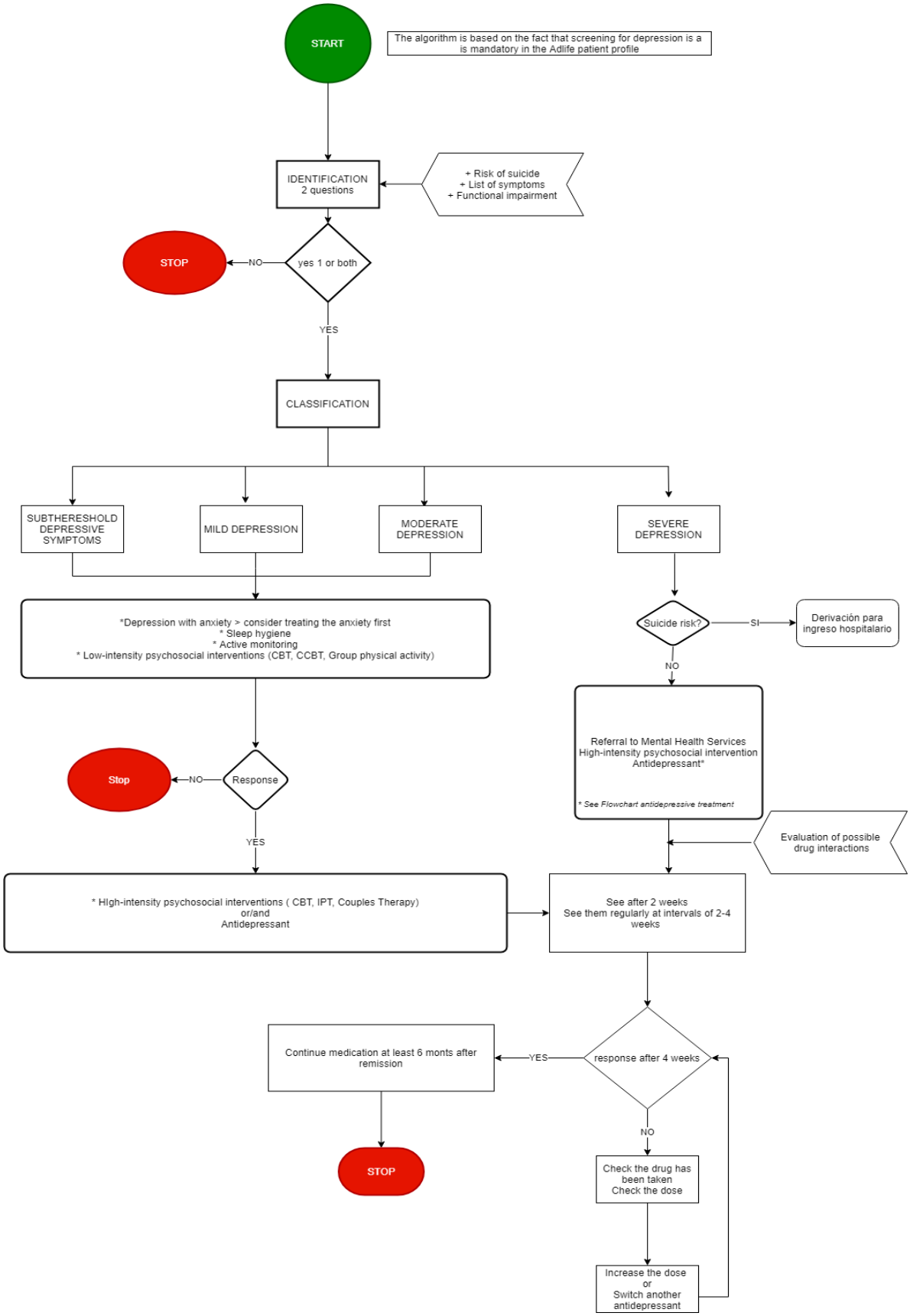


Figure 36: Depression - Classification and treatment overview

Abbreviations: CBT= cognitive behavioural therapy, CCBT= computerised cognitive behavioural therapy, IPT= interpersonal psychotherapy

Local deviations: RJH: Swedish guidelines also mention physical activity as a part of the treatment in mild to moderate depression. Lanarkshire: also refers to physical activity in recommendations.

1.5.8.2 Antidepressant treatment

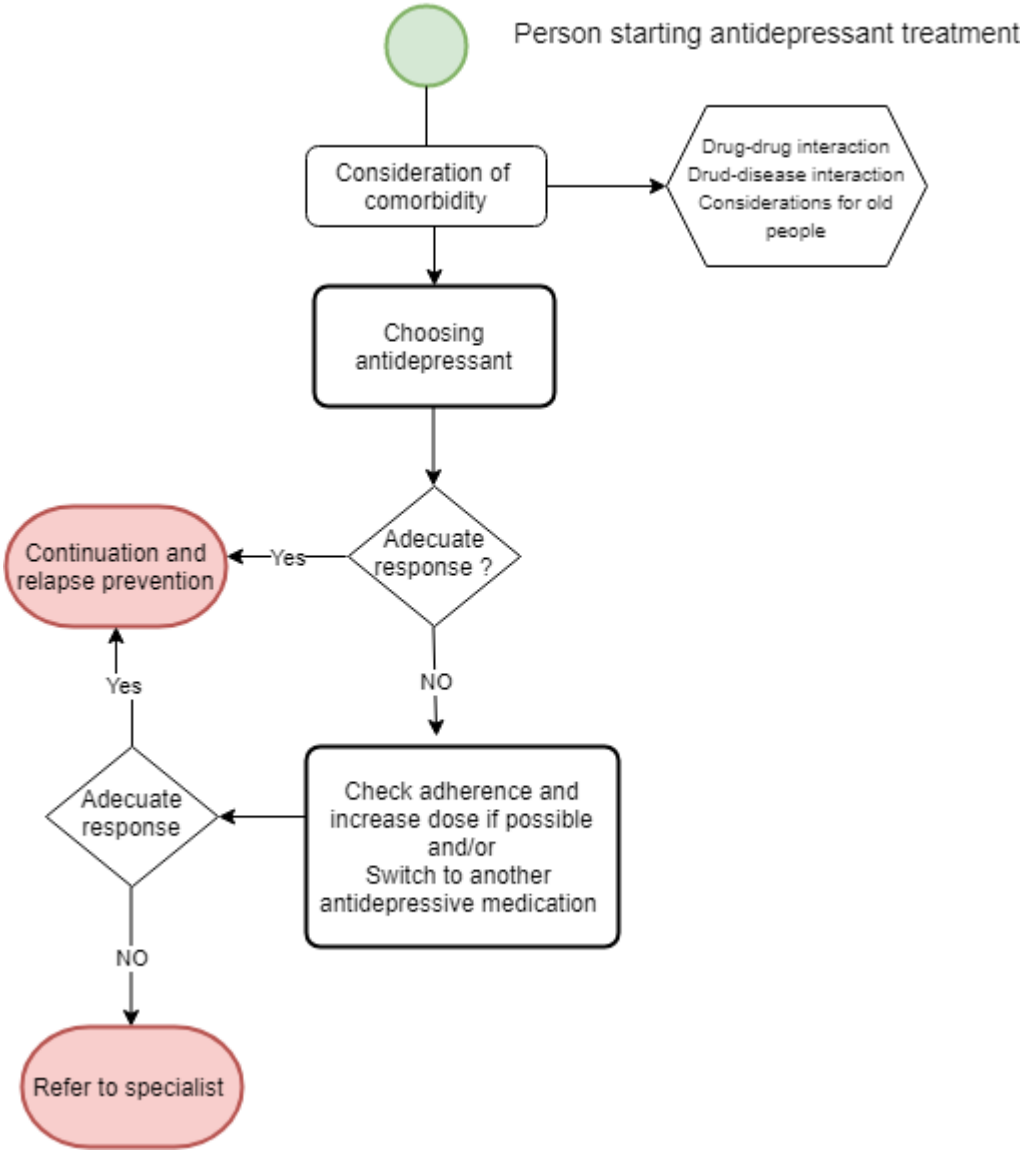


Figure 37: Depression - Antidepressant treatment

1.5.9 Flowchart mild cognitive disorder MCI)

These flowcharts are partially based on NICE guidelines on dementia NG97 [14] from 2018, in combination with input from clinical expertise. **Figure 38** focuses on behavioural changes in MCI, while **Figure 39** gives a care overview.

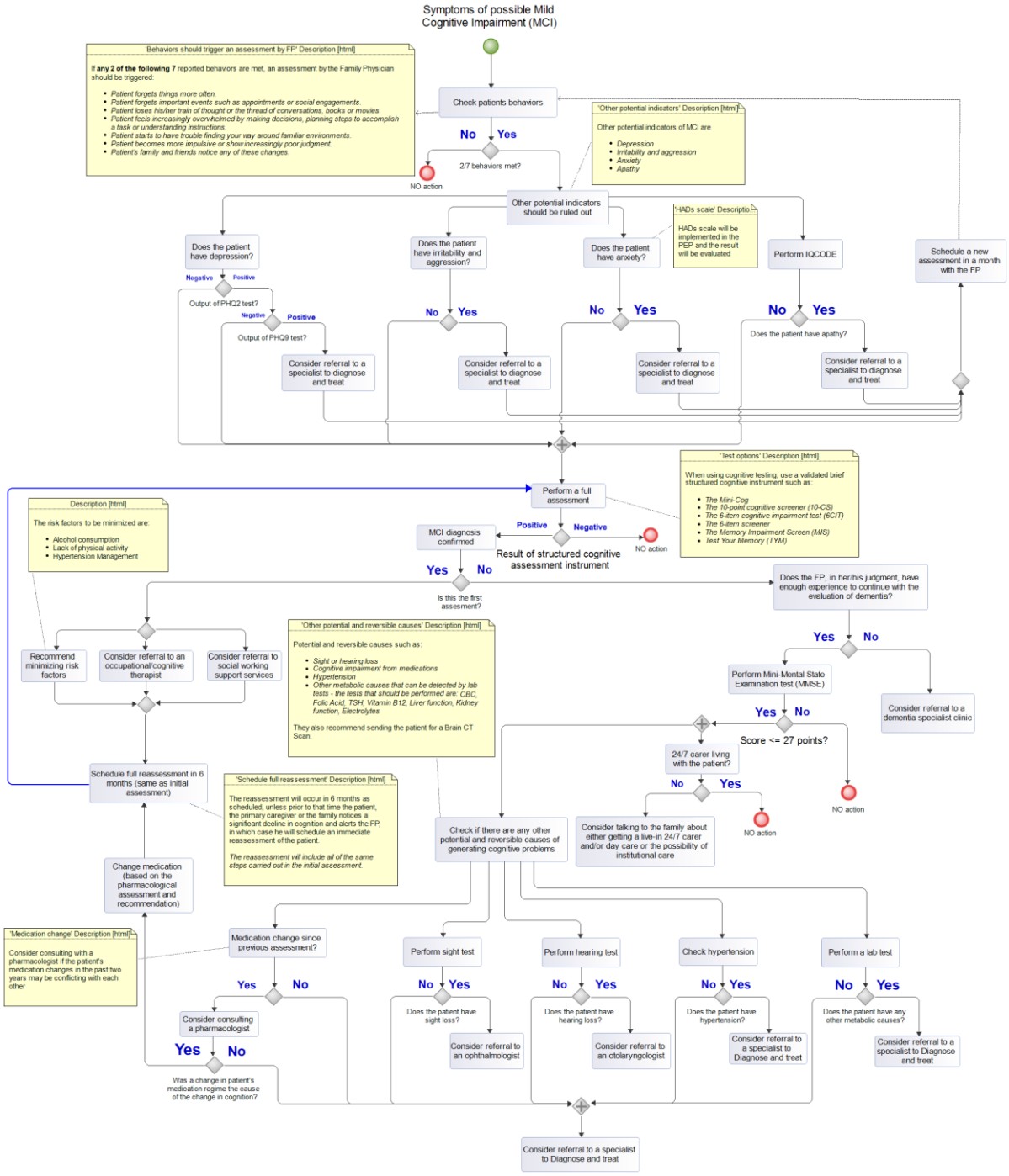


Figure 38: Mild cognitive impairment (MCI) – Behaviour

Abbreviations: HAD= hospital anxiety and depression (scale), IQCCE= Informant questionnaire on cognitive decline in the elderly, mini-Cog= mini cognition
Local deviations: RJH These patients are mostly taken care of in primary care, i.e., referral not common. IQCODE not commonly used. OSAKIDETZA The reported behaviours triggering an assessment requires an input from someone other than the patient to support the objectivity of the analysis. It can be the husband, the son, the boss, the GP We call it the Informant test. Test for full assessment is Mini mental state examination test (MMSE), no other. To evaluate other potential and reversible causes, the Brain CT scan is not required by the GP. This test is usually requested by neurologists.

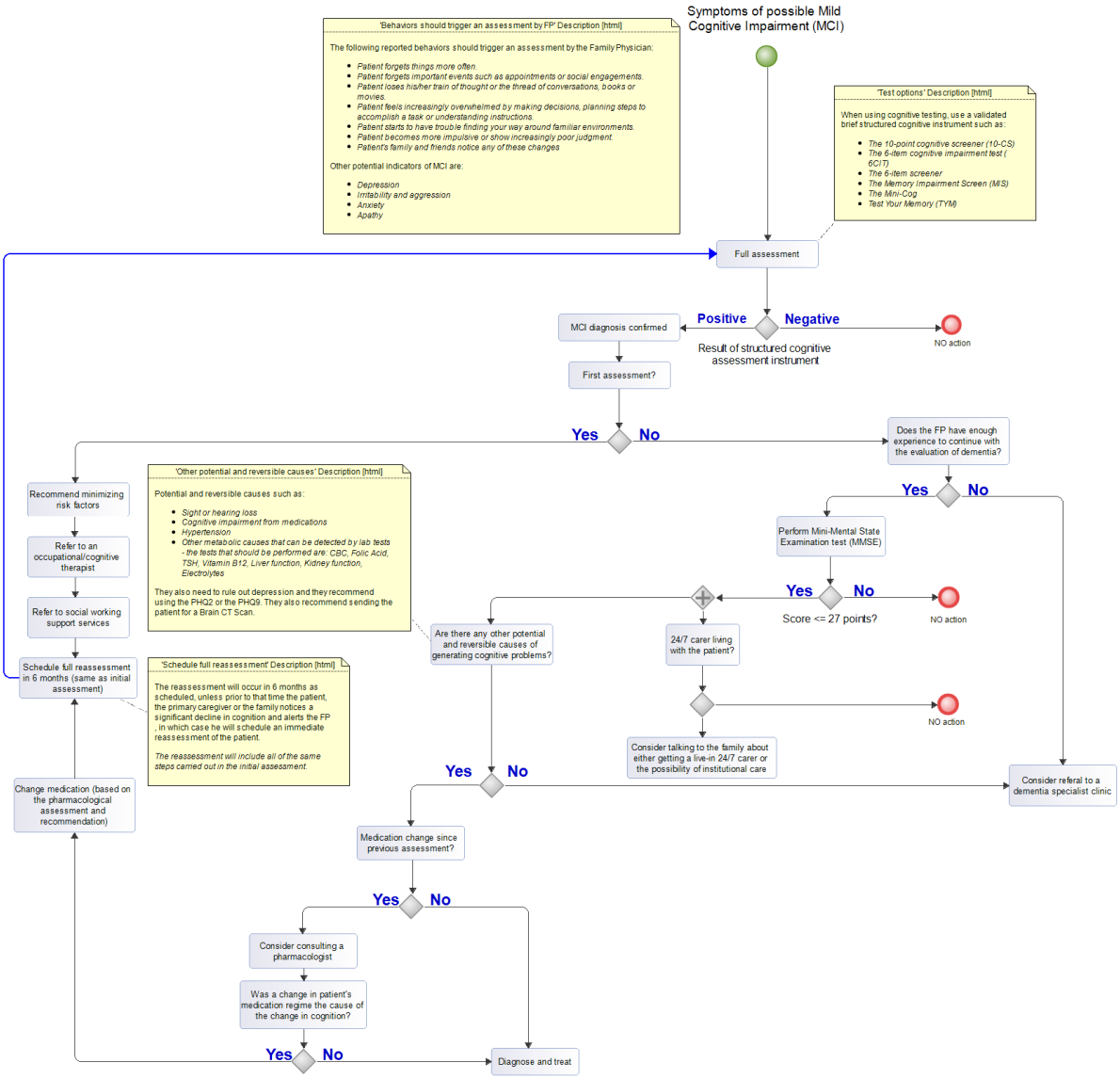


Figure 39 Mild cognitive impairment (MCI) – overview

Abbreviations: CBC= complete blood count, FP= family physician, MCI= mild cognitive impairment, TSH= thyroid stimulating hormone.
Local deviations: Similar as for figure 38.

1.5.10 Flowchart for possible stroke symptoms

The flowchart is based on NICE guidelines on stroke NG128 [15] from 2019.

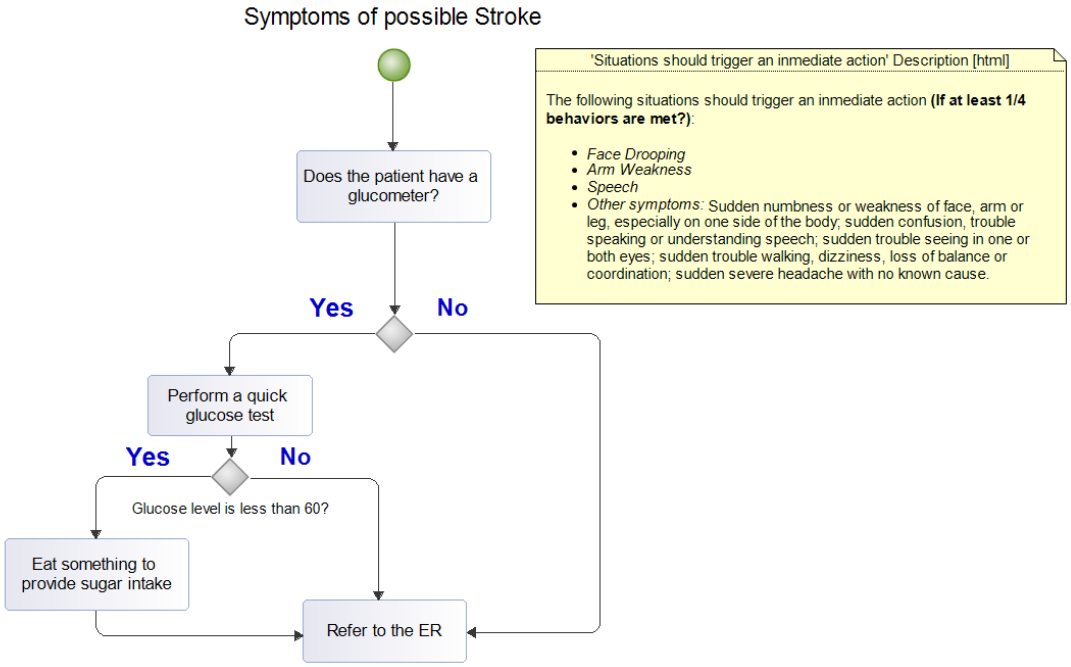


Figure 40: Possible stroke - Symptoms

Abbreviation: ER= Emergency room

1.5.11 Flowcharts for chronic hepatopathy

The flowcharts are based on NICE guidelines for Non-alcoholic fatty liver disease, NG49 [16] from 2016 and NICE guideline for cirrhosis in ages over 16, NG50 [17] from 2016.

1.5.11.1 Non-alcoholic fatty liver disease (NAFLD)

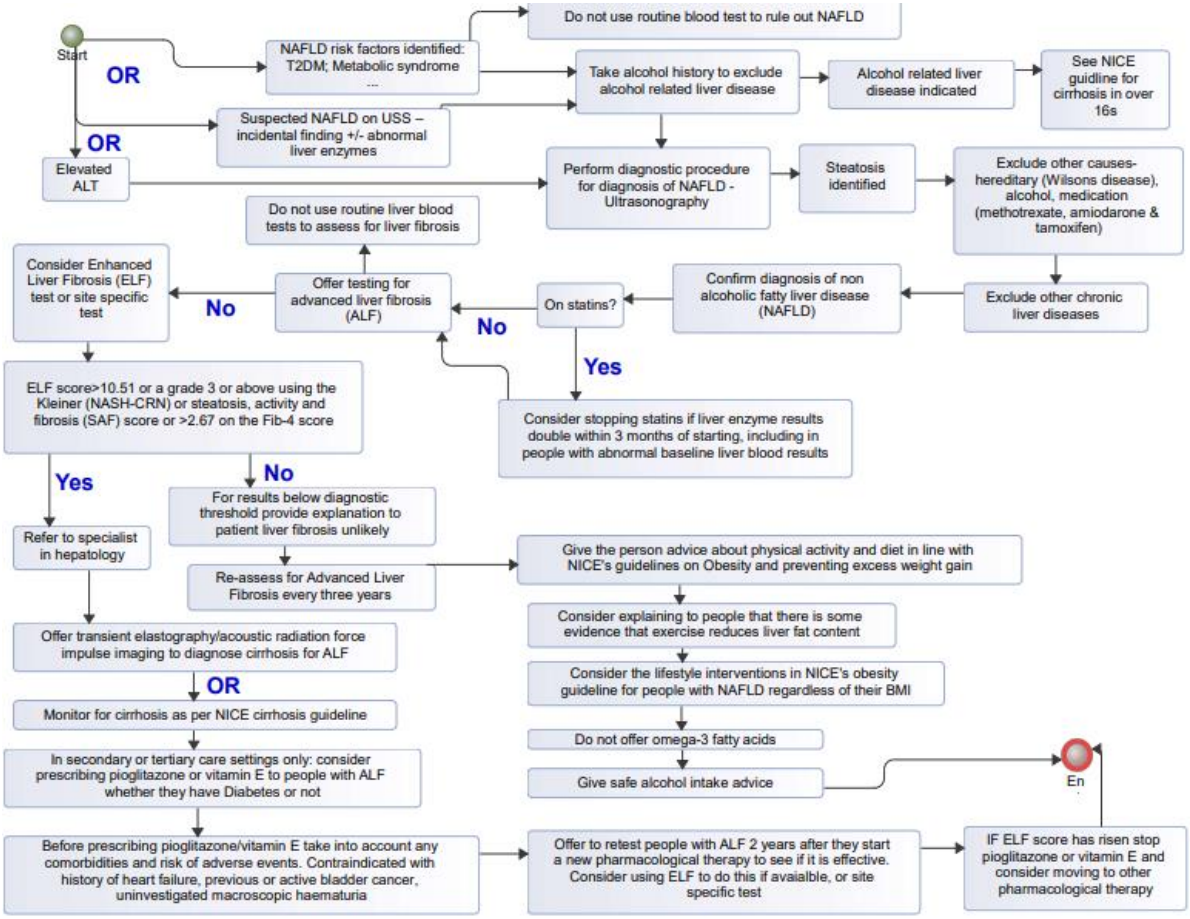


Figure 41: Non-alcoholic fatty liver disease (NAFLD) - Overview

Abbreviations: ALF= advanced liver fibrosis, BMI= body mass index, ELF= enhanced liver fibrosis, Fib= fibrosis, NAFLD= Non-alcoholic fatty liver disease, NASH-CRN= non-alcoholic steatohepatitis- clinical research network, NICE= National Institute for Health and Care Excellence, SAF = steatosis, activity, fibrosis, T2DM= type 2 diabetes mellitus

1.5.11.2 Cirrhosis in ages over 16

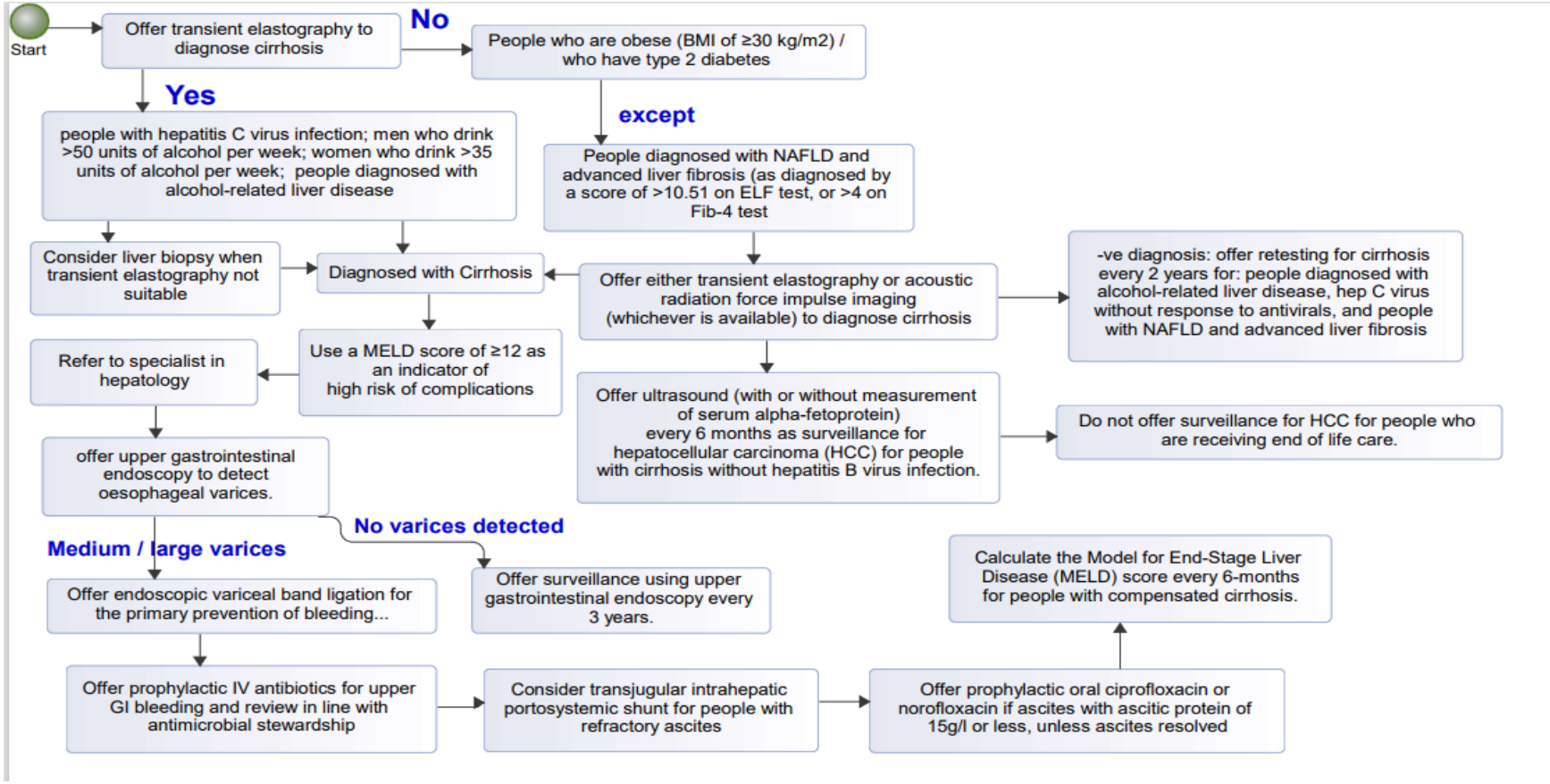


Figure 42 Cirrhosis

Abbreviations: BMI= body mass index, ELF= enhanced liver fibrosis, Fib= fibrosis, GI= Gastrointestinal NAFLD= Non-alcoholic fatty liver disease, MELD= Model for end stage liver disease, HCC= Hepatocellular carcinoma

Local deviations: RJH Fib-4 or ELF tests not in use. Lanarkshire: ELF testing not in use. AMCA Add beta blockers to the treatment for patients with medium/large varices.

1.5.12 Flowcharts for terminal care

These flowcharts are based on NICE guidelines; Service delivery at end of life, NG142 [18] and NICE guidelines; Care of dying, NG31 [19] from 2019 and 2015 respectively.

1.5.12.1 Recognition and initial steps

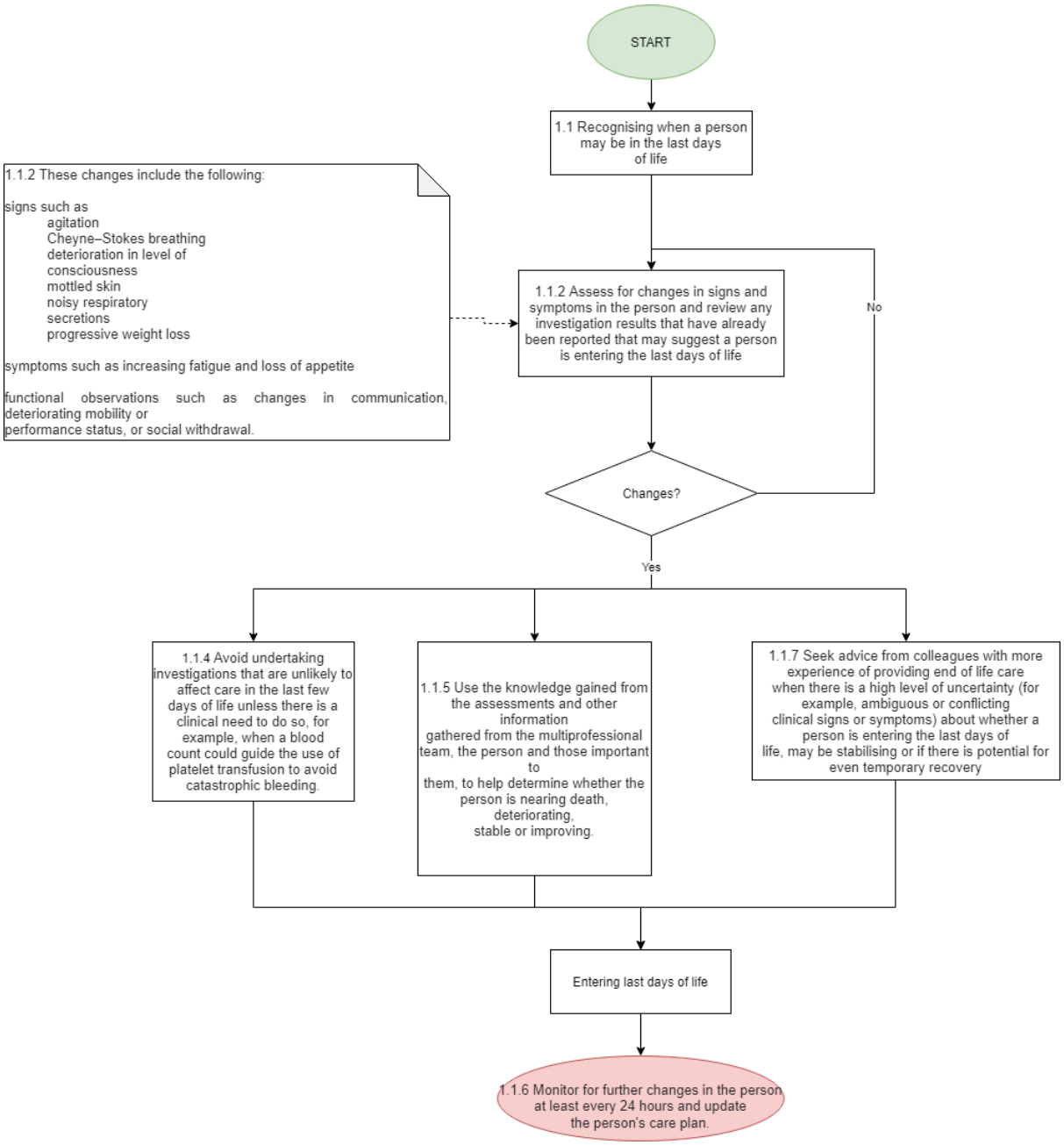


Figure 43: Terminal care - Recognition and initial steps

1.5.12.2 Hydration

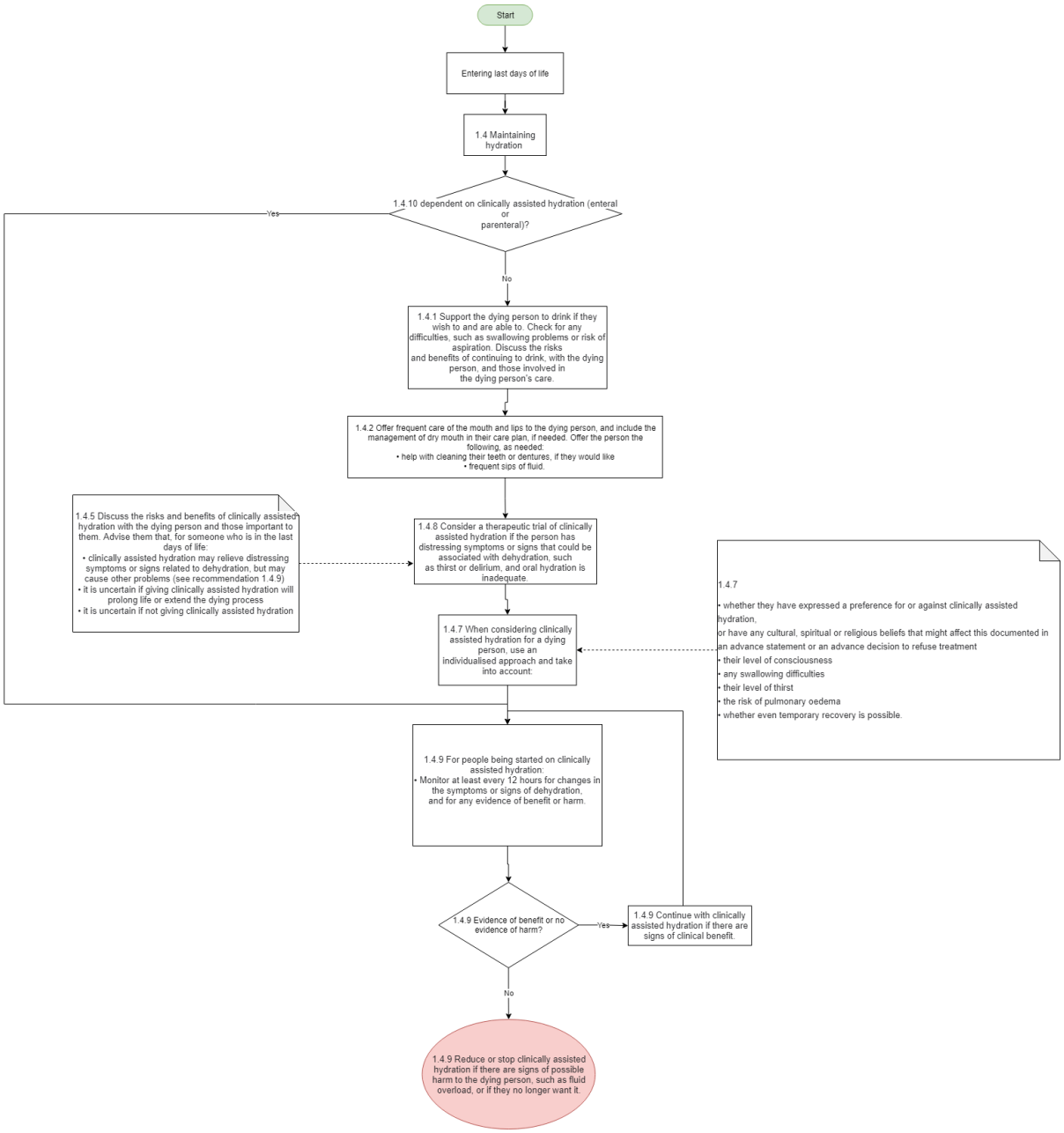


Figure 44: Terminal care - Hydration

1.5.12.3 Medication

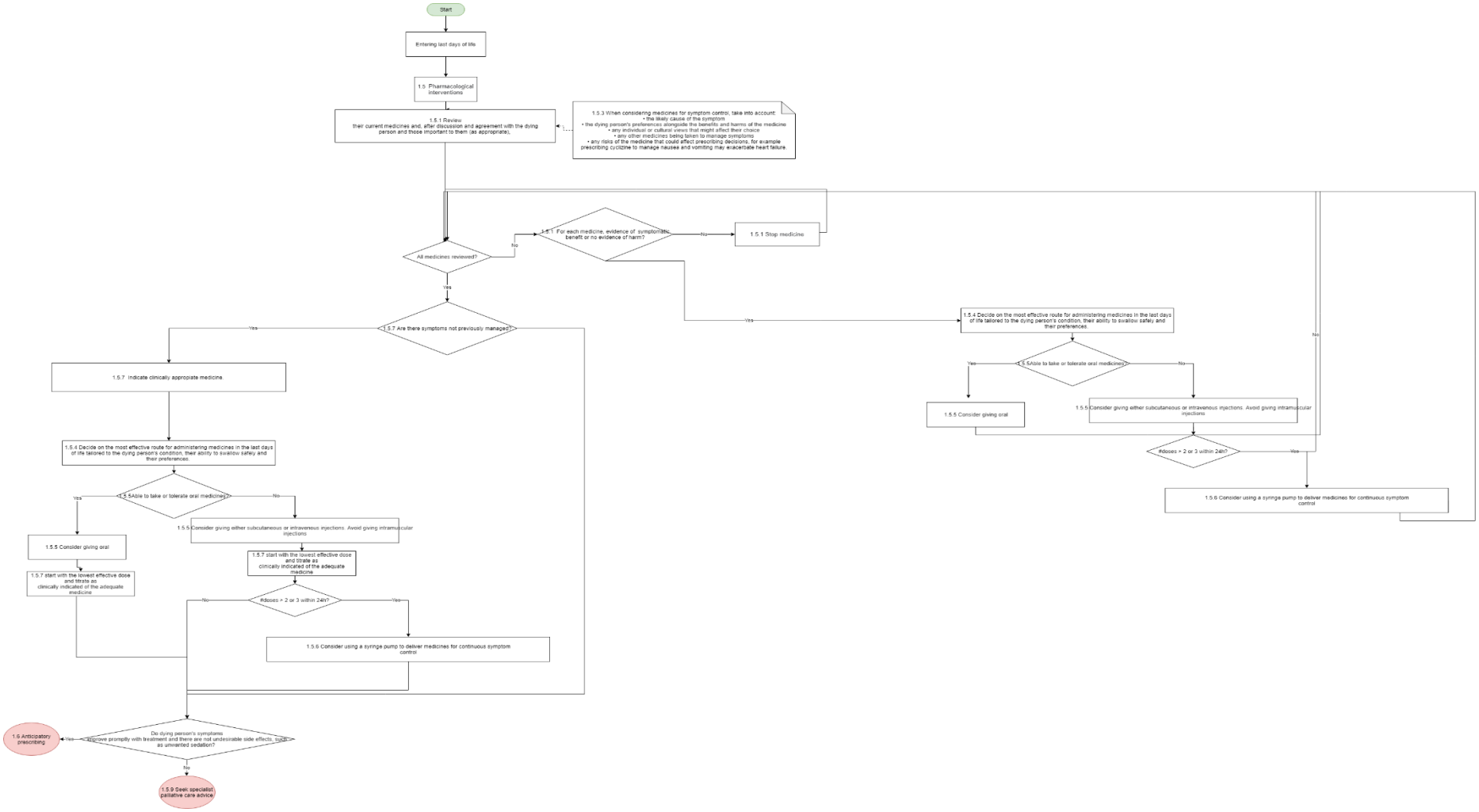


Figure 45: Terminal care - Medication

1.5.12.4 Care coordination

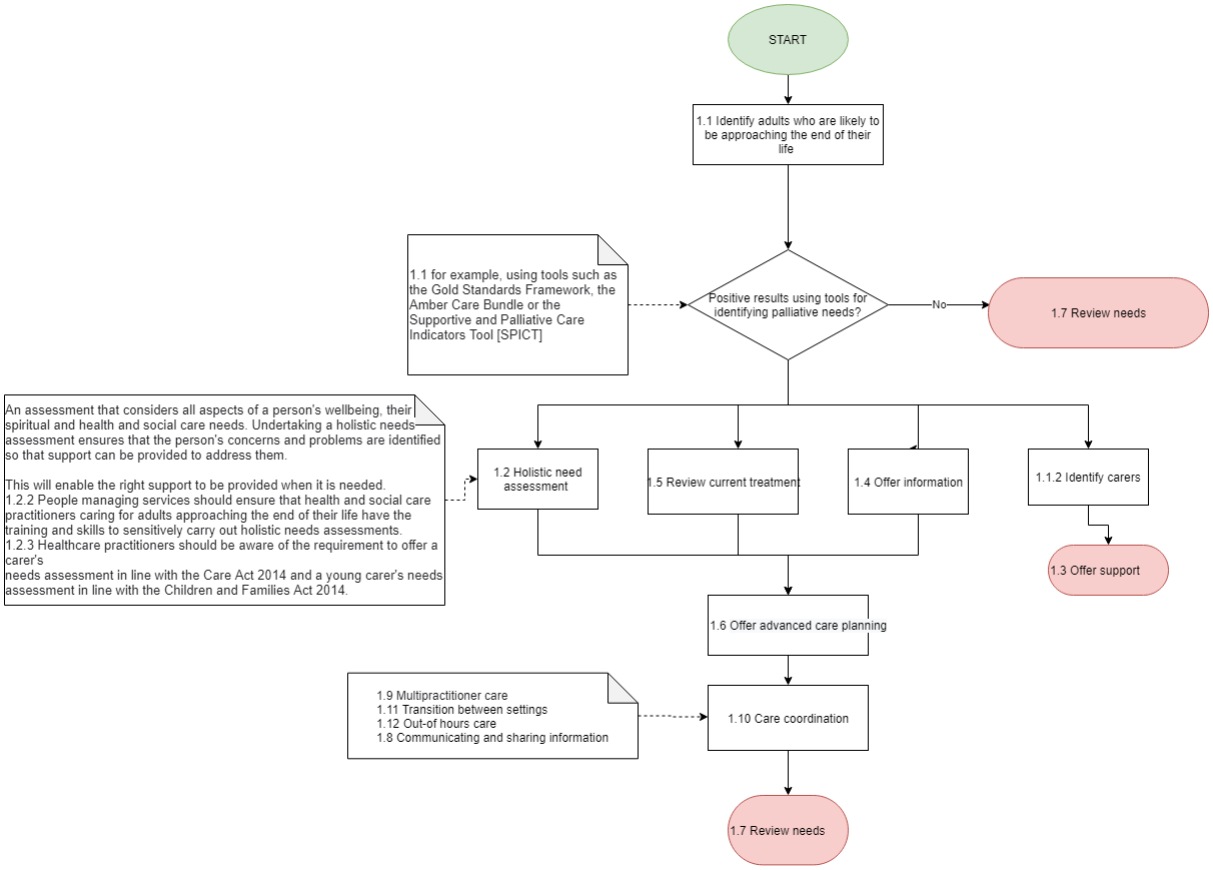


Figure 46: Terminal care - Care coordination

Local deviations: OSAKIDETZA: Tools for identifying palliative needs: NECPAL tool is used instead the suggested ones by NICE.

1.5.12.5 Breathlessness

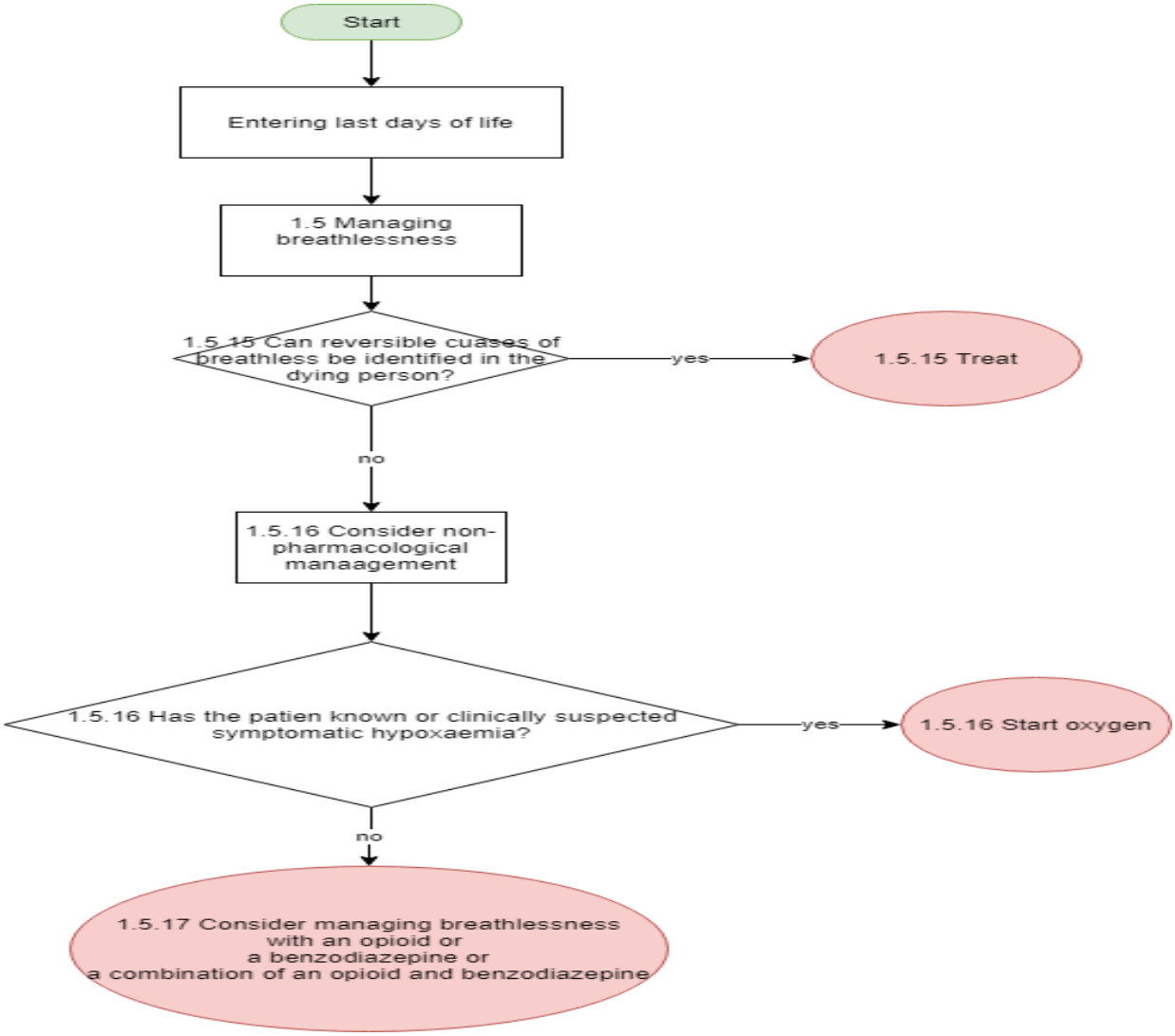


Figure 47 Terminal care - Breathlessness

1.5.12.6 Anxiety

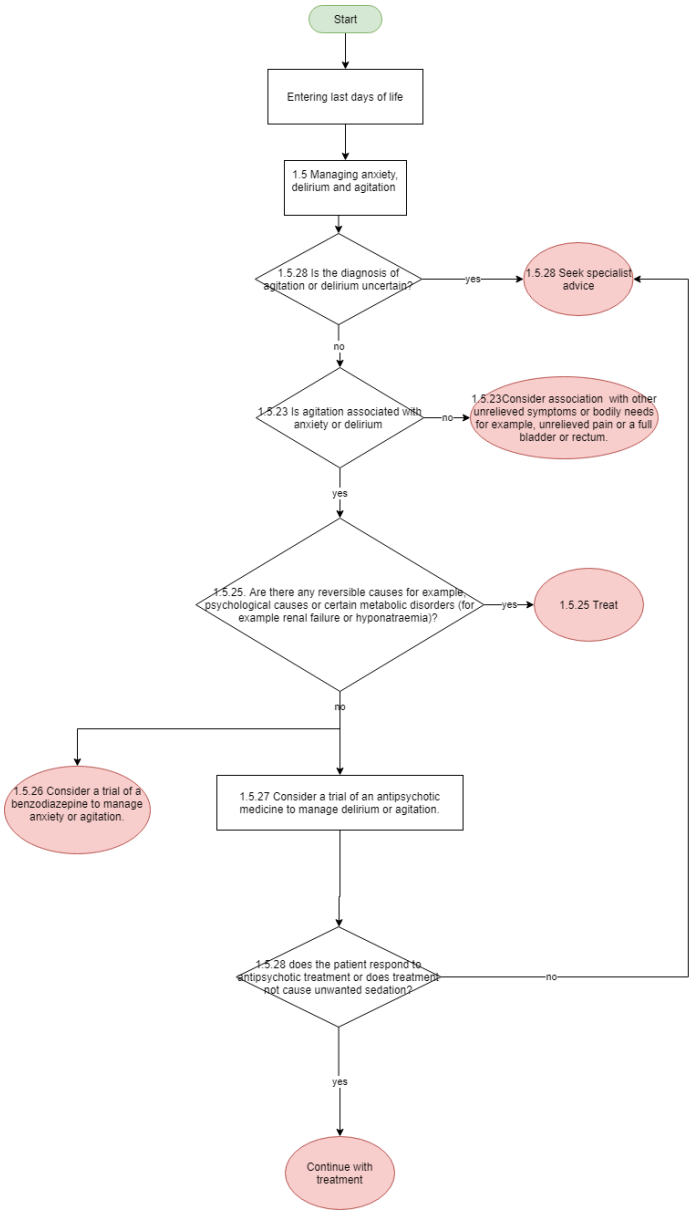


Figure 48: Terminal care - Anxiety

1.5.12.7 Respiratory secretion

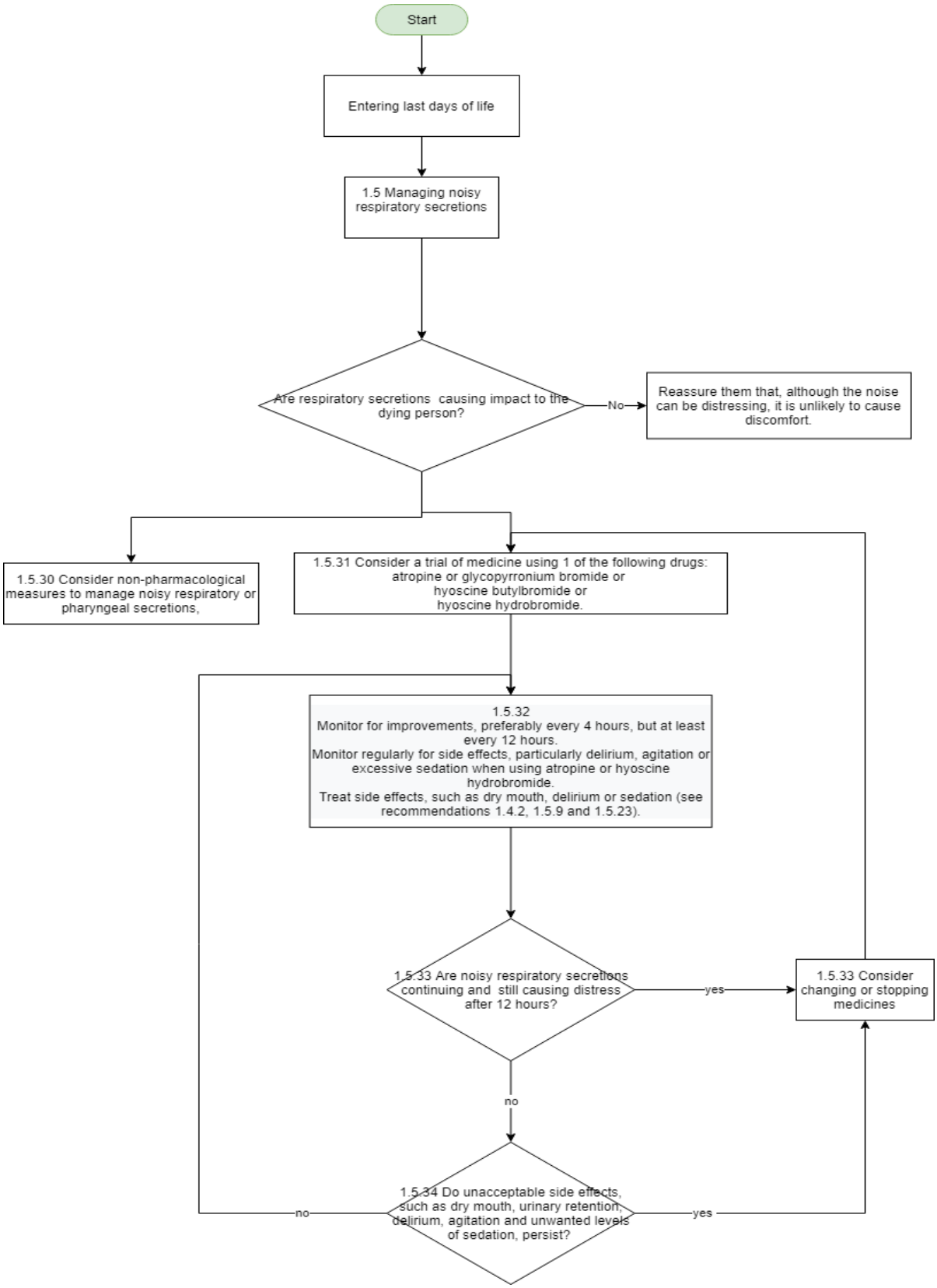


Figure 49: Terminal care - Respiratory secretion

1.5.13 Flowchart for social care needs in multi-morbidity

This flowchart is based on NICE guidelines for elderly with social needs and multimorbidity NG22 [20] from 2015.

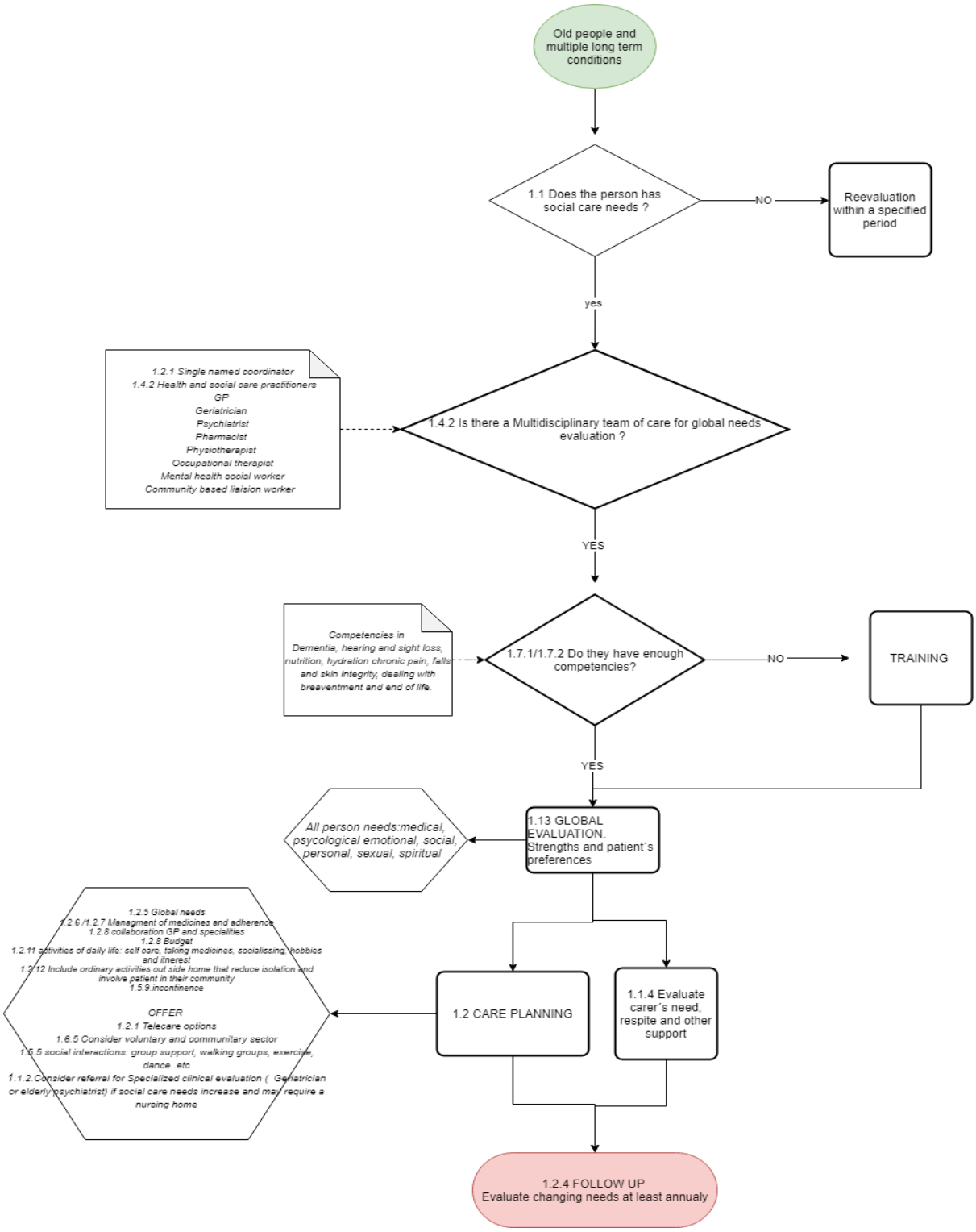


Figure 50: Social needs - Overview

Abbreviation: GP= general practitioner

1.5.14 Flowchart for supporting adult carers

This flowchart is based on NICE guidelines supporting adult carers NG150 [21] from 2020.

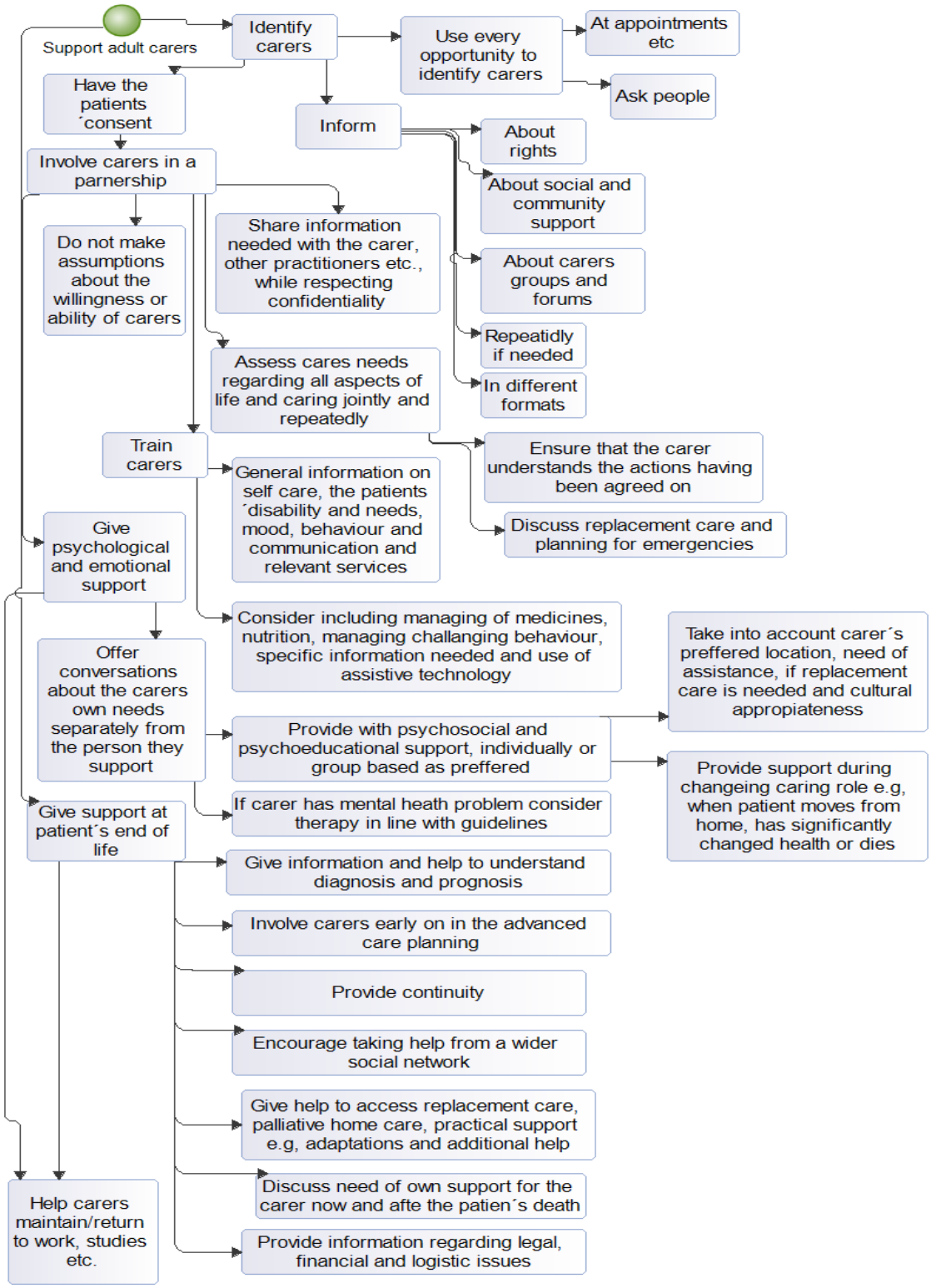


Figure 51: Supporting adult carers - Overview

1.6 Reconciliation of guidelines

The results of the reconciliations are presented in **Table 5,** with description of present single guideline context, type of interaction, relevant triggers and information and a resulting output or modified output needed. For eight of the reconciliations examined, there was no need for modifications. This was mostly due to that all interactions/problems already were identified at previous steps, i.e., reconciliation of two the guidelines involved. **Table 6** presents reconciliations undertaken without further interactions/problems being identified. To map all potential reconciliation alternatives with 48 flowcharts involved would not be doable. Based on medical knowledge the reconciliation alternatives were reduced. Further information regarding this can be found in **Table 2.**

Table 5 Output of guideline reconciliations with modifications and adaptations

Mapped single guideline	Context in the guideline	Type of interaction	Relevant clinical concepts/codes	Rule description	Trigger	Input needed	Resulting output	Reference
RECONCILED GUIDELINES T2DM + CKD								
Gastro-paresis Old rule								
New rule	If vomiting - use of metoclopramide	Disease to drug	ATC code + eGFR	IF treatment metoclopramide AND eGFR 15-60 ml/min THEN reduce metoclopramide by 50% to maximum 5 mg 3 times/day. IF eGFR <15 ml/min THEN reduce metoclopramide by 75% to maximum 3 mg 3 times/day	ATC code + eGFR	medication (ATC) including dosing and lab tests (eGFR)	Alert "GFR 15-60 ml/min THEN reduce metoclopramide by 50% to maximum 5 mg 3 times/day. IF eGFR <15 ml/min THEN reduce metoclopramide by 75% to maximum 3 mg 3 times/day"	Drug product sheet, www.fass.se

New rule	If vomiting - use of erythromycin	Drug-Drug	ATC-Codes	IF Simvastatin AND Erythromycin recommended/initiated Then Modify output	ATC-Codes	IF Simvastatin AND Erythromycin	Warning " Simvastatin contra-indicated together with erythromycin"	Drug product sheet, www.fass.se
Dietary advice Old rule	emphasise advice on healthy and balanced eating							
New rule		Disease-Disease CKD + T2DM	ICD-10, eGFR	IF eGFR <30 ml/min AND T2DM THEN modify output	IF eGFR <30 ml/min AND T2DM	ATC code AND eGFR	"Emphasise advise on healthy and balanced eating. Consider nutritional counselling by dietician"	
Diabetes EASD/ADA Old rule	Metformin at optimal dose. If contra-indicated move to next step							
New rule		Disease-Disease CKD + T2DM	ICD-10, eGFR, ATC code	IF eGFR 30-45 ml/min AND Metformin THEN modify output	IF eGFR 30-45 ml/min AND Metformin dosage is > 1000 mg/d	ATC code AND dosage (mg/d) AND eGFR	Warning " With the patients´ reduced renal function is maximum recommended Metformin dose 1000 mg/day"	Drug product sheet, www.fass.se
New rule		Disease-Disease CKD + T2DM	ICD-10, eGFR, ATC code	IF eGFR <30/min AND Metformin THEN modify output	IF eGFR <30 ml/min AND Metformin	ATC code AND eGFR	Warning " With the patients´ reduced renal function is Metformin contra-indicated"	Drug product sheet, www.fass.se

New rule	Use of sulfonylureas	Disease-Drug CKD + Sulfonylureas	ICD-10, eGFR, ATC code	IF eGFR <30/min AND Sulfonylureas THEN modify output	IF eGFR <30/min AND Sulfonylureas	ATC code AND eGFR	Warning " With the patients´ reduced renal function is Sulfonylureas not recommended"	Drug product sheet, www.fass.se
Lipid lowering New rule	Use of simvastatin	Drug disease interaction	ICD-10, ATC code	IF Simvastatin AND eGFR<30 ml/min THEN modify output	IF Simvastatin > 10 mg/day AND eGFR<30 ml/min	ICD-10, ATC code and dosage	Warning" With the patients´ reduced renal function is a Simvastatin dose of more than 10 mg/day not recommended"	Drug product sheet, www.fass.se
New rule	Use of Rosuvastatin	Drug disease interaction	ICD-10, ATC code	IF Rosuvastatin AND eGFR<30 ml/min THEN modify output	IF Rosuvastatin AND eGFR<30 ml/min	ICD-10, ATC code	Warning" With the patients´ reduced renal function is Rosuvastatin contra-indicated"	Drug product sheet, www.fass.se
New rule		Drug disease interaction	ICD-10, ATC code	IF Rosuvastatin AND eGFR 30-60 ml/min THEN modify output	IF Rosuvastatin >=40 mg/d AND eGFR 30-60ml/min	ICD-10, A code and dosage	Warning" With the patients´ reduced renal function is Rosuvastatin 40 mg/day contra-indicated"	Drug product sheet, www.fass.se
RECONCILED GUIDELINES COPD + T2DM								
Diabetes Dietary advise	"Emphasise advise on healthy and balanced eating"	Disease-Disease COPD + T2DM	ICD-10, Doctors staging of COPD	IF COPD >=3 AND DM2 THEN modify output	IF COPD >=3 AND T2DM		"Emphasise advise on healthy and balanced eating. Consider nutritional counselling by dietician"	Gold 2020

	COPD exacerbation	Disease-Disease COPD + T2DM	ICD-10	If DM2 AND exacerbation of COPD THEN display output	Exacerbation of COPD		"Schedule glucose monitoring, with a frequency adapted to medical history, present situation, and treatment given. Plan for extra tight controls if oral corticoids are used".	NICE
	COPD exacerbation	Disease-Disease COPD + T2DM	ICD-10 + ATC (insulin)	If DM2 AND exacerbation of COPD AND insulin treatment THEN display output	Exacerbation of COPD		"If the patient is insulin dependent consider hospitalisation, in particular if significant comorbidities exist"	NICE
Diabetes EASD/ADA Old rule	Metformin at optimal dose. If contra-indicated move to next step							
New rule		Disease-Disease CHF + DM2	ICD-10, ATC code	IF Metformin AND COPD >= 3 THEN modify output	IF Metformin AND COPD >=3	ICD-10, ATC code	Warning " Metformin is contra-indicated in respiratory de-compensation as exacerbations. Consider changing diabetes treatment"	Drug product sheet, www.fass.se

RECONCILED GUIDELINES CHF + T2DM								
Gastro-paresis Old rule	If vomiting - consider domperidone							
New rule		Drug to drug	ATC codes	IF treatment with digoxin AND treatment with domperidone is initiated THEN follow plasma concentration of digoxin	ATC codes, N.B. the importance of the order of prescription	medication (ATC) including order of prescription i.e., domperidone after digoxin	Alert	Drug product sheet, www.fass.se
New rule	If vomiting - consider erythromycin	Drug-Drug	ATC-Codes	IF Ivabradine AND Erythromycin recommended/initiated Then Modify output	ATC-Codes	IF Ivabradine AND Erythromycin	Warning " Ivabradine contra-indicated together with erythromycin"	Drug product sheet, www.fass.se
Dietary advice Old rule	emphasise advice on healthy and balanced eating							

New rule		Disease-Disease CHF + T2DM	ICD-10, eGFR	IF T2DM AND CHF with NYHA IV THEN modify output	IF T2DM AND CHF with NYHA IV	ICD codes AND NYHA classification	"Emphasise advise on healthy and balanced eating. Remind the patient to also reduce salt intake"	
Diabetes EASD/ADA Old rule	Metformin at optimal dose. If contra-indicated move to next step							
New rule		Disease-Disease CHF + T2DM	ICD-10, ATC code	IF Metformin AND NYHA III-IV THEN modify output	IF Metformin AND NYHA >=III	ICD-10, ATC code	Warning " Metformin is contra-indicated in cardiac de-compensation. Consider changing diabetes treatment"	Drug product sheet, www.fass.se
Diabetes EASD/ADA Old rule	Whenever SGLT-2i is recommended /initiated							
New rule	Whenever SGLT-2i is recommended /initiated	Drug-drug interaction	ICD-10, ATC code	IF diuretics are used and SGLT2i are recommended or initiated THEN modify output	IF diuretics followed by SGLT2i	ATC code	Add information " N.B. SGLT2i has a diuretic effect. Consider the need to reduce diuretics"	Drug product sheet, www.fass.se

New rule	Whenever Pioglitazone is recommended /initiated	Drug disease interaction	ICD-10, ATC code	IF CHF AND Pioglitazone is used/initiated/recommended THEN modify output	IF CHF AND Pioglitazone is used / initiated / recommended	ICD-10, ATC code	Warning "Pioglitazone increases the risk for cardiac de-compensation"	Drug product sheet, www.fass.se
New rule	Whenever Betablockers is recommended /initiated	Drug-drug interaction	ATC code	IF Insulin AND Betablocker is used / initiated / recommended THEN modify output	IF CHF AND Betablocker is used / initiated / recommended	ICD-10, ATC code	Alert "In insulin treated patients Betablockers might mask hypoglycaemic symptoms"	Drug product sheet, www.fass.se
RECONCILED GUIDELINES CHF + CKD								
Confirmed diagnosis of CHF Old rule	Consider prescribing digoxin							
New rule		Disease to drug	ATC codes, eGFR	IF treatment with digoxin AND renal failure THEN follow plasma concentration of digoxin	ATC codes, eGFR	ATC, eGFR	Alert: "Reduce dosage of digoxin and follow serum concentrations"	Drug product sheet, www.fass.se
RECONCILED GUIDELINES CHF + Hepatopathy								

	Treatment of ALF in patients with NAFLD in secondary and tertiary care setting	Drug to disease interaction: use of pioglitazone in people with NAFLD and/or ALF is contra-indicated with history of CHF		See NAFLD flowchart	ATC codes and ICD 10	ATC codes and ICD 10	Alert (contraindication)	

Abbreviations: ATC= Anatomic Therapeutic Chemical classification system, ALF= Advanced liver fibrosis, ADA= The American Diabetes Association, CHF= Congestive heart failure, CKD Chronic kidney disease, COPD= Chronic obstructive pulmonary disease, ICD= International Classification of Diseases, EASD= European Association for The Study of Diabetes, eGFR= Estimated Glomerular Filtration Rate, GOLD= Global Initiative for Chronic Obstructive Lung Disease, NAFLD= Non-alcoholic fatty liver disease, NICE= National Institute for Health and Care Excellence, NYHA= New York Heart Association Classification (Class I-IV), SGLT-2i sodium-glucose cotransporter 2 inhibitor, T2DM= Type 2 diabetes mellitus

Table 6 Performed reconciliation controls without new interactions/problems identified

Reconciliation levels		
2 diseases	**3 diseases**	**4 diseases**
CHF + Stroke	CHF + T2DM + CKD	COPD + CHF + T2DM + CKD
COPD + Stroke	COPD + CHF + Stroke	
COPD + CKD	COPD + CHF + T2DM	
	COPD + CHF + CKD	

Abbreviations: CHF= Congestive heart failure, CKD Chronic kidney disease, COPD= Chronic obstructive pulmonary disease, T2DM= Type 2 diabetes mellitus

1.7 Potentially preventable situations (PPS)

Table 7 presents the main results of the PPS task, where "identifier" represents the key event for AI to identify and a potentially avoidable event from a clinical perspective. Scales, questionnaires, laboratory tests, etc. present indicators that from a clinical judgement potentially could improve AI algorithms and similarly for demographic and social info were existence of informal caregivers and institutional living is considered relevant. In WP5 these results will be used in creating AI derived algorithms to hopefully prevent some of the unwanted outcomes (PPSs). The table presents potential sources for the algorithm creation from the EHRs and social and demographic information to be used. Not all pilot sites can contribute with information from e.g., all questionnaires and sub-division of care level is not relevant for all pilots. Information on suggested scales and questionnaires can be found at respective organisation website and in scientific papers; EQ-5D-5L [22], HADS [23], Zarit burden interview [24], Bartel index [25], and Lawton index [26].

A guide to CRGs on the development of PPS is provided in **Appendix** A7 and an example of the working material from the development of PPS in **Appendix A8**.

Table 7 Potentially preventable situations with potential predictive parameters

PPS	Identifier	Scales / questionnaires	Tests, measurements, laboratory, etc.	Resource use			Demographic / social info
Depression / anxiety	ICD10 F41.2 *Mixed anxiety and depression disorder*	EQ-5D-5L		A&E services	Social assistance	Psychiatry medium stay	Institutional living
	ATC N06A *Antidepressants*	HADS		Cardiologist	General surgery	Psychiatry rehabilitation	Social problems
				Respiratory	Palliative care	Internal medicine long stay	Social isolation
				Endocrinology	Infectious diseases	Nursing	
				Nephrology	Haematology	Primary care	
				Psychiatry	Rehabilitation	Home hospitalisation	
				Neurologist	Pain unit	Hospitalisation	
				Internal medicine	Psychiatry short stay	ICU	
				Geriatric			

Malnutrition	ICD10 R64 *Cachexia*	EQ-5D-5L	Haemoglobin	A&E services	Geriatric	Psychiatry medium stay	Caregiver
	ICD10 D50 *Iron deficiency anaemia*	NYHA	Albumin	Cardiology	General surgery	Psychiatry rehabilitation	Institutional living
	ICD10 D51 *Vitamin B12 deficiency anaemia*	Walking distance / number of steps / get up and go	Total Proteins	Respiratory	Palliative care	Internal medicine long stay	
	ICD10 D52 *Folate deficiency anaemia*	ZBI	Transferrin Saturation	Endocrine	Diet and nutrition	Nursing	
	ICD10 D53.9 *Nutritional anaemia, not specified*		Folate	Nephrology	Infectious diseases	Home hospitalisation	
			Weight	Psychiatry	Psychiatry short stay	Hospitalisation	
				Internal medicine			
Avoidable admission	ICD10 Z60 *Problems related to social environment*	ACCF/AHA		A&E services	Social assistance	Psychiatry medium stay	Caregiver

	ICD10 W19 *Falls*	EQ-5D-5L		Cardiology	General surgery	Psychiatry rehabilitation	Institutional living
	ICD10 Z91.8 *Risk of falls*	GOLD stages		Respiratory	Palliative care	Internal medicine long stay	
	ICD10 M80 *Osteoporosis with fracture*	HADS		Endocrinology	Infectious diseases	Nursing	
	At discharge no follow-up visit planned	NYHA		Nephrology	Haematology	Primary care	
	History of readmissions	Walking distance / number of steps / get up and go		Psychiatry	Rehabilitation	Home hospitalisation	
				Neurology	Pain unit	Hospitalisation	
				Internal medicine	Psychiatry short stay	ICU	
				Geriatric			
Readmission	Readmission within 30 days	ACCF/AHA	Weight	A&E services	Social assistance	Psychiatry medium stay	Caregiver
		EQ-5D-5L	Blood pressure	Cardiology	General surgery	Psychiatry rehabilitation	Institutional living

		GOLD	Creatinine /eGFR	Respiratory	Palliative care	Internal medicine long stay	
		HADS		Endocrinology	Infectious diseases	Nursing	
		NYHA		Nephrology	Haematology	Primary care	
		Walking distance / number of steps / get up and go		Psychiatry	Rehabilitation	Home hospitalisation	
				Neurology	Pain unit	Hospitalisation	
				Internal medicine	Psychiatry short stay	ICU	
				Geriatric			
Hypotension	ICD 10 I95 *hypotonia*	ATC CO2 *anti-hypertension*		A&E services	Social assistance	Psychiatry medium stay	
	ICD 10 R03.1 *Low blood pressure unspecified*	sodium		Cardiology	General surgery	Psychiatry rehabilitation	
		albumin		Respiratory	Palliative care	Internal medicine long stay	

		creatinine /e-GFR		Endocrinology	Infectious diseases	Nursing	
		Blood pressure		Nephrology	Haematology	Primary care	
				Psychiatry	Rehabilitation	Home hospitalisation	
				Neurology	Pain unit	Hospitalisation	
				Internal medicine	Psychiatry short stay	ICU	
				Geriatric			
Dependency	ICD10 Z70 *Care involving rehabilitation procedures*	EQ-5D-5L		A&E services	Geriatric	Psychiatry medium stay	Institutional living
	Rehabilitation admission	HADS		Cardiology	General surgery	Psychiatry rehabilitation	
	Transition to having an informal caregiver	Walking distance / number of steps / get up and go		Respiratory	Palliative care	Internal medicine long stay	
	ZBI score 61-66 severe burden	ZBI		Endocrinology	Infectious diseases	Nursing	
	ZBI score 41-60 moderate to severe burden	Barthel index		Nephrology	Haematology	Primary care	

	ICD10 Z51.10 *Palliative patient*	Lawton index		Psychiatry	Rehabilitation	Home hospitalisation	
	Visits to palliative care unit			Neurology	Psychiatry short stay	Hospitalisation	
	ICD10 F06.7 *MCI*			Internal medicine		ICU	
	ICD10 F00-F09 *Dementia, various types and confusion*						

Abbreviations: A&E= Accident and emergency, ACCF= American College of Cardiology Foundation, AHA= American Heart Association, ATC= Anatomical Therapeutic Chemical, COPD= Chronic obstructive pulmonary disease, CHF= Congestive heart failure, eGFR= Estimated glomerular filtration rate, EQ-5D-5L= European quality of life 5-dimension 5-level, GOLD= Global Initiative for Chronic Obstructive Lung Disease, HADS= Hospital anxiety and depression scale, ICD= International Classification of Diseases, ICU= Intensive care unit, MCI= Mild cognitive impairment, NYHA= New York Heart Association Classification, PPS= Potentially preventable situation, ZBI= Zarit burden interview.

1.8 Next steps

The content in this deliverable will primarily be used in WP5: Task 5.1 *Clinical decision support system design and implementation*, Task 5.2 *Integration of the scales and heuristic risk algorithms*, Task 5.3 *Integration of the clinical guidelines*, and Task 5.4 *Risk prediction model design and implementation* were the technical development of CDSS is continued. The flowcharts are computer executable fundaments, for the technical partners' work and scales/questionnaires and PROMs are to be used as information to feed CDSS. In the work developing prediction algorithms with the help of AI, aiming at avoiding many unwanted situations, the PPS work is an essential input to the technical partners' tasks.

1.9 References

1. National Institute for Health and Care Excellence (NICE). [Online]. Available: https://www.nice.org.uk/. [Accessed: 1-September-2021].

2. Global Initiative for Chronic Obstructive Lung Disease report 2021. [Online]. Available: https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.1-25Nov20_WMV.pdf. [Accessed: 31-Aug-2021].

3. National Institute for Health and Care Excellence (NICE), NICE guideline NG115, December 2018, last updated July 2019. [Online]. Available: https://www.nice.org.uk/guidance/ng115. [Accessed: 1-September-2021].

4. National Institute for Health and Care Excellence (NICE), NICE guideline NG28, December 2015, updated December 2020. Type 2 diabetes in adults: management. [Online]. Available: https://www.nice.org.uk/guidance/ng28. [Accessed: 31-Aug-2021].

5. Davies, M.J., D'Alessio, D.A., Fradkin, J. *et al.* Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia* 61**,** 2461–2498 (2018). https://doi.org/10.1007/s00125-018-4729-5.

6. National Institute for Health and Care Excellence (NICE), NICE guideline NG106, September 2018. Chronic heart failure in adults: diagnosis and management. [Online]. Available: https://www.nice.org.uk/guidance/ng106/evidence. [Accessed: 31-Aug-2021].

7. National Institute for Health and Care Excellence (NICE), NICE guideline NG19, August 2015, last updated October 2019. Diabetic foot problems: prevention and management. [Online]. Available: https://www.nice.org.uk/guidance/ng19. [Accessed: 31-Aug-2021].

8. National Institute for Health and Care Excellence (NICE), NICE clinical guideline CG173, November 2013 last updated September 2020. Neuropathic pain in adults: pharmacological management in non-specialist settings. [Online]. Available: https://www.nice.org.uk/Guidance/CG173. [Accessed: 31-Aug-2021].

9. National Institute for Health and Care Excellence (NICE), NICE guideline NG181, July 2014, September 2016. Cardiovascular disease: risk assessment and reduction, including lipid modification. [Online]. Available: https://www.nice.org.uk/guidance/cg181. [Accessed: 31-Aug-2021].

10. 'QRISK2-2017 risk calculator - Publications'. [Online]. Available: https://www.qrisk.org/2017/. [Accessed: 31-August 2021].

11. National Institute for Health and Care Excellence (NICE), NICE guideline NG136, August 2019. Hypertension in adults: diagnosis and management. [Online]. Available: https://www.nice.org.uk/guidance/NG136. [Accessed: 31-Aug-2021].

12. National Institute for Health and Care Excellence (NICE), NICE clinical guideline CG182, July 2014. Chronic kidney disease in adults: assessment and management. [Online]. Available: https://www.nice.org.uk/guidance/cg182. [Accessed: 31-Aug-2021].

13. National Institute for Health and Care Excellence (NICE), NICE clinical guideline CG90, October 2009. Depression in adults: recognition and management. [Online]. Available: https://www.nice.org.uk/guidance/CG90. [Accessed: 31-Aug-2021].

14. National Institute for Health and Care Excellence (NICE), NICE guideline NG97, June 2018. Dementia: assessment, management and support for people living with dementia and their careers. [Online]. Available: https://www.nice.org.uk/guidance/ng97. [Accessed: 31-Aug-2021].

15. National Institute for Health and Care Excellence (NICE), NICE guideline NG128, May 2019. Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. [Online]. Available: https://www.nice.org.uk/guidance/NG128. [Accessed: 31-Aug-2021].

16. National Institute for Health and Care Excellence (NICE), NICE guideline NG49, July 2016. Non-alcoholic fatty liver disease (NAFLD): assessment and management. [Online]. Available: https://www.nice.org.uk/guidance/ng49. [Accessed: 31-Aug-2021].

17. National Institute for Health and Care Excellence (NICE), NICE guideline NG50, July 2016. Cirrhosis in over 16s: assessment and management. https://www.nice.org.uk/guidance/ng50. [Accessed: 31-Aug-2021].

18. National Institute for Health and Care Excellence (NICE), NICE guideline NG142, October 2019. End of life care for adults: service delivery. [Online]. Available: https://www.nice.org.uk/guidance/NG142. [Accessed: 31-Aug-2021].

19. National Institute for Health and Care Excellence (NICE), NICE guideline NG31, December 2015. Care of dying adults in the last days of life. [Online]. Available: https://www.nice.org.uk/guidance/ng31. [Accessed: 31-Aug-2021].

20. National Institute for Health and Care Excellence (NICE), NICE guideline NG22, November 2015. Older people with social care needs and multiple long-term conditions. [Online]. Available: https://www.nice.org.uk/guidance/ng22. [Accessed: 31-Aug-2021].

21. National Institute for Health and Care Excellence (NICE), NICE guideline NG150, January 2020. Supporting adult carers. [Online]. Available: https://www.nice.org.uk/guidance/NG150. [Accessed: 31-Aug-2021].

22. EQ-5D. [Online]. Available: https://euroqol.org/eq-5d-instruments/eq-5d-5l-about. [Accessed: 1-September-2021].

23. Zigmond, AS; Snaith, RP (1983). "The hospital anxiety and depression scale". Acta Psychiatrica Scandinavica. 67 (6): 361–370. doi:10.1111/j.1600-0447.1983.tb09716.

24. Zarit, S. H., Reever, K. E., Back-Peterson, J. (1980). Relatives of the impaired elderly: correlates of feelings of burden. The Gerontologist, 20, 649-655.

25. Mahoney FI, Barthel D. Functional evaluation: The Barthel Index. Maryland State Medical Journal 1965; 14:56-61.

26. Lawton, M.P., & Brody, E.M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. The Gerontologist, 9(3), 179-186.

Appendix A

A.1 Participating clinicians in clinical reference groups

Table 8 Participating clinicians in CRGs

Pilot site	Name	Workplace	Speciality/experience
OUH	Anne Dichmann Sorknæs	Medical & emergency Department, OUH	Research nurse, PhD, Associated professor Specialist in Family nursing, Shared Decision-Making, Telemedicine and medical diseases especially COPD
OUH	Natassia Kamilla Juul		PhD student, Nursing specialist in heart disease, palliative care and participatory design.
Kronikgune/ Osakidetza	Laura de la Higuera Vila	Hospital Bidasoa (Gipuzkoa), Spain	MD Internist, PhD. Internal medicine and continuity of care unit for multimorbid patients in collaboration with primary care.
RJH	Mikael Lilja	R&D unit RJH	MD., PhD., Specialist in family medicine, associated professor
RJH	Eva-Pia Darsbo	The Mobile care team for elderly with multiple chronic diseases and frailty in their own homes. Department of medicine Östersund hospital and Odensala Health care centre	MD. Specialist in family medicine and geriatrics

RJH	Elsy Bäckström	Development organisation RJH	Specialist nurse, organisational changes and multimorbidity
USTRATH/ Lanarkshire	Gabriela Maxwell	NHS Lanarkshire	Primary care Advanced Nursing Practice Long term conditions Urgent in and out of hours care Primary Care Improvement Plan
AMCA	Nahir Barak	Assuta Medical Centre Ashdod	MD. Specialist in family medicine and Emergency medicine and is an active family practice physician in Jerusalem, Israel and a senior physician in the Internal Medicine Department A2 at Assuta Ashdod Hospital
AMCA/ Maccabi	Michal Yeshayahu	Maccabi HMO	Medical director of Maccabi's Integrated Care Unit and al so a practicing family physician, teaching studen ts and residents. Her main fields of interest are inter-professional education, collaboration and integra ted care
Werra-Meißner-Kreis	Janika Blömke	OptiMedis	Trained physiotherapist, BSc, Msc and PhD in Public Health, with expert knowledge on patient-reported outcome assessment in rare diseases
Werra-Meißner-Kreis	Fritz Arndt	Gesunder	Master of Science with an engineering background, specialist in health care programme development
Werra-Meißner-Kreis	Manfred Zahorka	OptiMedis	MD, specialist public health physician, senior expert in health system development with experience also working in developing countries

Werra-Meißner-Kreis	Jonah Grütters	OptiMedis	Research assistant, currently working as dual student with OptiMedis after six semesters of studying medicine

Abbreviations: AMCA= Assuta Ashdod LTD, COPD= Chronic obstructive pulmonary disease, OUH= Odense University Hospital, R&D= Research and development, RJH= Region Jämtland Härjedalen, USTRATH= University of Strathclyde

A.2 CRG – Scope, governance, and activities foreseen

ADLIFE Clinical Reference Group

This document describes the scope and activities of Clinical Reference Group (CRG) in ADLIFE project, as long as its structure, governance and organization.

Background

The Clinical Reference Group (CRG) is a multidisciplinary group of health professionals with representatives from the seven pilot sites of ADLIFE project. It aims to provide expert advice, support, and guidance on ADLIFE project in order to improve patient's health condition by an appropriately targeted and timely care. CRG will operate as a catalyst to provide personalized integrated care, implement intelligent tools for clinical decision-making support, ensure securely access, process, share and store patient's data and promote consistent and sustained active role of patients and caregivers across Europe focusing on outcomes.

Chair and membership

- Led by RJH
- Formed by at least 2 healthcare professionals (physicians and/or nurses) per pilot site
    - These 2 local healthcare professionals, act on behalf of their local CRG

Local CRG

- A clinical reference group will be created in each of the pilot sites
- In each site it includes at least three different healthcare roles for professionals: General practitioners (GP), Nurses, Specialist at hospitals

Scope

CRG is expected to:

- Guide ICT experts in the final design of the Personalized Care Plan Management Platform (PCPMP) in terms of personalized care plan requirements for the creation, update and follow-up of personalized integrated care plans for patients.
- Guide the process of defining and refining the Clinical Decision Support System (CDSS) to be used for estimation risk and poor evolution for the selected pathologies.
- Review and select patient-reported outcome measures (PROMs) to be used in the three platforms: PCPMP, PEP and CDSS.
- Enable the delivery of just in time adaptive interventions (JITAI) to ADLIFE pilot patients by sensing their context and delivering behavior change interventions accordingly.
- Review the technical specifications produced by Technological Partners and ensure real performance of the ICT tools complies with expected one.
- Support the increasing of patient centeredness allowing shared decision making by selecting decision aids and interventions to help people reflect on their needs and participate in decisions.
- Assist the definition of pilot site use cases describing how each pilot envisions ADLIFE deployment in its pilot.
- Support the development of pilot site scenarios (use cases) to describe the as-is and future wished to capture the intended use of ADLIFE
- Revise the evaluation indicators and decide on the final list

Activities of Clinical Reference Group

The Clinical Reference Group (CRG) will work in close collaboration with healthcare professional representatives of all Pilot Sites and/or with technical partners, depending on the service being addressed. The services encompassed by CRG include:

- Design of the Personalized Care Plan Management Platform (PCPMP)
  - Define the needs of advanced chronic disease care management to update and customize PCPMP
  - Provide feedback in terms of personalized care plan requirements
- Definition of Clinical Decision Support System (CDSS)
  - Review the most adequate assessment scales and select those that will be computerized
  - Select the most adequate Guidelines to provide evidence-based input to these CDSS
  - Review recommendations taking into account:
    - the Pilot sites´ reference Guidelines
    - a systematic process to reconcile conflicting recommendations for multimorbid patients
  - Adapt to local context and guides
  - Develop "If-else-then" programming flows and structure in decision trees
  - *Agree an initial and basic list of the symptoms/signs to be used by early warning systems*
  - Review the variables used for clinical prediction algorithms, including output (mortality, admission to ICU, re-admissions, complications...)
  - Review, asses and refine the reference predictive algorithms selected for COPD and CHF
  - Define the types of recommendations and alerts
  - Define CDSS visualization (in collaboration with technical partners from WP5)
- Review and selection of PROMs to be used in the three platforms (PCPMP; PEP and CDSS)
  - Decide the online PROM questionnaires to be available from the Patient Empowerment Platform
  - Agree on the actions and care strategies that can be activated according to the assessment scales scores and PROMs
- Agreement on the actions and information needed for just in time adaptive interventions (JITAI)
  - Define the information needed to sense patient context
  - Define adaptive interventions to be delivered in an individualized manner
- Confirmation and review of the technical specifications and readiness of the ADLIFE toolbox
  - Review the technical specification produced by Technological partners
  - Confirm the data availability in different sites (WP3, 4 and 5)
  - Validate translation to local languages
  - Test all functionalities of the ICT tools from a user perspective
- Review and selection of sharing decision making tools
  - Tailor shared decision-making tool to each group and each region taking into account all the specific features
- Assistance the definition of pilot site use cases with local clinical expert groups
- Support the development of pilot site scenarios
- Revision of the evaluation indicators
  - Select the final list of evaluation indicators

- Support to define the natural history of heart failure and COPD, considering two stages: compensated and decompensated

Activities of local clinical expert groups

- Healthcare professional representatives of all Pilots along with Clinical Reference Group (CRG) will guide the process of defining and refining CDSS.
- Assess final ADLIFE CDSM rules and algorithm
- Assess and map the variables identified in local care sites´ EHR systems for the design of the interoperability adopters (to be used to extract data from EHR sources and feed them to clinical decision support services)
- Validate final ADLIFE CDSM rules and algorithm in the different contexts of ADLIFE Pilot sites, checking local data sources.
- Test final ICT platforms deployed on the staging and production environments in each Pilot site with fake patients with realistic data, to ensure real performance complies with expected one.
  - Test scripts guiding each functionality will be developed

A.3 Example of review of flowcharts

Pilot CRGs have presented thorough evaluations of the guidelines in many steps. Enclosed below is an example of an analysis step before the finalisation of the flowcharts made by **OSAKIDETZA**. **AMCA** at this situation supported the OSAKIDETZA writing regarding CHF with reduced EF except for 1.8 “Interventional procedures” which they wanted to leave out.

Chronic heart failure in adults: diagnosis and management guideline (NG106) review by Osakidetza

This document shows the review of Osakidetza on the Heart Failure (HF) flowcharts developed after the analyses of Chronic heart failure in adults: diagnosis and management guideline (NICE NG106) in the ADLIFE project.
Osakidetza review includes local deviations in the Osakidetza practice and suggestions for the inclusion of sections of the guideline not addressed in the current flowcharts that we consider of interest when we think of an ADLIFE patient. In the latter, references to the NICE guideline NG106 are provided (in italic). The aim of these suggestions is to be considered by the pilot site responsible for the initial analyses of the guideline and further discussed, if considered.
There are two specific comments to be reviewed or updated after pilot site responsible for the initial analyses review.

GUIDELINES USED IN OSAKIDETZA

In Osakidetza recommendations are based in American (last update in 2017) and Europeans guidelines (last up date in 2016).
There are also Spanish guidelines which are based in those recommendations. Examples are:

- “Manual Práctico de manejo integral
  de paciente con insuficiencia cardiaca crónica de la SEMI 2018”
- Protocol from Ministerio de sanidad 2016).

Following one or the other depends on the organization you work and personal skills, patient and other circumstances.

CHF FLOWCHARTS REVIEW:

1. Patients with newly confirmed CHF flowchart.

These recommendations can be used for all chronic diseases.
In the project, this flow chart may be useful for COPD patients who have the new diagnosis of heart failure during the intervention. Because the rest of patients will be included after this diagnosis.

2. CHF with reduce fraction ejection flowchart

SUGGESTION: To include the following sections of NICE guideline NG106:
-1.4 Treating heart failure with reduced ejection fraction:

- SUGGESTION: To include more information regarding Diuretics (see 1.6 Managing all types of heart failure), not only for preserved ejection fraction, as they are indicated in all patients to relief symptoms.
- REVIEW/CORRECTION?: As it is the current flowchart, it seems that Beta Blockers (BB) are used only in some situations, while they are indicated in all patients if they have no contraindications. Please check.
- SUGGESTION: To include specialist. In ADLIFE, the specialists will be part of the health care professional team, and primary care teams should know when are indicated some specialist treatment, in order to start them or to refer the patients to the specialists.

SUGGESTION: To include in this flowchart the following sections from NICE guideline:

- *1.4.19 Ivabradine.*
- *1.4. 22 Sacubitril valsartan*
- *1.4.26 Digoxina.*
- *1.8 Interventional procedures:* I support the inclusion of this interventions in the treatment of heart failure of reduced ejection fraction. Indications for revascularization are only for symptomatic patients with preserved function and nowadays is no evidence for resynchronization or defibrillations in those group of patients.
    - *Coronary revascularization*
    - *Cardiac transplantation*
    - *1.8.2 Specialist referral for transplantation should be considered for people with severe refractory symptoms or refractory cardiogenic shock. [2003]*

    Patients in active list for transplantation are excluded of ADLIFE. However, it could be possible that after two or three months in the study they can have that option, so maybe we should add it transplantation/ palliative care.
    - *Implantable cardioverter defibrillators and cardiac resynchronization therapy*

- LOCAL DEVIATIONS: Those devices are always indicated by cardiologist and specialist in arrythmias. As it's not clear the benefit of defibrillators in reduced ejection fraction of no ischemic origin, its indication its individualized in each patient.

Flowcharts in American and European's guidelines are shown below as examples. The first one is the one from the American's (page 3) and the second (page 4) from the European's.

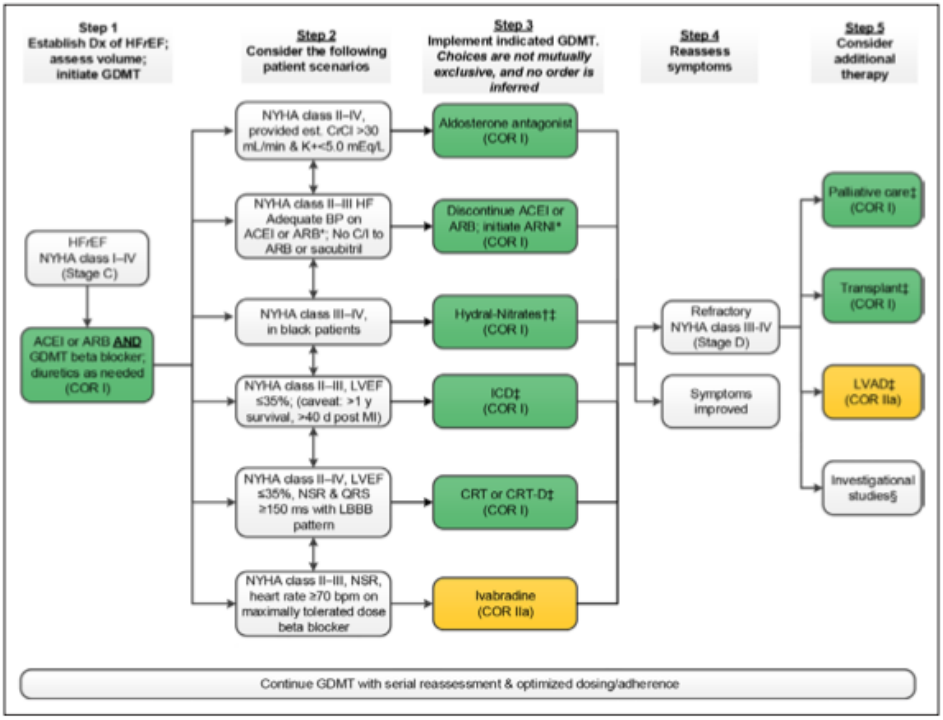


Figure 2. Treatment of HFrEF Stage C and D.
Colors correspond to COR in Table 1. For all medical therapies, dosing should be optimized and serial assessment exercised. *See text for important treatment directions. †Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored. ‡See 2013 HF guideline.[9] §Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.

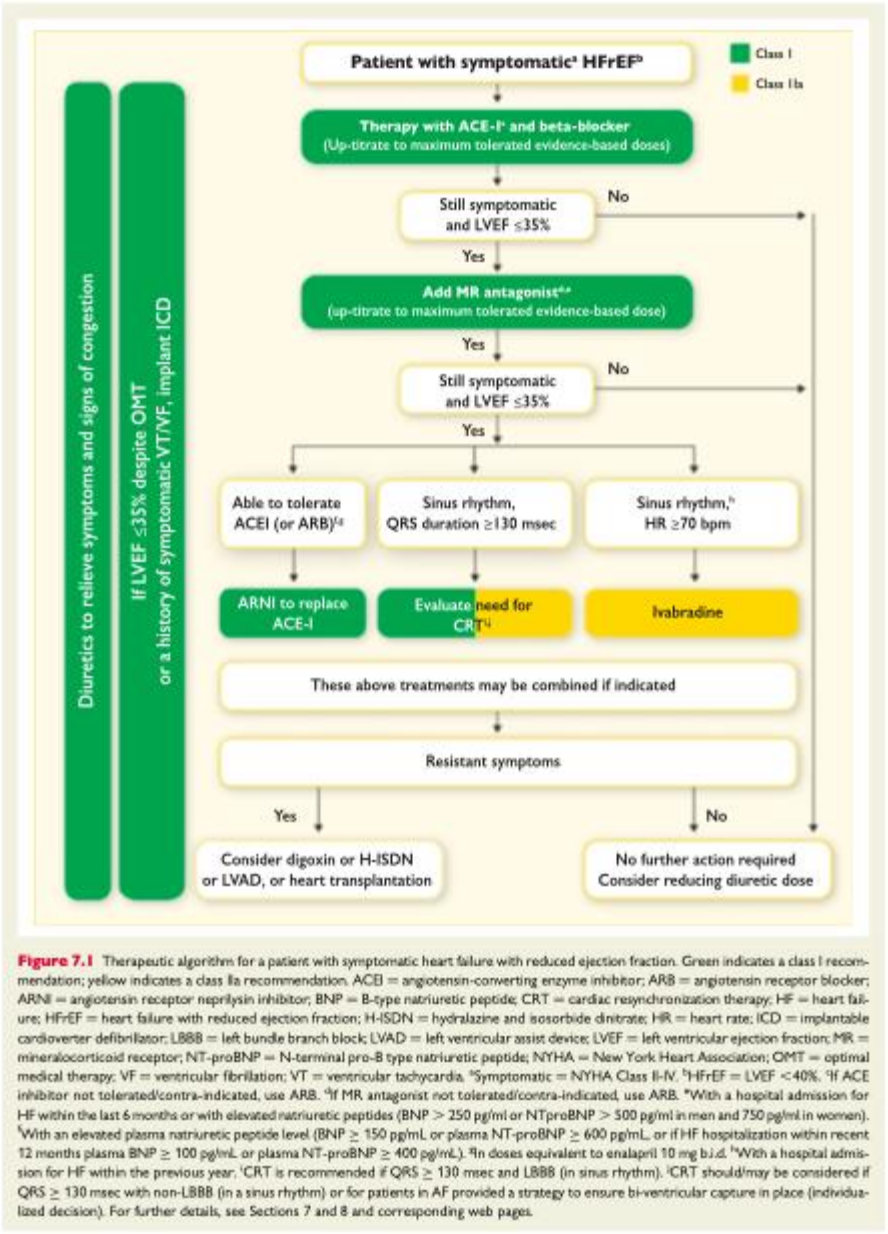


Figure 7.1 Therapeutic algorithm for a patient with symptomatic heart failure with reduced ejection fraction. Green indicates a class I recommendation; yellow indicates a class IIa recommendation. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; BNP = B-type natriuretic peptide; CRT = cardiac resynchronization therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; H-ISDN = hydralazine and isosorbide dinitrate; HR = heart rate; ICD = implantable cardioverter defibrillator; LBBB = left bundle branch block; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; MR = mineralocorticoid receptor; NT-proBNP = N-terminal pro-B type natriuretic peptide; NYHA = New York Heart Association; OMT = optimal medical therapy; VF = ventricular fibrillation; VT = ventricular tachycardia. [a]Symptomatic = NYHA Class II-IV. [b]HFrEF = LVEF <40%. [c]If ACE inhibitor not tolerated/contra-indicated, use ARB. [d]If MR antagonist not tolerated/contra-indicated, use ARB. [e]With a hospital admission for HF within the last 6 months or with elevated natriuretic peptides (BNP > 250 pg/ml or NTproBNP > 500 pg/ml in men and 750 pg/ml in women). [f]With an elevated plasma natriuretic peptide level (BNP ≥ 150 pg/mL or plasma NT-proBNP ≥ 600 pg/mL, or if HF hospitalization within recent 12 months plasma BNP ≥ 100 pg/mL or plasma NT-proBNP ≥ 400 pg/mL). [g]In doses equivalent to enalapril 10 mg b.i.d. [h]With a hospital admission for HF within the previous year. [i]CRT is recommended if QRS ≥ 130 msec and LBBB (in sinus rhythm). [j]CRT should/may be considered if QRS ≥ 130 msec with non-LBBB (in a sinus rhythm) or for patients in AF provided a strategy to ensure bi-ventricular capture in place (individualized decision). For further details, see Sections 7 and 8 and corresponding web pages.

3. <u>Patient with confirmed diagnosis CHF without reduced ejection fraction flowchart.</u>

REVIEW/CORRECTION?: This flowchart includes the recommendations 1.7.1,1.7.2, 1.7.3 and 1.7.4 from NICE guideline. These recommendations are for all patients, all types of heart failure. In this case, this flowchart could be adapted starting from Heart

Failure and then renamed as Monitoring treatment for all types of heart failure. How do you see it?
SUGGESTION: To create a new flow chart with recommendations of managing and monitoring treatment for all types of heart failure. Find below the NICE guideline sections suggested to be included.

1.6 Managing all types of heart failure

Diuretics.

1. *Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in people with heart failure, and titrated (up and down) according to need following the initiation of subsequent heart failure therapies. [2003]*
2. *People who have heart failure with preserved ejection fraction should usually be offered a low to medium dose of loop diuretics (for example, less than 80 mg furosemide per day). People whose heart failure does not respond to this treatment will need further specialist advice. [2003, amended 2018]*
3. *Avoid verapamil, diltiazem and short-acting dihydropyridine agents in people who have heart failure with reduced ejection fraction. [2003, amended 2018]*

Amiodarone

1.6.4 Make the decision to prescribe amiodarone in consultation with a specialist. [2003]

1.6.5 Review the need to continue the amiodarone prescription at the 6-monthly clinical review. [2003, amended 2018]

Vaccinations

1.6.9 Offer people with heart failure an annual vaccination against influenza. [2003]

COMMENT: It is the same for COPD patients, so it will be recommended for all ADLIFE patients.

1.6.10 Offer people with heart failure vaccination against pneumococcal disease (only required once). [2003]

Lifestyle advidce p18.

Salt and fluid restriction.

, Smoking and alcohol

7. *Monitoring treatment for all types of heart failure:*

1.7.1 All people with chronic heart failure need monitoring. This monitoring should include:

- *a clinical assessment of functional capacity, fluid status, cardiac rhythm (minimum of examining the pulse), cognitive status and nutritional status*
- *a review of medication, including need for changes and possible side effects*
- *an assessment of renal function[2]. [2010, amended 2018]*

1.7.2 More detailed monitoring will be needed if the person has significant comorbidity or if their condition has deteriorated since the previous review. [2003]

1.7.3 The frequency of monitoring should depend on the clinical status and stability of the person. The monitoring interval should be short (days to 2 weeks) if the clinical condition or medication has changed, but is needed at least 6-monthly for stable people with proven heart failure. [2003]

1.7.5 Consider measuring NT-proBNP (N-terminal pro-B-type natriuretic peptide) as part of a treatment optimisation protocol only in a specialist care setting for people aged under 75 who have heart failure with reduced ejection fraction and an eGFR above 60 ml/min/1.73 m2. [2018]

OTHER SECTIONS FROM NG106 TO BE CONSIDERED AS RECOMMENDATIONS FOR HF PATIENTS IN ADLIFE:

-1.9 Cardiac rehabilitation:

LOCAL DEVIATION: Physical exercise programs are more structured and not as well developed in our environment as post infarction rehabilitation..

-1.10 Palliative Care

-1.1 Team working in the management of heart failure

4. *The primary care team: recall the person at least every 6 months and update the clinical record. Arrange access to specialist hear failure services if needed.*

1.1.6 Care after an acute event: The primary care team should take over routine management of heart failure as soon as it has been stabilised and its management optimised. [2018]

Writing a care plan: 1.1.7 The specialist heart failure: diagnosis and etiology, medicines prescribed, monitoring when should be reviewed and any support the person needs. Functional abilities and social circumstances

A.4 Local CRG documents for single guidelines not included as local deviations

The DoA clarifies that NICE guidelines should be reference guidelines for the work in ADLIFE and also that creation of new guidelines or improvement of existing guidelines is not within the scope of the tasks. If local guidelines call for adaptations of the reference guidelines these requested adaptations are listed after each corresponding flowchart. Some of the material from the CRGs are complementary or describe improvements of the guidelines but outside the scope of ADLIFE. Such material is presented under this section of the Appendix. In section A.2.2 can also an example of how the work towards finalisation of flowcharts have been done. There, input from a local Clinical Reference Group on an initially proposed flowcharts can be found.

A.4.1 COPD

OSAKIDETZA provided some suggestions not included as local deviations and some references enclosed below.

COPD guidelines review by Osakidetza

This document shows the review of Osakidetza on the COPD flowcharts developed after the analyses of COPD guideline in the ADLIFE project. The review includes local deviations in

the Osakidetza general practice and suggestions for the inclusion of sections of the guideline not addressed in the current diagrams that we consider of interest when we think of an ADLIFE patient. In the latter, references to the specific pages of the guidelines are provided. The aim of these suggestions is to be considered by the pilot site responsible for the initial analyses of the guideline and further discussed, if considered.

GUIDELINES USED IN OSAKIDETZA

In Osakidetza the guidelines more used are GoLD (last version 2021) and GesEPOC (last version 2017).

The Spanish guidelines differs from the GoLD in the COPD classification. They define four fenotypes but the global treatment seems similar.

COPD FLOWCHARTS REVIEW:

Exacerbation and pharma treatment flowchart

SUGGESTIONS: Add some recomendations such as:

- When is indicated to use antibiotics: when the colour and the volume of the plemgh changes, more disypnea (pages 38-42 Pocket GOLD 2021)
- No more thant 5-7 days (pages 38-42 Pocket GOLD 2021)
- BDLD if the patient already uses them, during exacerbation they have to continue (pages 38-42 Pocket GOLD 2021)
- Tromboembolic venose profilaxys (heparine) in severe exacerbations (pages 38-42 Pocket GOLD 2021)
- Sistemic corticosteroids: No more than 5-7 days (pages 38-42 Pocket GOLD 2021).

Management of COPD flowchart

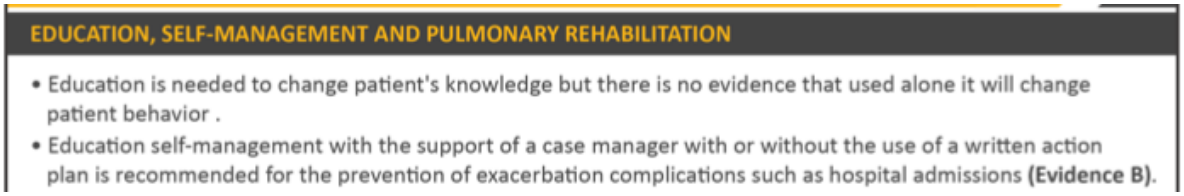
SUGGESTION: Inclusion of education self-management programmes could be considered. There is evidence in the literature about how these programmes can reduce hospital admission and quality of care.

IN GES EPOC it is explained in page 40 (see table 2 in Spanish).

Tabla 2
Aspectos que debería incluir un programa de educación terapéutica

- Conocer la enfermedad
- Asegurar la administración del tratamiento de forma correcta
- Saber identificar de forma temprana las exacerbaciones y saber cómo actuar
- Incorporar y mantener un estilo de vida con los cambios recomendados
- Evitar comportamientos de riesgo
- Acudir a las citas programadas
- Conocimiento y control de las comorbilidades
- Tener una actitud proactiva

In GoLD it is commented in page 35. And it can also be seen in tables in page 22 and page 37. *In GOLD refers to evidence B.*



EDUCATION, SELF-MANAGEMENT AND PULMONARY REHABILITATION

- Education is needed to change patient's knowledge but there is no evidence that used alone it will change patient behavior .
- Education self-management with the support of a case manager with or without the use of a written action plan is recommended for the prevention of exacerbation complications such as hospital admissions **(Evidence B)**.

5. Treatment at home or hospital flowchart

In Osakidetza we have a good Hospital at Home service, so this alternative permit to avoid hospital admission in some cases.
In COPD patients with palliative needs the main goal is symptoms control. In that case even with signs of alert we can offer hospital at home if the patient and his family desire that.

GENERAL COMMENT

To take into consideration the specially recommendations for COPD patients and COViD, as described in GOLD guidelines (last version 2021).

OVERALL KEY POINTS:

- *Patients with COPD presenting with new or worsening respiratory symptoms, fever, and/or any other symptoms that could be COVID-19 related, even if these are mild, should be tested for possible infection with SARS-CoV-2.*
- *Patients should keep taking their oral and inhaled respiratory medications for COPD as directed as there is no evidence that COPD medications should be changed during this COVID-19 pandemic.*
- *During periods of high prevalence of COVID-19 in the community, spirometry should be restricted to patients requiring urgent or essential tests for the diagnosis of COPD, and/or to assess lung function status for interventional procedures or surgery.*
- *Physical distancing and shielding, or sheltering-in-place, should not lead to social isolation and inactivity. Patients should stay in contact with their friends and families by telecommunication and continue to keep active. They should also ensure they have enough medication.*
- *Patients should be encouraged to use reputable resources for medical information regarding COVID-19 and its management.*
- *Guidance for remote (phone/virtual/online) COPD patient follow-up and a printable checklist are provided.*

AMCA provided the following not included as local deviations.

AMCA CRG – COPD Guidelines and Flow Chart

Exacerbation and pharma treatment

For all 3 groups (mild and moderate in the community, severe in the hospital or ER) there needs to be a decision tree step before the recommendation for treatment – "Bacterial Infection- yes/no". Indications of bacterial infection are: increased shortness of

breath, coughing, change in the color of sputum – if all 3 are present – good chance of a bacterial infection in which case an antibiotic need to be prescribed in addition to SABDs for the mild exacerbation and in addition to SABDs and oral corticosteroids for the moderate exacerbation.

Vaccination Stable COPD
There is third option, which is to give both vaccines – so this should be added as an option. The following is a link to the CDC website, and we have extracted the relevant recommendations
(https://www.cdc.gov/pneumonia/prevention.html#:~:text=Two%20vaccines%20offer%20protection%20against%20pneumococcal%20disease%3A%20PCV13%20and%20PPSV23.&text=CDC%20recommends%20all%20adults%2065,get%20a%20shot%20of%20PPSV23.&text=CDC%20recommends%20adults%2065%20years,that%20weakens%20the%20immune%20system)
The CDC recommendations are as follows:

If you are recommended to or want to receive both vaccines:
Get PCV13 first. Talk to your doctor about when to come back to get PPSV23.
If you've already received PPSV23, wait at least a year after that shot before you get PCV13.)

Follow up table
Overall ok but it is using the Old Gold classification (stages 1-4) as opposed to the new GOLD (A-D) which is preferable. The old classification is based on clinical findings, severity and lung function test results. The new classification is based only on clinical findings and severity. If we were to use the new classification, we would have to do some reordering of the flow chart,
In Israel, we have been using the new classification for 5 years and it is preferred so we would reorder the flow chart for Israel to reflect this. Barak and Rachelle will ask the Consortium CRG What is happening in the other pilot sites countries? Are they using the new GOLD classification or the old? The answer will determine whether the flow chart should be changed for everyone or only for those pilot sites that have adopted the new GOLD.

A.4.2 Congestive heart failure (CHF)

USTRATH / Lanarkshire provides the following information not included as local deviations.

Chronic heart failure in adults: diagnosis and management NG 106
Scottish equivalent: SIGN 147 Management of chronic heart failure
https://www.sign.ac.uk/assets/sign147.pdf

CHF	Implantable cardioverter defibrillators, cardiac resynchronisation therapy with defibrillator or cardiac resynchronisation therapy with pacing are recommended as treatment options for patients with heart failure with reduced ejection fraction, LVEF ≤35%, as specified

If Sacubitril/Valsartan initiated (Entresto)	Entresto should not be co-administered with an ACE inhibitor or an ARB. Potential risk of angioedema when used concomitantly with an ACE inhibitor. It must not be started for at **least 36 hours** after discontinuing ACE inhibitor therapy
Other medicines beneficial in HF	**Dapagliflozin –** Indication: symptomatic chronic heart failure with reduced EF in adult patients

A.4.3 Diabetes mellitus type 2

USTRATH / Lanarkshire provides the following information not included as local deviations.

Scotland follows Sign guideline 116: Management of diabetes – A national clinical guideline https://www.sign.ac.uk/assets/sign116.pdf
Sign guideline 154: Pharmacological management of glycaemic control in people with type 2 diabetes https://www.sign.ac.uk/media/1090/sign154.pdf

DIABETES FLOWCHARTS	DEVIATIONS
DM 2 medication	Sulphonylureas may be established in some patient's groups already and can also be considered
Erectile dysfunction	Erectile function assessment International Index of Erectile Function _ patient questionnaire or Sexual Health Inventory for Men (SHIM) questionnaire Exclude other causes (hypogonadism) Diagnosis following assessment
Local approved formulary	https://www.medednhsl.com/meded/nhsl_formulary/index.asp?T=06&S=6.01

AMCA provides the following, not included as local deviations.

Review of AMCA on Diabetes flowcharts developed in ADLIFE

DIABETES FLOWCHARTS	DEVIATIONS
Foot problem organisation	We disagree with the need to write in details or determine to healthcare professionals what the treatment flowcharts would be.
Lipid lowering	Israel uses the Israeli guidelines, which are based on the European guidelines as a low risk country.

A.4.4 Hypertension

USTRATH / Lanarkshire provides the following information regarding a potential use of home monitoring of blood pressure not included as local deviations.

Hypertension diagnosis	Blood pressure home monitoring via app alled Florence (Flo) – during initial high

	BP reading (not yet confirmed hypertension, also for control of newly diagnosed HTN) – patient given equipment and supplies readings via app

OSAKIDETZA has provided the following information not included as local deviations.

OSAKIDETZA REVIEW ON CHRONIC KIDNEY DISEASE AND HYPERTENSION FLOWCHARTS IN ADLIFE PROJECT

FLOWCHARTS	NICE GUIDELINE: CHAPTER	DEVIATIONS IN BASQUE COUNTRY IN ADLIFE	HIGH PRIORITY FOR OSAKIDETZA
Hypertension overview	NG 136	This algorithm is difficult to follow. It is better to talk about BP numbers according to age or comorbidity. Summary table of the NICE-136-HTA CPG *See comment 1 below*	
Hypertension treatment_step 2_4	NG 136	*I think it is basically the same as ours, but I find it difficult to understand.*	

COMMENTS:

Hypertension overview Flowchart seems similar to ours (Figure 1), but the one from ADLIFE seems to be more difficult to follow.

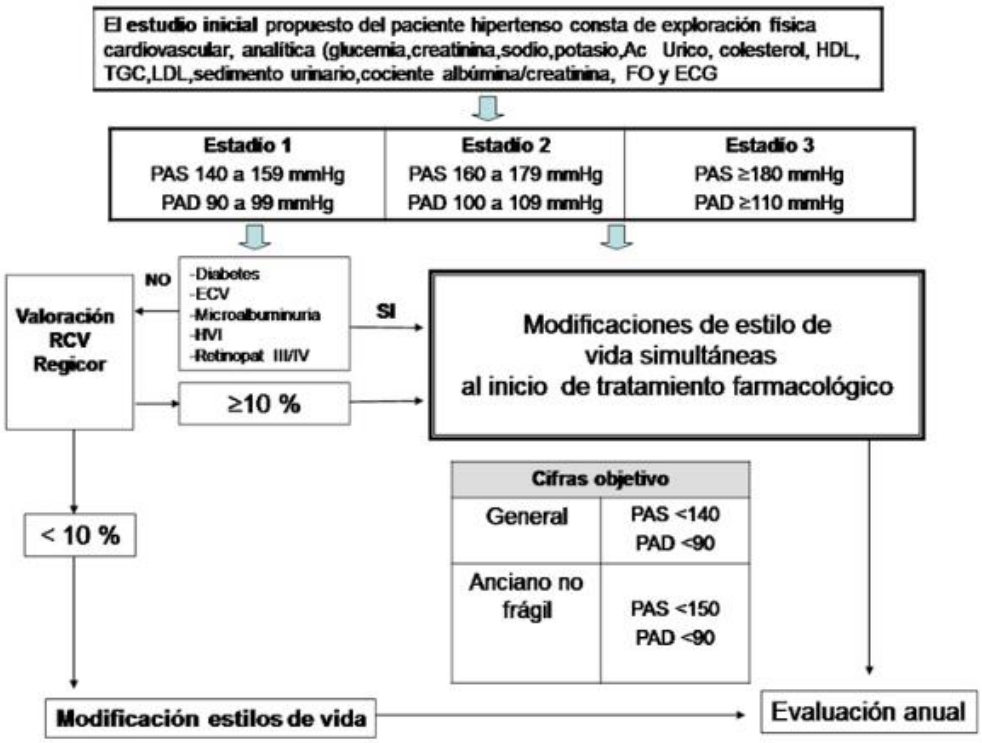


Figure 1. Proposed flow chart for the overview of hypertension in Osakidetza.

A.4.5 Lipid lowering

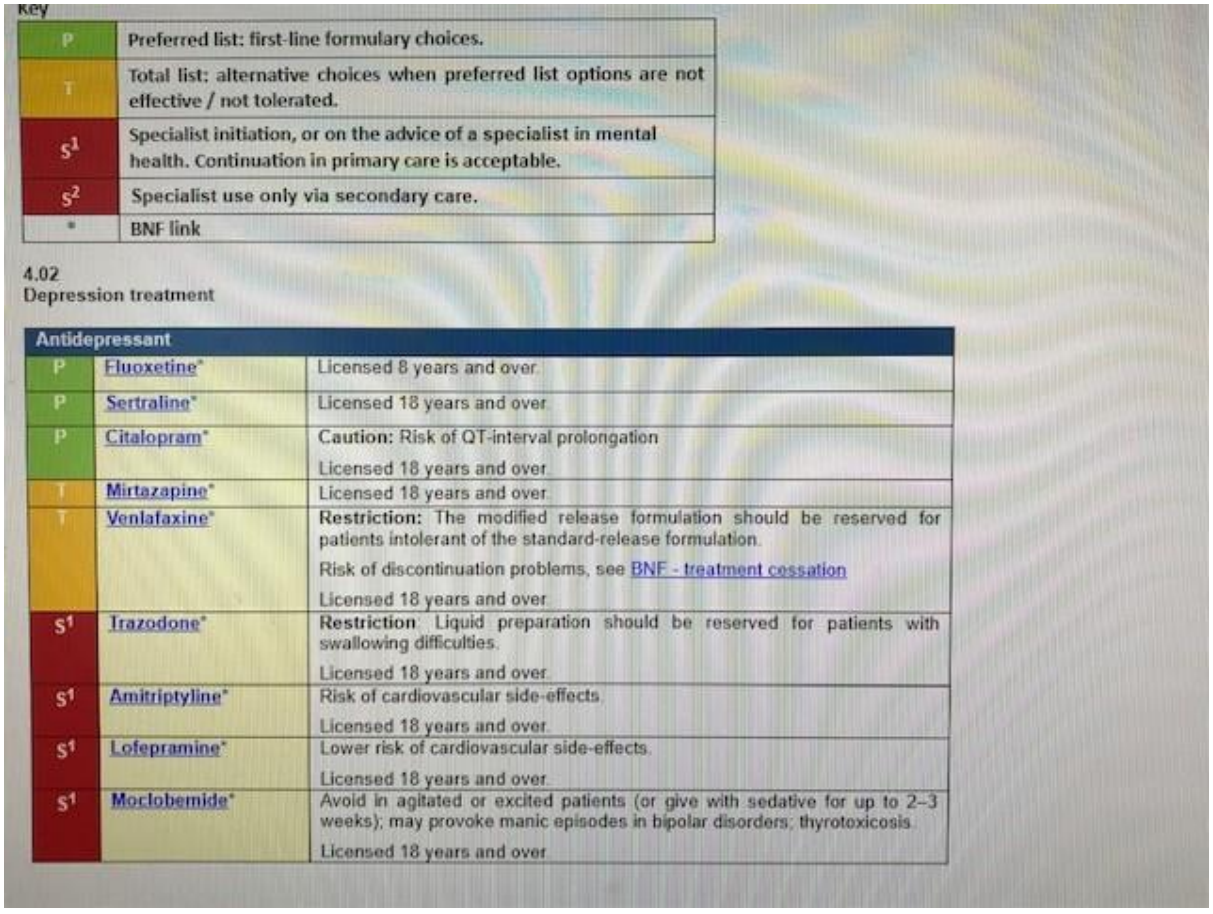
USTRATH / Lanarkshire provides the following information not included as local deviations.

Cardiovascular disease: risk assessment and reduction, including lipid modification CG181
Scottish equivalent: SIGN 149 Risk estimation and the prevention of cardiovascular disease
https://www.sign.ac.uk/media/1085/sign149.pdf

Lipid lowering therapy	Rules for different groups CVS risk CKD T2DM Pregnancy Existing atherosclerotic disease Familial hypercholersterolemia Agents

A.4.6 Depression

USTRATH / Lanarkshire refers to a local prescribing formula choices, enclosed.



Key

P	Preferred list: first-line formulary choices.
T	Total list: alternative choices when preferred list options are not effective / not tolerated.
S^1	Specialist initiation, or on the advice of a specialist in mental health. Continuation in primary care is acceptable.
S^2	Specialist use only via secondary care.
*	BNF link

4.02
Depression treatment

Antidepressant		
P	Fluoxetine*	Licensed 8 years and over
P	Sertraline*	Licensed 18 years and over
P	Citalopram*	**Caution:** Risk of QT-interval prolongation Licensed 18 years and over
T	Mirtazapine*	Licensed 18 years and over
T	Venlafaxine*	**Restriction:** The modified release formulation should be reserved for patients intolerant of the standard-release formulation. Risk of discontinuation problems, see BNF - treatment cessation Licensed 18 years and over
S^1	Trazodone*	**Restriction**: Liquid preparation should be reserved for patients with swallowing difficulties. Licensed 18 years and over
S^1	Amitriptyline*	Risk of cardiovascular side-effects. Licensed 18 years and over
S^1	Lofepramine*	Lower risk of cardiovascular side-effects. Licensed 18 years and over
S^1	Moclobemide*	Avoid in agitated or excited patients (or give with sedative for up to 2–3 weeks); may provoke manic episodes in bipolar disorders; thyrotoxicosis. Licensed 18 years and over

and to a booklet with information on treatment options including non-pharmacologic treatment https://www.sign.ac.uk/assets/pat114.pdf.

As diagnosis of depression is not within the scope of ADLIFE is a summary of practical aspects on diagnosis and treatment from the **OSAKIDETZA** perspective presented below.

PRACTICAL ASPECTS ADAPTATION TO OSAKIDETZA ENVIRONMENT

Diagnostic criteria and classification

- NICE decides in both guidelines for the DSM IV. While in our environment, we speak of the DSM V version and the ICD
- DSM_IV/V the person manifests a minimum of five symptoms, of which at least 1 must be depressed mood and/or decreased interest or pleasure in all or almost all activities for a period of at least 2 consecutive weeks.

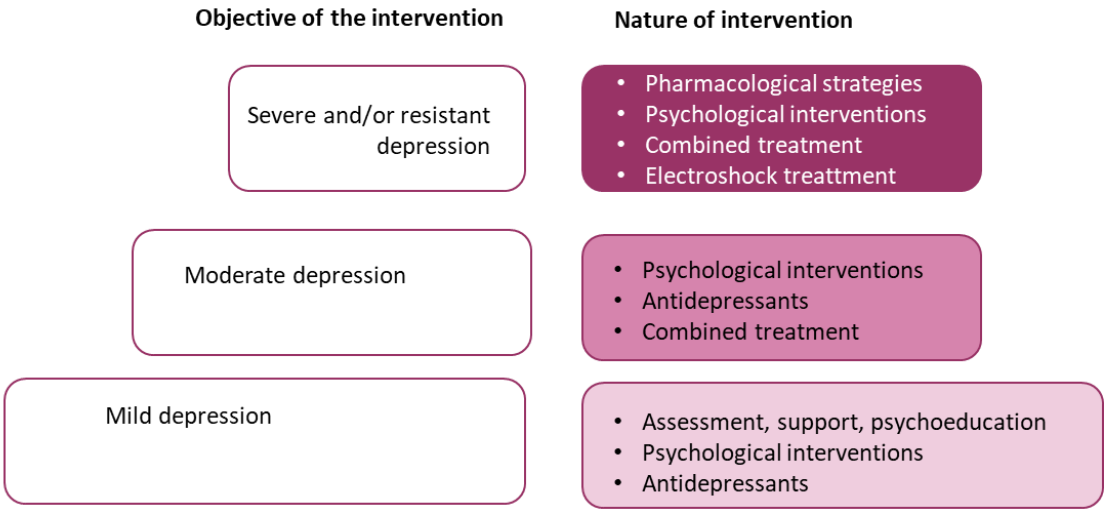
Five (or more) of the following symptoms must appear at the same time for two weeks, representing a change in the person's previous way of functioning that is seen in the depressed mood, or loss of interest in things, motivation or pleasure, in order to be determined to be a major depressive disorder:
1. A depressed mood should be noticeable for a large part of the day, almost every day.
2.There is a decrease in interest in the activities that used to generate this emotion, most of the day, most days.
3.Weight loss or weight gain.
4.Alterations in sleeping habits, such as insomnia or hypersomnia, almost every day.
5.Increased psychomotor agitation or slowing down, almost every day, observed by oneself and one's environment.
6.The person feels fatigued and/or lacking energy, almost every day.
7.Excessive feelings of guilt and worthlessness appear.
8.Difficulty in maintaining concentration or making decisions.
9.Recurrent thoughts of death, which may be suicidal ideation without a definite plan to carry it out, suicide attempts or meditations beforehand to carry out suicide.

ICD-11 diagnostic criteria
Depressed mood or lack of interest or pleasure in doing activities that were normally pleasurable, or both symptoms at the same time, lasting 2 weeks or more with sufficient intensity each day. The other symptoms accompanying these would be used to assess severity without requiring a specific number:

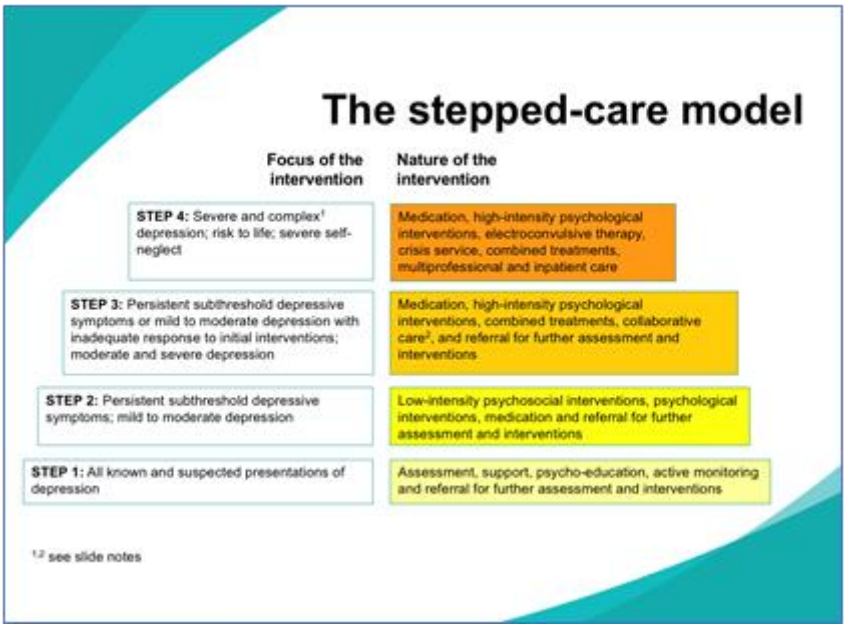
- Feelings of worthlessness or excessive or inappropriate guilt.
- Low self-confidence.
- Hopelessness, recurrent ideation of death or suicide.
- Changes in appetite or sleep.
- difficulty concentrating
- Asthenia, lack of energy or fatigue.

All of the above, without previous manic, hypomanic or mixed episodes that may indicate bipolar disorder.

Stepwise model in the management of depression in Osakidetza



NICE stepwise model



Non-pharmacological interventions in our setting are not available in many cases and in practice involve referral to mental health services, so that everything related to the frequency and combination of the different therapies could not be applied.

Practical aspects of considering depression in the ADLIFE project

- Since screening for depression in COPD/IC patients is mandatory, the initial global assessment of the patient should record whether he/she is already diagnosed with depression and in case of a negative response, screening should be carried out. If this is positive, the patient is classified by grade, which determines the treatment and follow-up plan.

- The most important alarms are the risk of suicide.

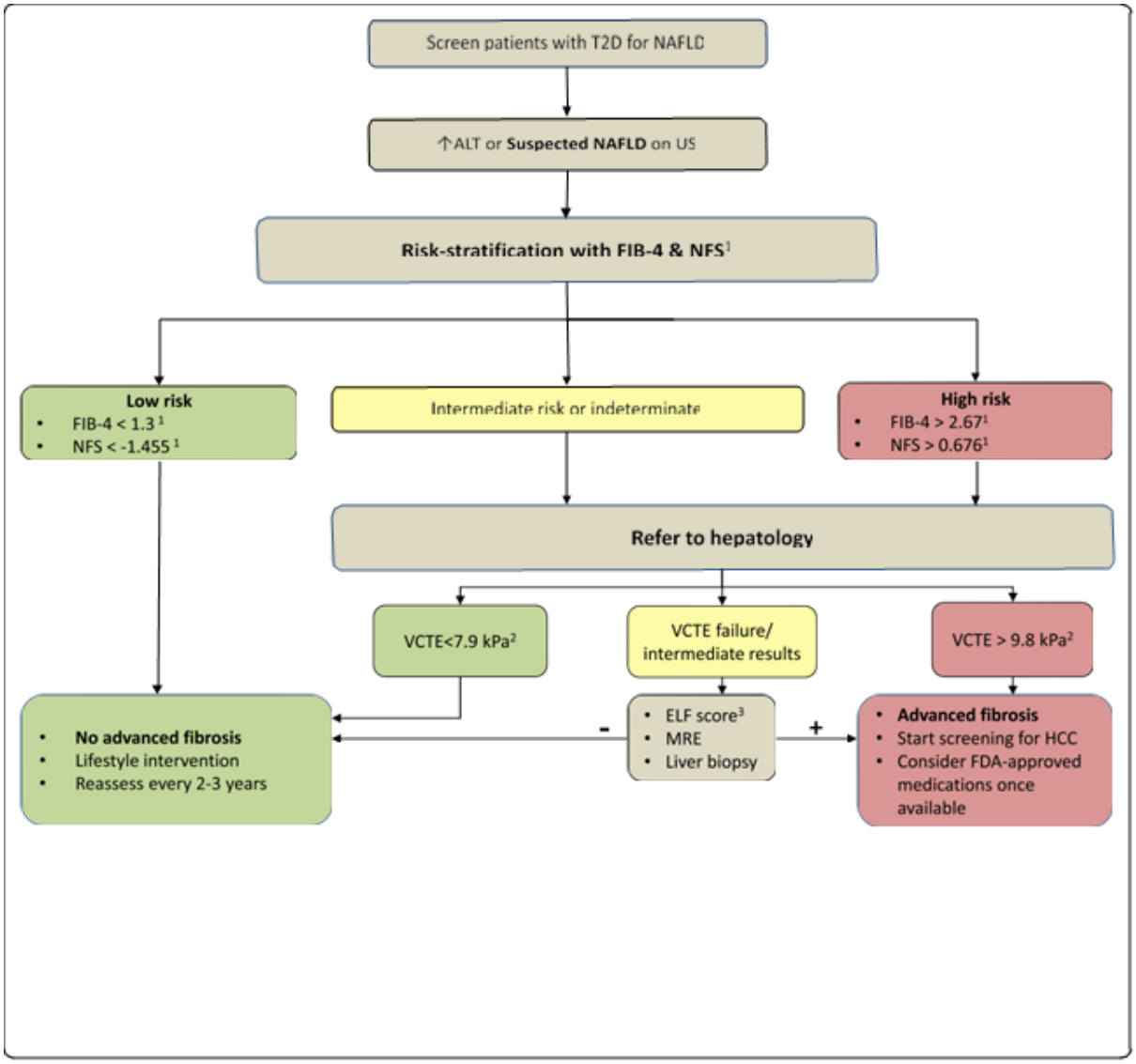
- In the case of exacerbations of the basic pathologies in which dyspnoea or asthenia predominate and the patient has a diagnosis of depression or this is suspected, it will always be an alternative to consider (illness/disease interaction).

- Treatment of depression leads to:
    - Drug-disease interactions:
        - Drugs with a sedative effect increase dyspnea in the advanced stages of COPD and HF.
        - Arrhythmogenic capacity of antidepressants
    - Drug-to-drug interactions
        - Increased bleeding risk of SSRIs and antiplatelet agents
    - Interactions with anticoagulants
    - Other interactions

A.4.7 Cirrhosis

This section is presented in the figures 41 where further information on flowcharts and included local deviations can be found.

USTRATH / Lanarkshire locally promotes the following screening pathway for patients with co-existing Type 2 diabetes mellitus.



A.4.8 Terminal care

This section is presented in the figures 42-48 where further information on flowcharts and included local deviations can be found.

USTRATH / Lanarkshire uses the Scottish palliative Care Guidelines https://www.palliativecareguidelines.scot.nhs.uk/ with a summary presented below.

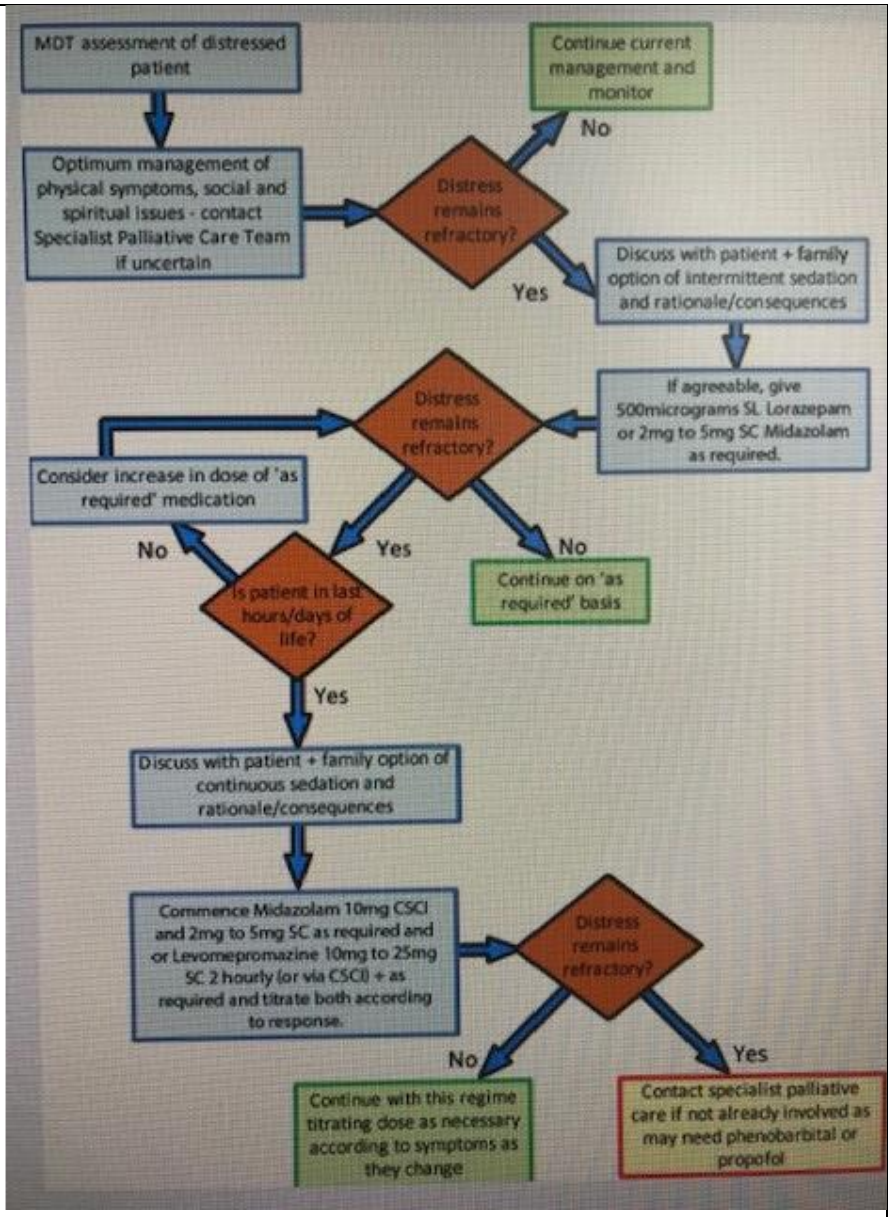
Managing breathlessness

Any actions should prompt review ie. treat & review, start oxygen & review.

Managing anxiety, delirium and agitation

Assessment – consider causes	drugs (opioids, anticholinergics, corticosteroids, benzodiazepines, antidepressants, sedatives), drug withdrawal (alcohol, sedatives, antidepressants, nicotine), dehydration, constipation, urinary retention, uncontrolled paint, liver or renal impairment, electrolyte disturbance (sodium, glucose), hypercalcaemia, infection, hypoxia, cerebral tumour or cerebrovascular disease, visual impairment and deafness, differential diagnosis: depression, dementia

Investigations	full blood count and biochemistry incl. calcium, check for infection (urine), review all medication and stop any non-essential drugs, assess for sensory impairment, check for opioid toxicity (drowsiness, agitation, myoclonus, hypersensitivity to touch), reduce opioid dose by 1/3rd, consider switching to another opioid if delirium persists, check for constipation, urinary retention or catheter problems
Management	Treat underlying causes If terminal delirium refer to last days of life guideline Maintain hydration, oral nutrition and mobility If nicotine dependent, consider using replacement patches
Non-pharmacological management	Explain cause to patient, relatives and carers Address anxiety Environmental factors/stimulation (lightning, noise, position, reorientation) Try to maintain normal sleep-wake cycle Explain the organic cause of behaviour and symptoms
Medication	Review regularly and withdraw medication as soon as the patient recovers 1/ haloperidol (500mcgs – 3mg oral or subcutaneous once daily, repeat after 2 hours if necessary. Maintenance treatment may be needed if cause cannot be reversed, use lowest effective dose. 2/ benzodiazepines do not improve cognition, may help anxiety, use with caution, used in alcohol withdrawal, sedative and antidepressant withdrawals, preferred in Parkinson's disease. Lorazepam 500mcgs to 1mg oral or sublingual, Midazolam subcutaneous 2mg-5mg 1-2hrly or diazepam orally or rectally (5mg 8-12 hrly) If increased sedation is desirable and appropriate seek specialist advice
Practice Points	Attention to environment Opioid toxicity is a common cause of delirium, particularly in the elderly Corticosteroids can cause florid delirium The Adults with Incapacity (AWI) Act covers the medical treatment of patients with cognitive impairment, completion of AWI and care plan will be required In acute situation emergency treatment can be given without AWI Encourage oral fluids if able Relative or friend support
Severe uncontrolled distress	https://www.palliativecareguidelines.scot.nhs.uk/media/71364/2019-distress-flowchart.png



Management of respiratory tract secretions

Non-pharmacological management	Reduce risk by avoiding fluid overload: review any assisted hydration or nutrition (IV/SC fluids/feeding) Position changing – head down or lateral positions
Medication	Intermittent SC injection works or SC infusion (be aware of dry mouth – apply mouth care guideline) Fist line: hyoscine butylbromide 20mg SC hourly PRN (up to 120mg/24hrs) Second line: glycopyrronium bromide 200mcgs SC, 6-6 hourly PRN Third line: hyoscine hydrobromide 400mcgs SC, 2 hrly PRN

A.4.9 Supporting adult carers

This section is presented in the figure 50 where further information on flowcharts and included local deviations can be found.

Here **USTRAT / Lanarkshire** refers to that the NICE guidelines NG150 refers to England and their Carer Act 2014 while for Scotland corresponding legislation is the Carers (Scotland) Act 2016. This is not included as a local deviation as the mapping purposely omitted references to a single country.

A.5 Analysis of single clinical guidelines – work description

Here an information document to CRGs is presented.

T6.2 Analysis 1: single clinical guidelines

Scope and content of ADLIFE Clinical Decision Support Services

The CDSS will provide information about two main diagnoses in their most severe stages, COPD and CHF, including common comorbidities as diabetes, chronic renal failure, chronic hepatopathy, stroke, cognitive disorder, and depression. Limitations are shown in table 1. Since ADLIFE is C3 Cloud-based, a lot of material can be re-used. Still, new ADLIFE perspectives must be considered, as early warning signs (EWS) and adaptive interventions used in the patient empowerment platform (PEP).

The scope of the CDSS is limited as follows:

Diagnosis	Limitation
Overall	Patients over 55 years
COPD	FEV1<50, >2 GOLD scale
CHF, hypertension	Heart failure in functional stage III/IV according to the NYHA scale and stages C and D of the ACCF/AHA classification, stable phase (at least two months without decompensation). Acute heart failure will not be included.
Diabetes	Diabetes type 2 only.
Chronic renal failure	Both mild/moderate (GFR 30-59 ml/min) and severe stage (GFR 15-29 ml/min). GFR <15 ml/min will not be included.
Chronic hepatopathy	Mild/moderate stage. Will be analyzed reconciled with CHF only. *Focus on medications, nutrition, and alcohol.*
Stroke	Will be analyzed regarding EWS and reconciled with COPD/CHF only. *Focus on how post stroke symptoms impact care of COPD/CHF: nutrition, depression, and physical activity.*
Cognitive disorder	Will be analyzed as single guideline, not reconciled with others.
Depression	Mild/moderate stage. Will be analyzed as single guideline, not reconciled with others
Terminal care	Will be analyzed as single guideline, not reconciled with others.

Table 1: Scope of CDSS

Reference guidelines

According to the project proposal, the reference guidelines will be the NICE and GOLD guidelines. Suggested guidelines are shown in table 2. The responsible pilot sites can add other guidelines, and local reference guidelines will also be considered.

Responsibilities of CRG

The analyze work of the single guidelines will be divided between the pilots as suggested in table 2. The review will be done from both medical and caring perspective including physical,

psychological, social, and spiritual aspects, why it is important that the local CRG includes both general practitioners, nurses, and specialists.

Single guidelines (n=10)	Clinical review	Technical implementation	Due date step 1 and 2
COPD (NG115, GOLD)	OUH	Warwick	M12
CHF* (NG106, CG181, NG136)	Optimedis	Warwick	M10*
Depression* (CG90, CG91)	KG	Warwick	M10*
Diabetes* (NG28, NG19, CG173)	RJH	SRDC	M10*
Chronic renal failure* (CG182, NICE pathways)	RJH	SRDC	M10*
Chronic hepatopathy (NG50, NG49)	Strathclyde	Warwick	M12
Stroke (CG162, NG128)	AMCA	EVERIS	M12
Mild cognitive disorder (NG16, NG97)	AMCA	EVERIS	M12
Terminal care, care of elderly (NG142, NG22, NG31)	KG	SRDC	M12
Supporting carers (NG150)	Falkievitz	SRDC	M12

*Table 2: shared responsibility between pilots – single guidelines. More guidelines can be added, e.g. guidelines for nurses. *already done in C3 Cloud, to be validated.*

Work plan step 1: review single guidelines

The diagnoses are first reviewed one by one. By detailed analysis of the texts the CRG will study the assigned guidelines (linked in table 2, also downloaded at Sharepoint T6.2) and select **what is relevant to include in the CDSS**. They will also review any flowcharts that may be included in the guidelines, since they will be a good help in developing the ADLIFE flowcharts in Modelio in step 2.

As for the guidelines previous studied in C3Cloud, they both need to be updated to today's date, but also include new ADLIFE perspectives: severity and new sections (red and grey).

1. **Mark sections to be included in the CDSS** by six different colors following this scheme:
   - Yellow: diagnostic recommendations,
   - Blue: medication and other therapeutic recommendations,
   - Green: recommendations of monitoring and follow-up,
   - Purple: possible interactions with other guidelines, including comorbidities
   - Red: early warning signs, estimation of risk and poor evolution (EWS),
   - Grey: adaptive interventions (JITAI, PEP)

2. **Summarize** the result of the reviewed guidelines in the spreadsheet "List of proposed single flowcharts ADLIFE CDSS" with reference to the original clinical guideline/chapter for validation. Each diagnosis has its own tab, add subject(s), source(s) and type of purpose. The spreadsheet, including examples from C3 Cloud, is uploaded on SharePoint, T6.2.

3. **The CRGs will make a joint agreement** of what recommendations should be forwarded to step 2 (column "in/out of scope"). Those considered outside the project scope will not be made into flowcharts.

4. **On the agreed recommendations, each CRG will comment** on the other pilots' tabs if their region uses other recommendations than mentioned in the guidelines which must be considered in the final CDSS. Minor differences should not be addressed (columns "regional adaptions").

Work plan step 2: develop flowchart diagrams


Each pilot site will develop if-else-then programming flows structured in decision trees for their diagnoses, with help and feedback from technical partners. Examples from C3 Cloud is uploaded on Sharepoint, T6.2. Be sure to use the decided symbols for start , stop and decision Yes/No

Upload the finished flowcharts on SharePoint, T6.2.

Time plan

M10 2020-10-31 Step 1 and 2 done for the single guidelines from C3 Cloud
M12 2020-12-31 Step 1 and 2 done for new single guidelines

Further work

The work will proceed according to the next manual: "Analysis 2 reconciled clinical guidelines".

A.6 Analysis of reconciled guidelines – work description

Here information material to the CRGs is presented.

T6.2 Analysis 2: reconciled clinical guidelines

Previous work

The initial work of T6.2, including scope, limitations and work plan step 1 + 2, is described in the manual "Analysis 1: single clinical guidelines"
Single diseases flowcharts and information can be extracted from ADLIFE flowcharts.

Work plan step 3: review reconciled guidelines

After the analysis of single guidelines, the agreed recommendations will be reconciled to see how they influence each other. Based on table 3, each CRG reviews the flowcharts for their assigned diseases and combination of diseases. Not all combinations will be computerized, limitations can be seen in table 1 in the previous manual.
In ADLIFE the multimorbidity scope targets the following conditions: COPD, CHF, Diabetes, Renal Failure (RF), Hepatopathy, Stroke and Depression, 7 in total. Special consideration is going to be provided to high blood pressure.
Taking into account the selected diseases, the overall work addresses 17 patterns of comorbidity, generated by the combination of the target conditions.

Reconciled guidelines (n=17)		
Two diagnoses	**Three diagnoses**	**Four diagnoses**
COPD + CHF *(OUH)*	COPD + CHF + Diabetes *(KG)*	COPD + CHF + Diabetes + RF *(RJH)*
COPD + Diabetes *(RJH)*	COPD + CHF + RF *(KG)*	
COPD + RF *(OUH)*	COPD + CHF + Stroke *(AMCA)*	
COPD + Stroke *(AMCA)*	COPD + Diabetes + RF *(RJH)*	
CHF + Diabetes* *(OM)*	CHF + Diabetes + RF* *(RJH)*	
CHF + RF* *(OM)*	CHF + COPD + Depression *(KG)*	
CHF + Hepatopathy *(Strat)*		

CHF + Stroke *(AMCA)*		
CHF + Depression *(KG)*		
COPD + Depression *(KG)*		

*Table 3: shared responsibility between pilots – reconciled guidelines. *already done in C3 Cloud, to be validated.*

1. **Study the summary** of guidelines on SharePoint ("List of proposed flowcharts ADLIFE CDSS") and the developed flowcharts, looking for possible interactions and conflicts between single recommendations. Select the critical issues where interactions can occur and we want to address and reconcile. We have to focus on a few conflicts/constraints taking into account the effects of the interaction (symptoms, safety and potential harm). They include establishing the risk of the patient, setting goals, defining activities for the care plan or the pharmacological treatment. Issues to consider:
    - Type of interactions: Disease Disease; Disease to drug; Drug to disease:
        i. Disease-Disease interaction: The presence of a disease is a risk factor to develop comorbidity or when it is already, it worsens its prognosis (i.e. RF increases the risk of developing HF but if RF and HF both are present, HF has a worse prognosis) or both diseases overlap their symptoms (Asthenia as a symptom in a person with heart and renal failure) or may interfere with the diagnosis by altering lab tests results.
        ii. Disease to Drug/ Drug to disease interactions: The presence of a second disease (i.e. nephropathy) determines some type of contraindication, interaction or dose adjustment in people who need pharmacological treatment (Drug) derived from their index disease (i.e. diabetes) or its complications (i.e. complications Micro / macro of diabetes). Pharmacological treatment of comorbidity (i.e. nephropathy) conditions the evolution of the index disease (i.e. diabetes)
        iii. Drug-drug interaction will be dealt separately.
    - Possible conflicts: repetition; wrong sequence or overlaps; contradictory goals or activities; inconsistencies; constraints and potential synergies both in care and pharmacological treatment.
        i. Examples of conflicts include:
            1. Overlaps (medication, tasks, …)
            2. Wrong sequence of activities
                a. Detected based on the timestamps for each activity
            3. Medication interactions
                a. Check drug interactions database (requires connection of the decision support modules to the DB)
            4. Location inconsistencies
                a. (e.g., home hospitalisation vs. hospital admission)
    - Critical issues: Severity and stage classification (functional assessment); interventions on lifestyles, training, and self-care (JITAI, risk prediction); pharmacotherapy and follow-up plan.

2. **When conflicts are identified,** adjust the evidence based clinical guidelines recommendations to mitigate the conflict and develop reconciled rules. To make new modified recommendations, use available knowledge and some of these means:
    - Select one of the recommendations before the other,
    - Merge the recommendations to a joint one,
    - Remove the recommendation,
    - Substitute or modify the recommendations with extra input and output.

For this, a template (Table 4) for each combination of diseases to be reconciled (i.e. COPD + CHF) is provided on SharePoint ("Template reconciled

guidelines ADLIFE CDSS"), where the selected interactions lead to new rules. The template (one tab for each combination) includes examples from C3 Cloud.

A.7 Guide for CRGs to develop PPS

A guide for CRGs for the development of PPS is enclosed below.

GUIDE TO DEVELOP PPS

Introduction

This guide aims to define Potential Preventable Situations (PPS) and identify data that could alert the upcoming situation while it is still is preventable. In a later stage the technological partners, with the use of AI on anonymized real EHR data, will develop algorithms and computerise them.

To do the work required in each step, you have to use to documents linked to this guide:

- "STEP1_PreventableSituations (Annex 1)
- "STEP2_PPS_traceable data template (Annex 2)"

Scope:

On February 23, the scope of PPS was accepted by the CRG. It includes the following events: Preventable admissions, re-admissions, increase dependency need, malnutrition, and depression/anxiety. We need to define the PPS in a clear and identifiable way. Each of them can cover different clinical situations, defined by different diagnosis (ICD codes) or even by drug prescriptions (ATC codes). We need to review the definitions provided, add or delete codes to the different PPS so that they can be complete and easily computerized. Next, we need to describe the EHR data that may indicate in advance the risk of occurrence for each of the PPSs. In other words, the signs of evolving care needs have to be associated with EHR data.

Process:

Step 1:

These PPS (avoidable admission, dependency, malnutrition, depression/anxiety, hypotension), what different clinical events can cover? How can we identify them: ICD codes, a specific prescription (ATC code), other…?

- To work on **step 1** "to identify the preventable situations": add events, remove events proposed in the template provided in Annex 1 ("STEP1_PreventableSituations")
    - Please complete and send your results to RJH **no later than April 6th**

Step 2:

What EHR traceable data (measurements, test results (threshold values or delta value = trend), diagnosis) could potentially be used to early identify that a PPS will occur?

- To work on step 2 "To identify the ways of measuring the signs/indications of evolving care needs from longitudinal EHR data" and completing for **each PPS** the template provided in Annex 2 ("STEP2_PPS_traceabledata_templates)"
    - Please complete a template per PPS and send them to RJH **no later than April 20th**

Step 3:

For each preventable care need, estimate the duration for early action window. How early does the care provider need to receive a signal that a risk situation may arise?

- INSTRUCTIONS TO BE PROVIDED ON APRIL 20
    - Compilation of your results to RJH **no later than April 27th**

Please upload your revised and completed templates to the PPS folder on SharePoint. It can be found under WP6 - Clinical Reference Group- Working docs – PPS definition
NB! It´s important that the work not will be delayed in relation to the time plan, as the result of the work must form the basis for technical solutions in ADLIFE.

Sidbrytning

Annex 1: Definition of Preventable Situations

PPS	AVOIDABLE ADMISSION	RE-ADMISSION	DEPENDENCY	MALNUTRITION	DEPRESSION /ANXIETY
CLINICAL SITUATIONS	Z60.* Problems related with social environment *Early action window – at reporting – cannot always be predicted and can arise suddenly*	Admission that occur within 30 days after previous discharge from hospital with no visit to primary/specialized care within two weeks from previous discharge (is 30 days too long a gap??? shorten the period for association with 'failed discharge'). *Early action window – at reporting, cannot always be predicted and can arise suddenly.*	Rehabilitation care: ICD10 Z50 Care involving rehabilitation procedures Rehabilitation admission Reduction in function . Change in cognition. *Early action window: self-reporting of activity, if below achieved and agreed activity level (personalised care plan) to prompt review (1 week of reduced level?)*	R64 Cachexia *Early action window - ? personalised care plan to include fluid and diet plan – self reported and weight monitoring. Early alarm at agreed % of weight loss??*	ICD10 F41.2 Mixed anxiety and depression disorders *Early action window???*
	W19.* Fall, falling (accidental) *Early action window: self-reporting of activity, if below achieved and agreed activity level (personalised care plan) to prompt review (1 week of reduced level?)*	…….	Transition from not having to having caregiver Carer stress – not coping – loss of caregiver Delay in access to equipment to ensure safety at residence	D50 Iron deficiency anaemia	Social problems, social isolation
	Z91.8 At risk for fall (history of fall) *A/A*		Zarit score 41 - 60 moderate to severe burden 61 - 88 severe burden	D51 Vitamin	Antidepressants prescriptions

	M80 Osteoporosis with pathological fracture		Institutionalization (nursing home) Delay in decisions in relation to preferred/most appropriate plac e of care	B12 deficiency anaemia	…….
	…….		ICD10 Z51.10 Palliative patient	D52 Folate deficiency anaemia	
			Visits to specialized palliative units	D53.9 Nutritional anaemia, not specified	
			Total, severe dependency scores in Barthel or Lawton	Additional malnutrition codes...	
			Diagnoses for cognitive impairment, diagnosis of dementia, Alzheimer's, confusional disorde r.	……..	
	……	……..	…….	……..	

Annex 2: EHR Traceable data for Potentially preventable situation (PPS)

Threatening PPS	This form is for Elija un elemento. If other, explain here
EHR traceable data	• List of diagnoses by ICD10 codes Diagnosis (ICD10 coded) will be available through GP Systems and pulled in from Vision360 and Emis
	• List of drug treatment by ATC codes Existing GP systems/ECD list
	• Demographic info ☐Care giver ☐Institutionalization Others Access through existing GP system if Pt permission has been given to upload as part of KIS.
	• Scales and questionnaires ☐ACCF/AHA ☐Barthel ☐CAT ☐EQ-5D-5L (COPD & CHF) ☐GOLD ☐HADS ☐Kansas City Cardiomyopathy Questionnaire (KCCQ) ☐Lawton ☐NYHA ☐Walking distance / number of steps / get up and go ☐Zarit Others Separate uploads might be required for this or links embeded within the platform for this. *If looking to analyise previously answered questionnaires, any that exist in current Acute Pt Record will only be able to be viewed as scanned documents in PDF format through Clinical Portal. There is currently no analytical capibility here*

- Tests and measurements

☐Cough
☐Dyspnea
☐Oedema
☐eGFR
☐FEV1
☐MRC
☐Sputum
☐Systolic Blood pressure
☐VO2 peak
☐Weight
Others
Some mearusements avialable within existing registry, but some might need to be input separately.

- Analytics

☐Creatinine
☐Glycemia
☐HbA1c
☐Hemoglobin
☐INR
☐NT-proBNP
☐Platelets
☐Potassium
☐Sodium
☐Urea
☐Albumin
☐Prealbumin
☐Total Proteins
☐Cholesterol
☐Cholesterol LDL
☐Cholesterol HDL
☐Ferritin
☐Transferrin
☐Transferrin Saturation
☐Folate
☐B12
☐TSH
Others

Accessible through existing GP systems

- Resource use

☐A&E services
☐Cardiologist
☐Respiratory
☐Endocrine
☐Nephrologist
☐Psychiatry
☐Neurologist
☐Internal medicine
☐Geriatric
☐Social assistance
☐General surgery
☐Health advice
☐Palliative care
☐Dietic and nutrition
☐Infectious diseases

☐Haematology
☐Rehabilitation
☐Transfusion, tissues, cells
☐Pain unit
☐Psychiatry short stay
☐Psychiatry medium stay
☐Psychiatry rehabilitation
☐Internal medicine long stay
☐Nursing
☐Primary care
☐Home hospitalisation
☐Hospitalisation
☐ICU
Others Social care and carer's input – this would not be accessible through existing systems.

Some of this will be accessible through existing systems and platforms. *We will need to fully scope this out as the information may be across multiple platforms.*

A.8 Working material from PPS development – example

An example of an ongoing development of PPS with shared information and discussion between Osakidetza and RJH is provided below.

Early warning signs

Warnings, alarms and notifications that can (1) anticipate evolving needs of the patient and (2) suggest specific services for early action facing prospective events of the disease progression

Describe events based on your experiences							
No	**Health status**	**Where?**	**What?**	**When?**	**How?**	**How often?**	**Crucial knowledge?**
	Think of a visit of a patient with COPD and / or heart failure as the main diagnosis. What is his/her health status?	Describe the encounter scenario, the setting …	List the worst-case scenarios, your concerns with this patient, what you want to prevent from happening	For each of the points arose in "What?", define an estimated timeline, when will it happen if we do nothing? In a week, month, year?	For each of the points arose in what? describe the tools/indicators/scales you rely on as predictors. How do you assess the probability of happening? What triggers your concerns?	For each of the points arose in "What?", determine when the patient status will be re-assessed. What is the follow up frequency?	For each of the points arose in "What?", determine the priority of an early warning to assess them: "Must be" / "If possible" / "Not mandatory"
Suggestions from Kronikgune							

1	Patient with Severe COPD	Outpatient, Primary Care	Hospital admission	Hospital admission within a week (short term)	DOSE-index: Dyspnoea, obstruction, smoking, exacerbation.	Comment from RJH on DOSE: Lung function, FEV1, is seldom used at home in Sweden within this senior/fragile group.	
			Respiratory failure	Respiratory failure within a month (midterm)			
			Exacerbations	Exacerbations in the subsequent year (long term)	https://www.ncbi.nlm.nih.gov/pubmed/22786813		
			Mortality	Mortality in the subsequent year (long term)			

2	Acute heart failure	Specialist visit (Cardiologist)	Poor course	Poor course within a week (short term)	AHFRS score (comorbidities, oedema, ED visits in the past 24M, glycemia, blood urea nitrogen levels)	Comment from RJH on AHFRS: this scale does not seem applicable at home, only in ER?	
			Death		https://www.ncbi.nlm.nih.gov/pubmed/27730492		
			Admission in ICU	Admission in ICU within a week (short term)			
			Mechanical ventilation (invasive or non-invasive)	IMV or NIMV within a month (midterm)			

3	Patient QoL	Outpatient	Low physical activity	Physical activity within a month (midterm)	HADO-index (Health, Activity, Dyspnoea, Obstruction)	Comment from RJH on HADO/BODE: this scale is important as risk stratification in a background measurement, but maybe not as EWS?	
			Low perceived health	Perceived health within a month (midterm)			
			Mortality	Mortality in the subsequent year (long term)	https://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-8-28		
Suggestions from RJH							
4	Stable patient with severe HF condition	Patient at home, with support from primary care or outpatient	Prevent respiratory failure and possible associated	Within days to weeks (weight gain).	Assessment of:	Every day	Must be (daily weight. Breathing frequency if possible).

		teams from the medicine clinic	oedema, which leads to functional impairment such as bed rest, increased care dependency at home and possibly hospital care. Long term concern: malnutrition.		- **Daily weight** to directly insert extra-dose diuretics (with an additional notice of current blood pressure to know the right dose of diuretics, not as EWS though). Weight gain is most important to follow. Would also be good with a message back from the patient that he/she has increased the diuretics.		

				Months (weight loss due to malnutrition)	- Breathing frequency might be interesting to know, but this metric requires staff to get an objective value?		
5	Patient with impaired heart failure	When visiting a cardiologist / cardiologist	Prevent respiratory failure and possible oedema, which leads to functional impairment such as bed rest, increased care dependency at home and	Within days. If the patient is unstable two days in a row, the health care should act.	Assessment of: - Weight gain - Impaired energy / perceived physical ability - Hard to breathe	Every day	Must be

			possibly hospital care		- Ankle oedema, wounds, erysipelas (more long term follow up, maybe not as EWS)		

6	Stable patient with severe COPD	Patient at home, with support from primary care or outpatient teams from the medicine clinic	Prevent respiratory failure with subsequent functional impairment such as bed rest, increased dependence on home care or hospital care	Within days to weeks	**Breathing frequency** and **oxygen saturation**. Symptoms such as increased production of mucus, coloured mucus, increased shortness of breath during walking, increased nocturnal shortness of breath. The patient should be advised to take an antibiotic or cortisone dose and contact the health care the next day.	Weekly and with reported symptom increase (shortness of breath, fever)	Must be

7	Patient with impaired COPD	When visiting a lung doctor / lung nurse in hospital or COPD nurse in primary care	Prevent respiratory failure with subsequent functional impairment such as bed rest, increased dependence on home care or hospital care. Risk of osteoporosis? Depression?	Within weeks to months	Assessment of: - Swallowing difficulties	Fever and hardness to breathe: daily. Others, weekly.	Must be.

					- Smoking habits - Hard to breathe - Anxiety - Weight loss - Decreased physical activity - Ankle Edema - Fever due to increased breathing or respiratory infections		

8	Patient in terminal stage (CHF and/or COPD)	Patient at home, with support from primary care or outpatient teams from the medicine clinic (as the Palliative Team), or living in a municipal housing.	Prevent suffering (relieve pain, shortness of breath, anxiety, nausea and mucous breathing)	Within hours to a day	ESAS estimate, VAS or Abbey Pain scale. Daily question about other symptoms (for example resting hours > active hours) for quick adjustment of on-demand drugs	Every day, to structure the need for palliative efforts and communication within the team	Must be