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DEC	Websites, patent fillings, videos etc.	
OTHER		
Dissemination Level		
PU	Public	**X**
CO	Confidential (Consortium members including the Commission Services)	
CI	Classified Information (Commission Decision 2015/444/EC)	

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Table of Contents

List of Figures

List of Tables

1 Versions History

Version	Date	Author	Comments
0.5	01-12-2022	Silvana Quaglini Ronald Cornet Lucia Sacchi Silvia Panzarasa Savannah Glaser	Merging separate versions
0.7	28-12-2022	Silvana Quaglini Ronald Cornet Lucia Sacchi Silvia Panzarasa Savannah Glaser	Version for internal review
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2 Executive Summary

In this deliverable we describe the knowledge engineering process used to formalize the clinical practice guidelines implemented in CAPABLE. More precisely the following steps will be illustrated:

1. **Choice of the guidelines -** Selecting the most compatible guidelines for the system.

2. **Text processing mechanism** - detecting recommendations and translate them into a set of computer-interpretable rules.

3. **Analysis of each recommendation** - detecting what raw data type was involved, which vocabulary is mostly suitable for coding, what abstractions need to be performed on this raw data. This allows achieving clearer representation, at the same time producing reusable pieces of knowledge. The detected raw data also represent the minimum data set needed by the CAPABLE DSS (Decision Support System), so this step has been fundamental for the development of other CAPABLE components

4. **Translation of each recommendation** into a set of computer-interpretable rules, organization of rules into a logical flow, and their representation using the Composer tool, i.e., the authoring tool developed by one of the project partners. In this step, adaptations have been implemented to allow a smooth guideline implementation in the different healthcare settings

5. **Validation of the represented knowledge** by simulating realistic clinical scenarios (oncologists have been involved in this phase). Particular attention has been put to multimorbidity management, since running guidelines for different pathologies may lead to contradictory recommendations, which must be resolved

6. **Handover to the implementation team and refinement iterations** with the team itself.

The guideline formalization activity was carried out since the very beginning of the project, involving four master thesis students who, in collaboration with the medical counterpart and under the supervision of UNIPV tutors, each developed the model of a specific guideline. The immunotherapy guideline has been analyzed by the KNI team.

The deliverable will then provide the actual description of the formalized guidelines, through a set of flowcharts, and links to their representation in Composer.

3 Introduction

The CAPABLE objective includes the following goals:

For doctors:

• Facilitating doctors' access to the most up-to-date evidence-based medical knowledge existing in CAPABLE DB and the latest Clinical Guidelines.

• Allowing doctors' access to patients' data, in-between control visits, in order to early manage possible problems and to reduce control visit duration and complexity.

• Improving clinical processes, through a better understanding of patients' conditions which allows the identification of patients who need priority treatment.

• Reduce manual physicians' interventions by using AI components which recommend the patient different approaches to reduce disease symptoms.

• Prevent physician mistakes by giving treatment recommendations based on the latest guidelines

• Facilitating multidisciplinary management of oncological patients, by harmonizing medical actions by oncologists, psychologists, nutritionists, and physical therapists.

For patients:

• helping the disease management from home, meeting the needs of patients and their caregivers, without making its use too heavy a commitment in an already delicate condition.

• encouraging patient involvement through a virtual coaching system, based on a behavioral change model;

• Reducing and preventing treatment side effects by using different approaches and recommendations (e.g., "Virtual Capsules", i.e. non-pharmacological well-being interventions).

• Better connection with the caregivers using the patient's App to improve the treatment.

• providing emotional support to the patient when the data collected by the application on the quality of life and psychological state suggest a worsening of the patient's condition;

From the list above, it is clear that one of the main CAPABLE foundations is represented by clinical practice guidelines, i.e., documents reporting recommendations based on up-to-date scientific evidence. It is also clear that there is a need for a deep and careful guidelines analysis and harmonization, (i) to manage possible conflicts generated by running multiple guidelines in case of multi-morbidities, (ii) to separate recommendations that in the same guidelines are directed to different targets (e.g., to doctors or to patients), and (iii) to separate recommendations related to different medical experts, in the meanwhile guaranteeing their cooperation in the patient's overall management.

Computer-Interpretable Clinical Practice Guidelines (CIGs) are one of the two pillars of the Capable DSS (the other one being predictive models based on data-driven tools, see D5.4).

Figure 1 illustrates the excerpt of the CAPABLE architecture specific to the DSS for doctors.

Figure 2 refers to the DSS for patients (please note that when we talk about patients, we implicitly mean patients and their home caregivers), also called Virtual Coach (VC). It emphasizes the patient coaching context, in particular the psychological context and its possible trajectory based on the Trans-Theoretical Model (TTM). This allows the system to send very personalized messages according to the patient's propensity to accept the system recommendations and accordingly modify some behaviors.

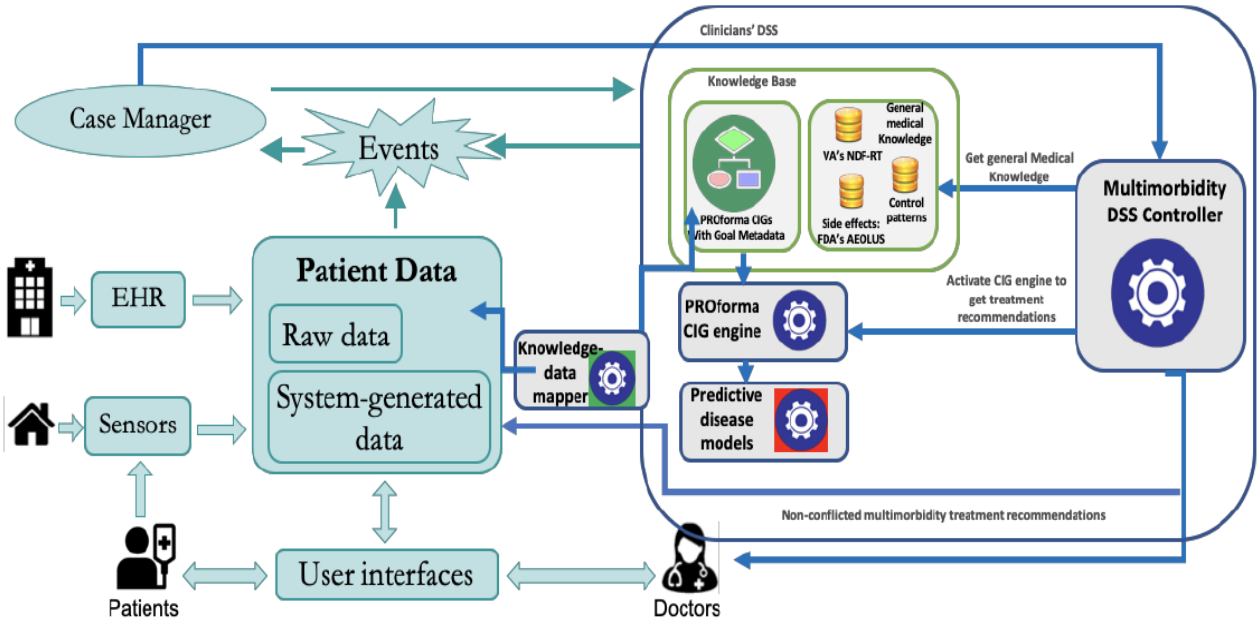


Figure 1 - The CAPABLE architecture and the focus (on the right) on the Decision Support System for clinicians

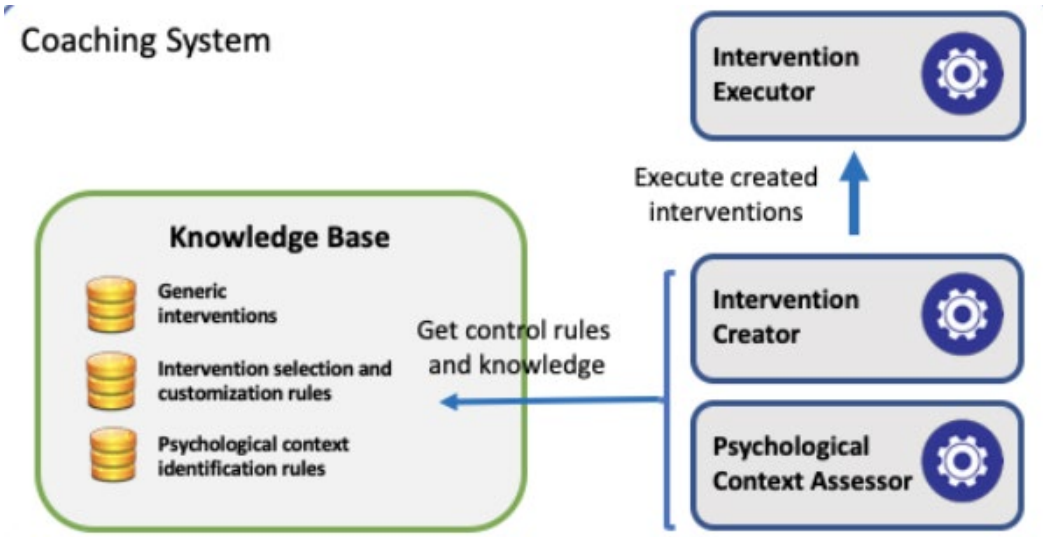


Figure 2 - The focus on the Decision Support System for patients and their caregivers, i.e., the CAPABLE Virtual Coach

In Chapter 4 we briefly illustrate the clinical practice guidelines implemented in the system, and provide justification for their choice.

In Chapter 5 we describe the principles of the knowledge extraction process from the guidelines text until the final Composer representation.

In Chapter 6 the specific processes for the five above mentioned guidelines are described.

4 Overview of the CAPABLE Clinical Practice Guidelines

Since the main goal of CAPABLE is to support the home-patients management, the focus has been, as declared from the beginning, on the management of the side effects of the oncological treatments. As a matter of fact, those are the main causes of a decreased quality of life of cancer patients, and also cause a decreased adherence to treatments (in order to mitigate side effects, patients tend to self-adjusting drug dosages or even decide to stop the therapy).

For this reason, the medical team involved in the project decided to implement in CAPABLE the ESMO guidelines for supportive and palliative care, which means all those treatments, beyond the actual treatment for cancer, that alleviate signs and symptoms (from here-on "symptoms") due to cancer treatment itself, or due to the impaired psychological condition (https://www.esmo.org/guidelines/guidelines-by-topic/supportive-and-palliative-care).

ESMO is the European Society for Medical Oncology (www.esmo.org), and this ensures that guidelines reported in the ESMO website are developed by teams of leading experts in the various oncological areas, following a rigorous evidence-based process (namely, the GRADE approach [Stavros 2020]), and that guidelines are regularly updated according to new scientific knowledge discovered.

Among the ESMO guidelines, the following ones have been chosen for computerization:

- Diarrhoea in adult cancer patients [Bossi 2018]
- Management of oral and gastrointestinal mucosal injury [Peterson 2015]
- Prevention and management of dermatological toxicities related to anticancer agents [Lacouture 2021]
- Cancer-related fatigue [Fabi 2020]
- Management of toxicities from immunotherapy [Haanen 2022]

The choice has been done by the medical teams involved in CAPABLE. According to them, the 5 above guidelines cover a set of side effects that are both frequent and challenging for oncologists to manage. Other guidelines refer to symptoms that are usually managed by other medical specialists (e.g., dyspnoea managed by pneumologists, severe gastrointestinal symptoms managed by gastroenterologists) not involved in the CABABLE project.

The ESMO guidelines are meant to provide recommendations mainly to medical professionals, even if a careful interpretation of the text often highlights recommendations that can also be provided to patients. This text analysis is one of the knowledge engineering tasks that we performed on the above cited GL documents.

However, we had the need for explicit and specific recommendations for patients, and to this purpose we relied on the AIMAC booklets (https://www.aimac.it/libretti-tumore) that guarantee evidence-based suggestions or, in case of absence of scientific evidence, suggestions based on the expert consensus. The source of information is reported in each booklet. The following booklets (original versions in Italian) have been considered:

I diritti del malato di cancro (The cancer patient's rights)

La nutrizione nel malato oncologico (The nutrition for cancer patients)

La sessualità nel malato oncologico (Sexuality in the oncological patient)

Il tumore negli anziani e il ruolo dei caregiver (Cancer in the elderly and the role of caregivers)

Il cancro del rene (The renal cancer)

Il cancro del polmone (The lung cancer)

Il cancro della mammella (The breast cancer)
Il cancro della tiroide (The thyroid cancer)
Nuova cura per il tumore testa-collo (New treatment for head and neck cancer)
La chemioterapia (Chemotherapy)
Le terapie immuno-oncologiche (Immuno-oncological therapies)
La fatigue (The fatigue)

5 The process of knowledge extraction

Knowledge engineering is the branch of artificial intelligence that deals with the creation of knowledge-based systems, such as the CIGS. These systems are built through a modeling activity which consists in the development of rules to be applied to the data in order to support the decision-making process.

The goal of the knowledge engineer is therefore to build models that are equipped with problem-solving capabilities as comparable as possible to those of a domain expert. Modeling is a cyclical process that can be modified or perfected at each stage, and which can lead to the acquisition of further knowledge. As a matter of fact, knowledge is usually classified as explicit or tacit:

• Explicit knowledge can be represented through a formal language and therefore more easily transmitted between individuals. In clinical practice guidelines, this is the knowledge reported as recommendations, which also carries information about the studies behind and level of scientific evidence supporting the recommendation itself, which depend on the reliability of those studies.

• Tacit knowledge is personal knowledge embedded in an individual's experience and context that is difficult to represent and communicate. It often makes up the majority of available knowledge; in clinical practice guidelines, this is the knowledge that must be "read between the lines". It is not explicitly written because the experts give it for granted, as it belongs to the common background of medical doctors, i.e., the intended guideline users. Examples of this implicit knowledge is "before prescribing a drug, check for possible allergies/intolerance of the patient for that drug". Guidelines explicitly reports recommendations like "IF condition y THAN Drug x", while the rule about allergic risk is implied. Another example is "IF obesity THAN alert for risk of pressure ulcers", but obesity is a risk for pressure ulcers only if it impairs the patient's mobility. So the complete rule, that explicitates the implicit knowledge should be: "IF obesity impairing mobility THAN alert for risk of pressure ulcers".

CIGS formalization of course requires taking into account both types of knowledge, and this requires the ability of knowledge engineers to interact with medical experts in order to enhance the explicit recommendations with the "hidden" and necessary implicit knowledge. Often, discussing with different medical experts it turns out that each of them gives a different interpretation to the guidelines text, thus meaning that text is ambiguous. In this case a disambiguation process is needed, which requires further documents reading and eventually leading to a better textual knowledge representation in the further guideline versions.

Independently from the specific guideline, the formalization process is made by the following steps:

1. Careful reading of the guideline text
    a. Detection of the portions of the text that are "interesting" for the formalization, i.e., that contain recommendations
    b. Resolution of uncertainties with the help of medical experts
2. Semi-formal representation of the knowledge contained in the guideline
    a. Tables
    b. Flowcharts
3. First iteration with medical experts to validate the semi-formal representation
4. Identification of precise data items and abstractions needed
    a. Use of the vocabularies chosen in CAPABLE for data representation
5. Enrichment of every recommendation with attributes that specify the target of the recommendation (doctor, nurse, patient, caregiver, etc.), the timing, and the grade of scientific evidence

6. Formal knowledge representation using the CIG language chosen in CAPABLE (Proforma through Composer)
7. Development of validation scenarios to be submitted to medical experts and CIG refinement after feedback
8. Implementation and integration of the CIG into the overall system. From the methodological point of view, this last step is not part of the conceptual formalisation of the guideline, because it depends on the specific system components the CIG wll be integrated into. Thus it will not be illustrated in this deliverable (see D5.3 and D5.6).
9. Finally, there must be a continuous monitoring of the scientific websites in order to detect any update of the published guidelines. As a matter of fact, guidelines are "living documents" that are updated as soon as new scientific evidence becomes available that refines/contradicts what was assumed to be the best practice in the past

We now illustrate in more detail the previous steps.

Step 1.a is not trivial, because several guidelines report a lot of information about the clinical trials that have been analyzed to develop the guideline itself. Sometimes there are also references to previous versions of the guideline. Some guidelines facilitate this step because, after the description of the studies, they report a "summary table" with the recommendations. Other guidelines do not offer this facility, and the summarisation must be performed by the knowledge engineer.

Moreover, recommendations are not only for diagnosis and treatments, they could also be alerts, and these are more difficult to detect. For example, if a guideline reports the percentage of a certain adverse event in patients undergoing a certain treatment, this is not a recommendation, it is just information. However, showing this information to the doctors prescribing that drug is useful to alert the doctor for the need of a tight monitoring for that side effect if its probability is high. Thus, some information must be translated into a recommendation of type "alert".

Step 1.b requires the knowledge engineer to detect possible incongruences, not only within the same guideline, but also among different guidelines. Often incongruences are due to the fact that each guideline is specific for one particular problem, and does not foresee all the possible comorbidities that a patient may suffer from. In our case, the main challenge is posed by the fact that the immunotoxicity guideline addresses several adverse events, among which diarrhoea and skin toxicity, that are also addressed in their two additional specific guidelines. Taking the example of the diarrhoea, this means that:

- the "diarrhoea guideline" reports general recommendations for the symptom and also specific recommendations for diarrhoea caused by immunotherapy

- the "Immunotoxicity guideline" reports different sections, each one for a different toxicity, among which there is diarrhoea

So, the two guidelines must be harmonised (the same for the skin toxicity).

Step 2 does not require any specific formalism, because the main purpose of this step is to ensure that the guideline has been interpreted correctly. Often guidelines report some schema, which may be proficiently used as the starting point for this step. In step 2, knowledge engineers report all the knowledge contained in the guideline in a way that is absolutely unambiguous. Since natural language is often ambiguous, this step consists in translating recommendations written in natural language into a non-ambiguous formalism. We can do that using tables, diagrams, rules written in a semi-formal language, etc.

Step 3 Since the semi-formal representation does not imply using technical tools or languages, medical experts can be smoothly involved in this step, to validate the informal "guideline translation". On the contrary, once the CIG is represented using a software tool like the Composer, formal validation becomes more difficult, and it is usually performed by simulation, i.e., creating a set of scenarios (step 7).

Step 4 is necessary because CIGs must be integrated with the Electronic Health Record (EHR) so the vocabularies must be shared among all the CAPABLE components. Every recommendation implies doing a match with the patient's data. In this step, those data are detected and matched with the chosen vocabulary (e.g., in CAPABLE, with CTCAE, RXnorm and SNOMED). Moreover, some recommendation do not use raw data, but concepts that put together more than one data item, so-called *abstractions.* An abstraction can be for example "Anemia" that is defined according to Hemoglobin thresholds that are different for males and females (so Anemia is an abstraction based on Hemoglobin and sex). Other abstractions may use only one variable, but with multiple measures, such as "persistent fever", which requires only the *temperature* variable, but more than one observation (so Persistent Fever is an abstraction based on temperature and a definition of what "persistent" means, for example 3 days).

Step 5 is necessary in order to classify each recommendation to be included either in the clinicians' guideline or in the patients' guideline, i.e. the Virtual Coach (VC). As a matter of fact, each guideline eventually leads to two parallel flows, for the two target users. Sometimes, the same recommendation can be declined for both target users. For example, if a guideline reports a suggestion for the patient like "To prevent side effect X, you can do Y", this will become a recommendation for the patient in the VC, but also could be a recommendation for the physician like "During the next control visit, remind the patient to do Y to prevent X". So, the guidelines have been analysed also to detect such recommendations that deserve "reinforcement" by the doctors.

We also addressed the problem of when and how to alert the guideline users in critical situations. For example, in case a patient enters symptoms that, according to the guidelines, require hospitalization, how to alert the users? It's important to avoid alarming patients and their relatives, but at the same time it's important that the symptoms are appropriately treated as soon as possible. Thus, we choose to use a double communication channel. The VC will recommend the patient to call his doctor, while the physician's DSS will recommend the doctor to hospitalise the patient. Thus, the first user (either the patient or the doctor) that complies with the received recommendation will "activate" the actual hospitalisation process.

Step 6 is the actual formalisation step in the chosen language. CAPABLE adopts the ProForma language implemented through the Composer tool developed by Deontics, and illustrated in detail in the previous deliverable D5.3.

In this phase, guideline represented through the Composer are enriched with a (even rough) GUI for data input and for simulating a patient's journey over some time, in such a way to allows medical expert to test the represented knowledge as a whole (and not a recommendation at a time, like in the previous steps).

Step 7 is the actual validation of the represented knowledge. It is performed by representing several realistic clinical cases, and letting the medical experts to "play" with them, i.e. entering data and looking at the results, that are the recommendations automatically generated. They also can play the role of a patient entering symptoms from remote, and check what is recommended to the patient. Eventually they can simulate time passing, change data and see how results change.

Step 8. Once the guidelines have been validated through step 7, they must be integrated into the overall CAPABLE system, so connecting them to the other components. This step requires also to change the Composer representation, eliminating all the additional parts introduced in step 6 to simulate the final system as explained in step 7 (for example the GUIs). As a matter of fact, the final system will gather data directly from the Hospital electronic patient record or from the CAPABLE doctor Dashboard.

The next chapter described this process for the above mentioned guidelines.

6 The implemented guidelines

In the following sections, we show how the five guidelines mentioned above have been formalized following the steps described in the previous section. For sake of space, and to avoid unnecessary redundancy, the entire formalization process will not be illustrated for all the guidelines, thus we will elaborate more on the first guideline and show some examples of both semi-formal and formal representations for each of the other ones. The full formalisation processes are available in the master thesis documents of students who graduated after working on this aspect of the CAPABLE project [Pilia2022, Vitale2020, Palo2022, Brungiu2022] under our supervision, while the results, i.e. the Composer representations, are available in the GIT repository of the project (visible upon the reviewers' request).

6.1 Diarrhoea guideline

As already mentioned, the formalisation of this guideline has been developed after harmonizing its recommendations with those reported in the section "diarrhoea" of the Immunotoxicity guideline. Fortunately, we did not find true contradictory recommendations, but only a different phrasing and different detail that required some encounters with the oncologists to achieve the final formulation of the rules.

After that process, to summarise the diarrhoea guideline, we first developed the flowchart shown in Figure 3.

This representation highlights the target users (patients/doctors) and the type of the tasks (patient assessment, further exams, treatment). From the figure it's immediate to realise that only grade 1-2 uncomplicated diarrhoea may be treated at home, while higher grades require hospitalization.

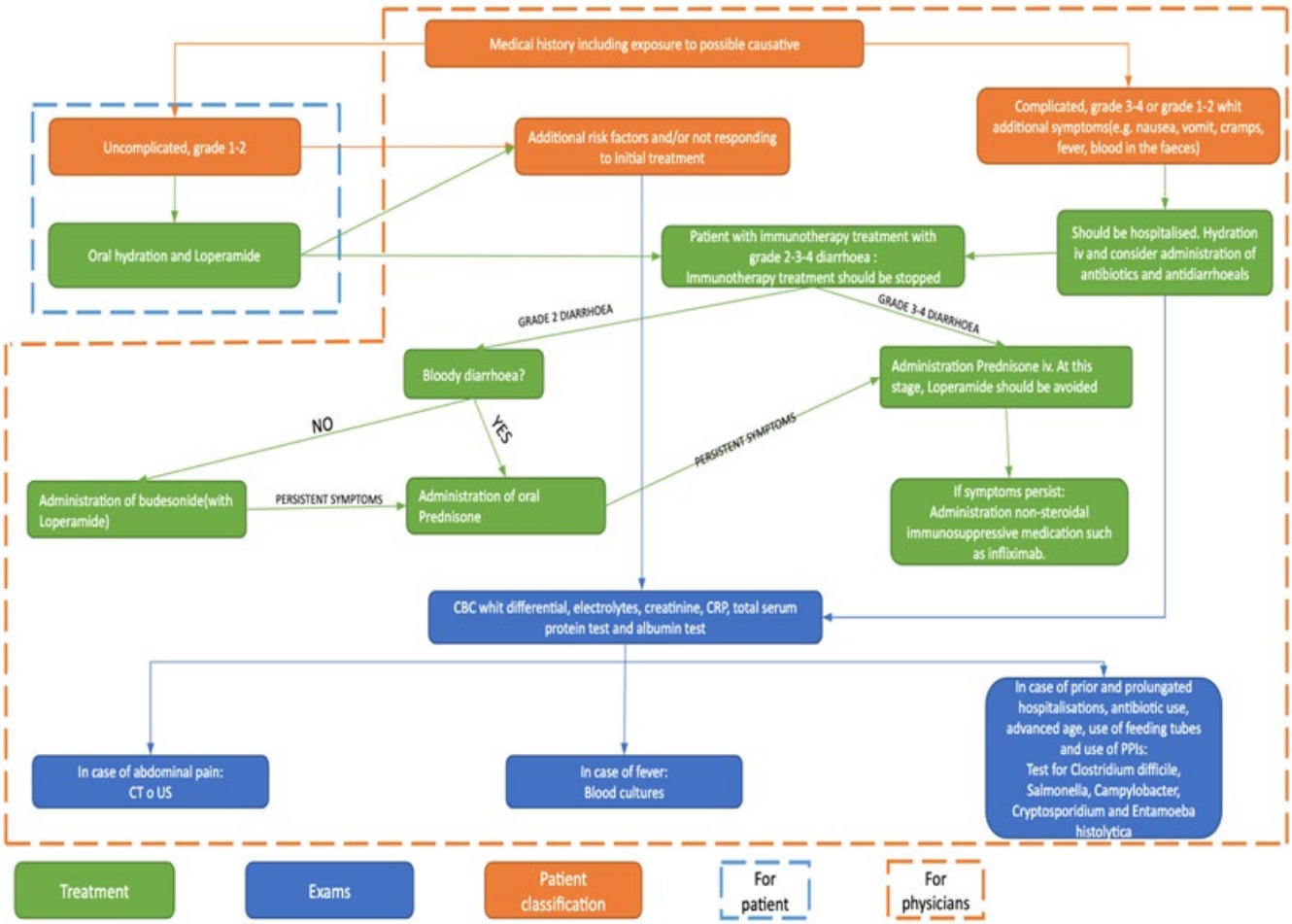


Figure 3 - High level flowchart of the diarrhoea guideline

In case of uncomplicated diarrhoea of grade 1 or 2, Figure 4 illustrates the detailed flowchart

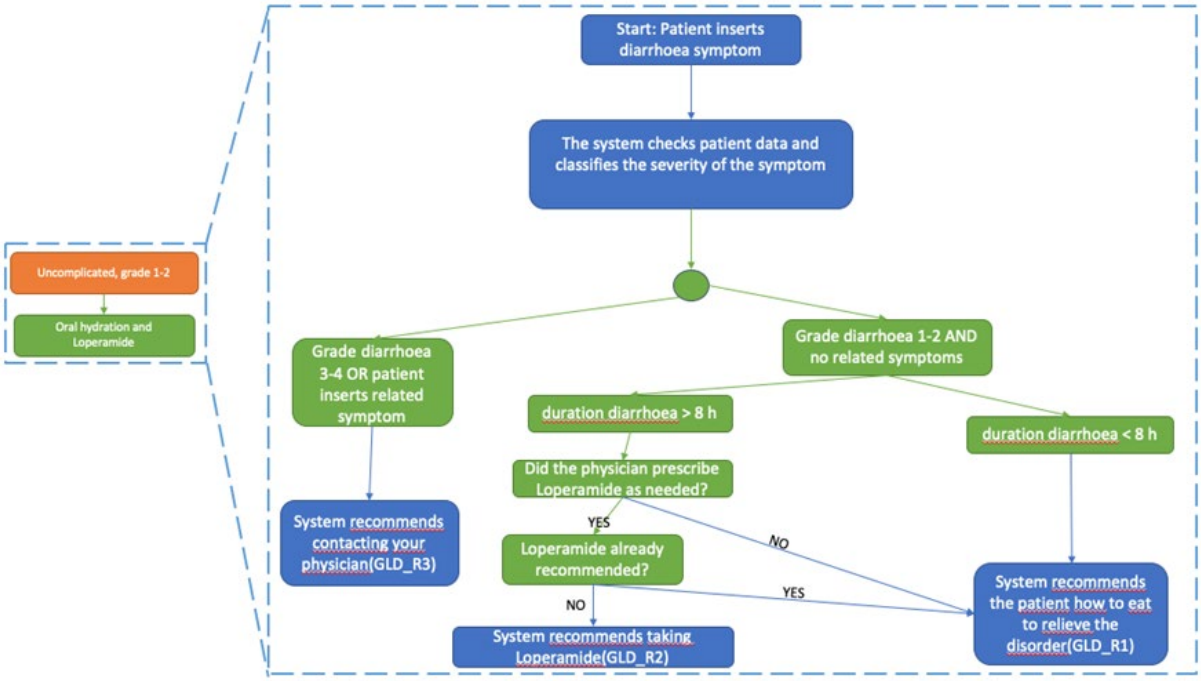


Figure 4 - Details of the management of uncomplicated diarrhoea grade 1-2 (left)

Therefore, if the diarrhoea is grade 1 or 2 with no related symptoms and if the symptom persists for less than 8 hours, the system sends recommendations to the patient regarding lifestyle such as advice on how to eat to alleviate the disorder (recommendation GLD_R1); if, on the other hand, the symptom persists for more than 8 hours, the system checks whether Loperamide has been prescribed as needed by the doctor (this prescription can be done either at the patient's enrollment or also afterwards, after prescribing a cancer treatment known to cause diarrhoea). If it has not been prescribed, the system recommends only GLD_R1 to the patient, otherwise it checks if the recommendation to take Loperamide has already been sent to the patient. If not, it sends the recommendation.

To help the patient in everyday life we have decided to integrate the ESMO_diarrhoea guideline with the AIMAC booklet on diarrhoea.

Eight practical recommendations were selected to be given to the patient to help manage the effects of diarrhoea (each recommendation has been given a code):

· GLD_R7: Eat small and frequent meals throughout the day;

· GLD_R8: Drink frequently to replenish lost liquids (water, infusions, water flavored with lemon, vegetable broth);

· GLD_R9: Take lactic ferments on doctor's instructions;

· GLD_R11: Avoid foods or drinks sweetened with sugar like sorbitol, mannitol, xylitol, etc.;

· GLD_R12: Do not limit the use of salt in the preparation and seasoning of dishes;

· GLD_R13: Limit the consumption of fruit, vegetables and cereals, with the exception of carrots, potatoes, apples, bananas and barley;

· GLD_R14: Consume drinks and food at room temperature;

· GLD_R15: Avoid very fatty foods and spicy foods.

Furthermore, once the symptom has been entered for the first time, it is essential to keep the situation monitored by asking the patient for periodic updates, including on any related symptoms. We have therefore modeled the monitoring process as shown in Figure 5 (high

level model) and Figure 6 (detailed model). Monitoring will be carried out by the Virtual Coach component.

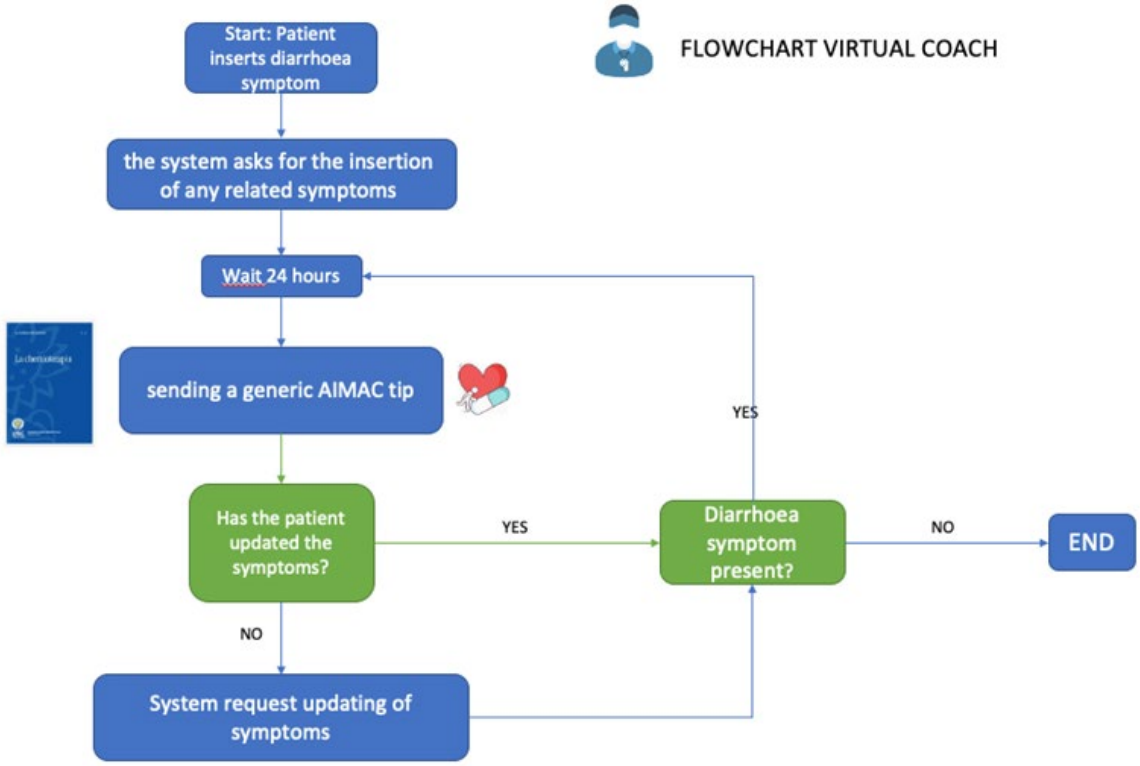


Figure 5 - The monitoring process for a patient suffering from diarrhoea (high level)

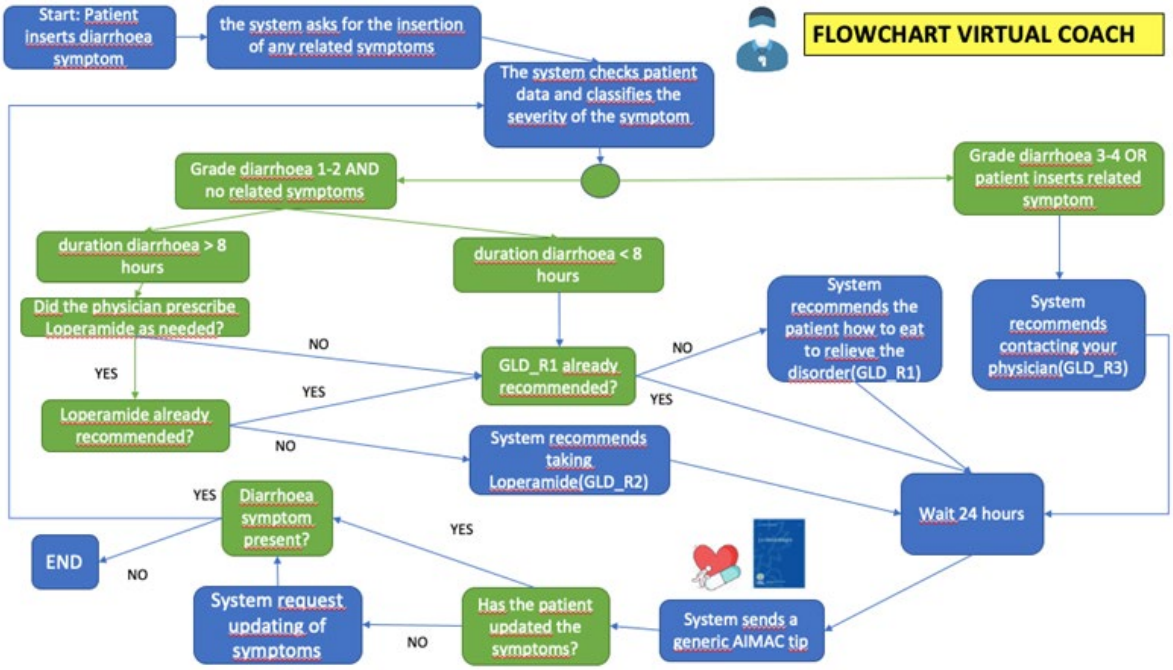


Figure 6 - The monitoring process for a patient suffering from diarrhoea (detailed level)

In the event that the diarrhoea is complicated, according to the *double communication channel strategy* explained in step 5, the guideline area reserved for the physician is fired (see Figure 3, orange dotted border) and the patient will only be notified to contact the physician. Contemporary, the latter will be advised to hospitalize the patient and rehydrate him intravenously. In addition, the system will also recommend to consider antibiotics and antidiarrhoeals.

If the patient has risk factors or does not respond to the first treatment, the system recommends further blood tests. In the presence of abdominal pain, the DSS recommends to perform a computer tomography (CT) or an ultrasound (US) examination; blood cultures in case of fever; in case of previous and prolonged hospitalization, use of antibiotics, advanced age, use of feeding tube or proton pump inhibitor, it will be recommended to test for Clostridium difficile and to consider testing for Shigella, Salmonella, Campylobacter etc.

A very important factor to consider in the management of the adverse event diarrhoea is immunotherapy.

If the patient is receiving immunotherapy and a Grade 2 or higher diarrhoea symptom is entered into the system, the physician will be advised to discontinue such treatment. Furthermore, the presence of this factor also changes the treatment of diarrhoea which will no longer be through Loperamide but will depend on the diarrhoea grade.

If the diarrhoea is grade 2, it is necessary to evaluate the presence or absence of blood in the stool. If so, it is advisable to administer oral Prednisone otherwise Budesonide together with Loperamide. If with the latter treatment there is no improvement within 3 days, the treatment should be changed and oral prednisone should be administered.

If the diarrhoea is grade 3 or 4 or treatment with oral Prednisone does not improve within 3 days, the doctor will be advised to switch to the intravenous route by stopping the intake of Loperamide. In conclusion, even if this treatment does not improve and the symptom persists, a non-steroidal immunosuppressant such as infliximab is administered.

After detecting all the recommendations in the guideline, and after the semi-formalisation process, we detected all the variables managed in those recommendations. They are shown in Table 1. We report both raw data and the necessary abstractions. The table also highlights the importance of dates for the correct formulation of rules, given that guidelines are continuously running "behind the scene" and must provide the correct recommendation according to the moment when the doctor or the patient accesses their applications.

Table 1- The complete list of clinical and non-clinical parameters needed to implement the guideline for the diarrhoea management

Data item	**Data type**	**Notes**
Name		
Surname		
Date of Birth	date	
Gender		
CapablePatientID	text	Internal id of the patient
CapableAppId	text	Internal id of the patient app

Diabetes	boolean	
Hypertension	boolean	
Collagen vascular	boolean	
IBD	boolean	
Years as a smoker	float	0 if no smoker
Current Weight (kg)	float	weight + reporting date
Height (cm)	float	
Bmi	float	weight/height^2
Previous intestinal surgery	boolean	physician will decide if the surgeries undergone by patient are relevant
Loperamide as needed prescription		start validity, end validity, drug name, max daily dosage, interval between administrations, way of administration
Loperamide as needed prescribed		Loperamide as needed prescription.end validity > now()
ANC	Integer	
Abdominal syndromes	boolean	
bowel wall thickening	float	
hypovoleamia	boolean	
tachycardia	boolean	
severely dehydrated	boolean	
diarrhoea		start date, end date, update date
Symptom Grade	0(Absent)/1/2/3/4	diarrhoea and Vomiting 0-4, the other symptoms 0-3
Nausea		start date, end date, update date
Fever		start date, end date, update date
Vomit		start date, end date, update date
Abdominal pain		start date, end date, update date
Dizziness		start date, end date, update date
Abdominal Cramps		start date, end date, update date
Blood in faeces	boolean (0=false, 1=true)	reporting date
Additional_symptoms	boolean (0=false, 1=true)	TRUE if Abstraction verified ABSTRACTION: (Fever == true) or (Nausea == true) or (Vomit == true) or (Abdominal pain == true) or (Dizziness == true) or (Abdominal Cramps == true) or (Blood in faeces == true)
Complicated diarrhoea	boolean (0=false, 1=true)	TRUE if corresponding abstraction verified ABSTRACTION: (diarrhoea grade == 2 and on_immunotherapy = TRUE) or (diarrhoea grade<=2 and ((Additional_symptoms == true)

		or (Warning_signs == true)) or (diarrhoea grade>2)
Intervention Sent		sent_date, end_validity_date (depends on recommendation validity), recipient_ID (patient_ID/physician_ID), recommendation_ID, recommendation_text
Intervention Response		response_date, response (Accept/Deny)
Grade 2 Persistent diarrhoea	boolean	TRUE if Abstraction verified ABSTRACTION: (diarrhoea.end_date != null) and ((diarrhoea grade ==2) and start(diarrhoea grade 2)>=3 days)
Persistent diarrhoea for scenario	boolean	TRUE if Abstraction verified ABSTRACTION: (diarrhoea.end_date != null) and ((diarrhoea == true) and start(diarrhoea) >= 3 days)
On Loperamide	boolean	TRUE if Abstraction verified ABSTRACTION: (Intervention_sent.recommendation_ID == GLD_R1) and (Intervention_response.response == Accept) and (Intervention_response.response_date<=Intervention_sent.end_validity_date)
On Immunotherapy	boolean	TRUE if Abstraction verified ABSTRACTION: ongoing cancer medication list in(Ipilimumab, Nivolumab, Pembrolizumab, Atezolizumab, Avelumab, Ipilimumab+nivolumab)
On chemotherapy	boolean	TRUE if Abstraction verified ABSTRACTION: (cancer_treatment.drug = Chemotherapy) and (cancer_treatment.end_date != null)
Oral Prednisone never prescribed	boolean	TRUE if Abstraction verified ABSTRACTION: _treatmentRecivedForCurrentEpisodeOfDiarrhoea not in Oral Prednisone
Neutropaenia	boolean	TRUE if Abstraction verified ABSTRACTION: (ANC < 500) and (Abdominal syndromes = FALSE) and (bowel wall thickening > 4)
Risk factor	boolean	TRUE if Abstraction verified ABSTRACTION: Smoker = "yes" OR Comorbid_desease = "yes" OR Previous_intestinal_surgery = "yes" OR bmi < 17
prior prolungated hospitalization	boolean	
previous_admission_for_diarrhoea	boolean	
ongoing use of feeding tube	boolean	Procedure
Other treatments/ Ongoing non cancer medication list	set of text	

Peritonitis	boolean	Warning sign
Blood loss	boolean	Warning sign
Delirium	boolean	Warning sign
Renal impairment	boolean	Warning sign
Sepsis	boolean	Warning sign
Shock	boolean	Warning sign
Electrolyte disturbances	boolean	Warning sign
Inability to eat	boolean	Warning sign
Persistent_nausea_vomiting_dehydration_accompanied_by_reduced_urine_output	boolean	Warning sign
Warning signs	boolean	TRUE if Abstraction verified ABSTRACTION: (Severely dehydration==true) or (Fever == true) or (Peritonitis == true) or (Blood loss == true) or (Delirium == true) or (Renal impairment == true) or (Sepsis == true) or (Shock == true) or (Electrolyte disturbances == true) or (Abdominal cramps == true) or (Inability to eat == true) or (Previous admission for diarrhoea == true) or (Neutropaenia == true) or (Persistent_nausea_vomiting_dehydration_accompanied_by_reduced_urine_output == true)
Clinical_finding_list	set of text	
Clostridium_difficile_associated_colitis	boolean	
GvHD_colitis	boolean	
Coeliac_plexus_block_in_last_few_days	boolean	
Ischemic_colitis	boolean	
Localised_tenderness	boolean	
Ongoing_use_of_PPI	boolean	
Ongoing_use_of_antibiotics	boolean	
Radiation_proctopathy	boolean	
Rebound_tenderness	boolean	
Received_pelvic_RT_in_the_past	boolean	
Receiving_pelvic_RT	boolean	
LoperamideProblem	boolean	TRUE if Abstraction verified ABSTRACTION: allergyOrIntoleranceList includes Loperamide
Ongoing recent procedure list	set of text	Range: Ongoing use of feeding tube Coeliac plexus block in last few days
Ongoing cancer medication list	set of text	
_diagnosisConfirmedList	set of text	

_testPerformed	set of text	
_treatmentRecivedForCurrentEpisodeOfDiarrhoea	set of text	
allergyOrIntoleranceList	set of text	
patientSymptomsList	set of text	
Sleep Problem	boolean	
Insomnia SeverityIndex	integer	
past procedure list	set of text	Range: Surgical bowel resection in the past Organ transplant in the past
Diarrhoea_recurrent	boolean	TRUE if Abstraction verified ABSTRACTION: previous_admission_for_diarrhoea == true
Diagnosis_of_one_of_the_six_types_of_cancers_that_cause_diarrhoea	boolean	TRUE if Abstraction verified ABSTRACTION: Problem_active_list includesAny includesAny [Carcinoid syndrome],[Malignant tumor of colon], [Lymphoma finding], [Medullary thyroid carcinoma], [Malignant tumor of pancreas], [Pheochromocytoma]
Problem_active_list	set of text	
Grade 1 Persistent diarrhoea	boolean	TRUE if Abstraction verified ABSTRACTION: (diarrhoea.end_date != null) and ((diarrhoea grade ==1) and start(diarrhoea grade 1)>=14 days)

6.1.1 Modeling the guideline through the Composer

Clinical practice guidelines (CPGs) contain evidence-based recommendations intended to improve patient care. Specifying CPGs formally as computer-interpretable guidelines (CIG) enables their execution over a patient's Electronic health record (EHR) to deliver patient-specific recommendations, thus supporting clinicians. CIG languages are formal knowledge representation languages capable of capturing the task-network structure and content of a clinical guideline in a form that can be interpreted by a computer. CIG languages have been developed over the years. These include, among others, GLIF, Guide, Asbru, GASTON, GLARE, HELEN, PROforma, and SAGE [Peleg 2003].

We used the PROforma language [Fox 1998] with its (already mentioned) Composer editor to implement the CIGs.

The PROforma language incorporates the versatility and expressiveness of procedural languages (e.g., the Arden syntax) with the semantic consistency of defined information roles. PROforma is a CIG formalism that has a deliberately small number of task classes in order to ease its learning by modelers. Task classes include enquiries, actions, decisions, and plans. All tasks have common attributes, including goals, pre- and post-conditions, and scheduling constraints. PROforma allows the specification of flexible guideline models in which tasks are enacted in parallel as long as their preconditions and scheduling constraints are met. Decisions are based on argumentation rules that have varying levels of support for candidates. The engine has an API and a user interface that can be used to match the CIG to a patient's data and suggest to the physician user the tasks whose preconditions and scheduling constraints are met. When decision tasks are reached, the engine calculates the net support of all of the arguments for the patient's data items, and

candidates that meet the net support are recommended. PROforma is one of the most highly cited CIG languages and its commercial and supported authoring and enactment tools have been used to develop applications that have been deployed by commercial companies at scale in several countries [Fux 2020].

As a first step, all the data and abstractions extracted from the guideline and shown in Table 1 were created in the Composer. Furthermore, all the recommendations (or claims in Composer's terminology) with the related scientific evidence have also been defined. To create these fundamental elements for the modeling, the Composer markup function was used, which allows highlighting and classifying the text of the guideline from the Document Markup window (Figure 7).

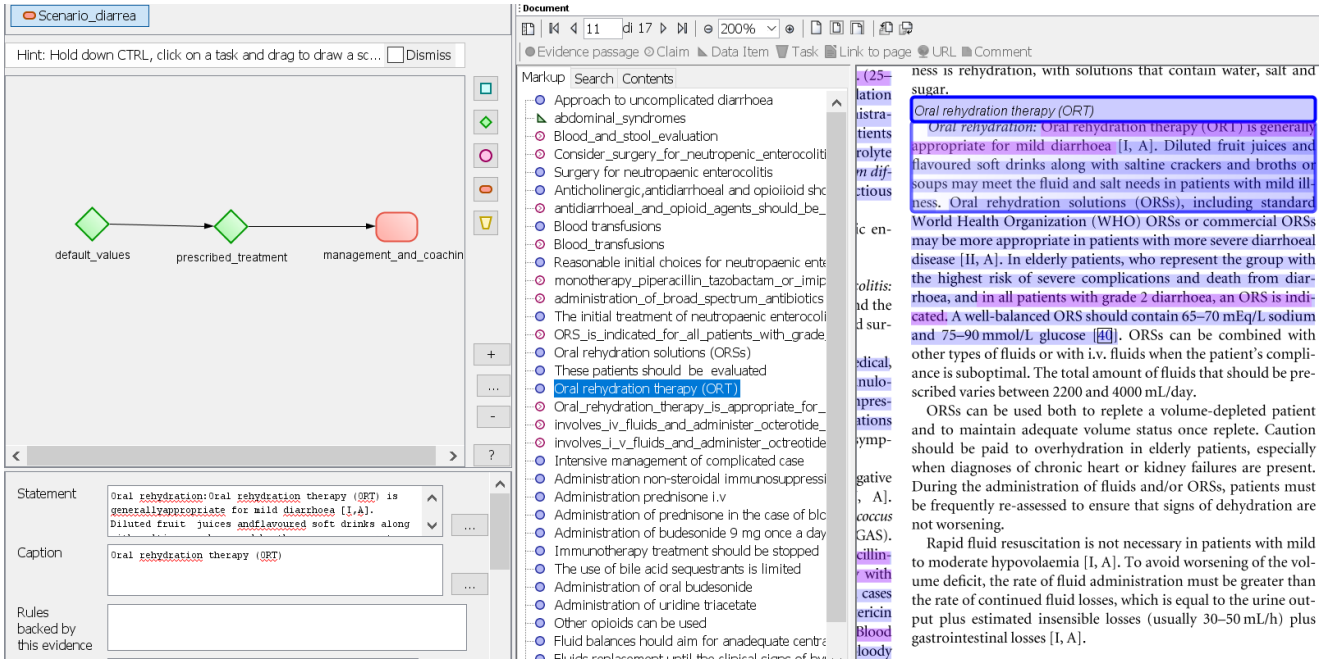


Figure 7 - The Markup functionality of the Composer tool, allowing to associate a formalized recommendation to the corresponding piece of text in the guideline document

Data, claims or evidence that could not be marked up directly from the guideline text were entered manually.

After that, functions were created with the goal of both populating the data items and defining the abstractions. For example, the following box reports the code for calculating the abstraction "presence of risk factors":

```
if (Smoker = "yes" OR
Comorbid_desease = "yes" OR
Previous_intestinal_surgery = "yes" OR
bmi < 17, "yes", "no")
```

while the following one reports the code for calculating the abstraction "complicated diarrhoea":

```
1 if(('Diarrhoea' = 3 or 'Diarrhoea' = 4) or (('Diarrhoea' = 1
  or 'Diarrhoea' = 2) and (('Abdominal_pain' = "yes" or
  'Abdominal_Cramps' = "yes" or 'Dizziness' = "yes" or 'Fever' =
  "yes" or 'Nausea' = "yes" or 'Bloody_stools' = "yes" or
  'Vomit' = "yes") or Warning_signs = "true")) or
2 ('Diarrhoea' = 2 and 'on_immunotherapy' = "yes"), "yes", "no")
```

After defining all the data and abstraction needed, two plans have been created: the Patient_data_collection and the diarrhoea_management (Figure 8). The first one will allow the insertion of all the personal data of the patient enrolled in the CAPABLE project, while the second one contains all the management tasks of the diarrhoea, with the sections dedicated to the patient and the doctor.

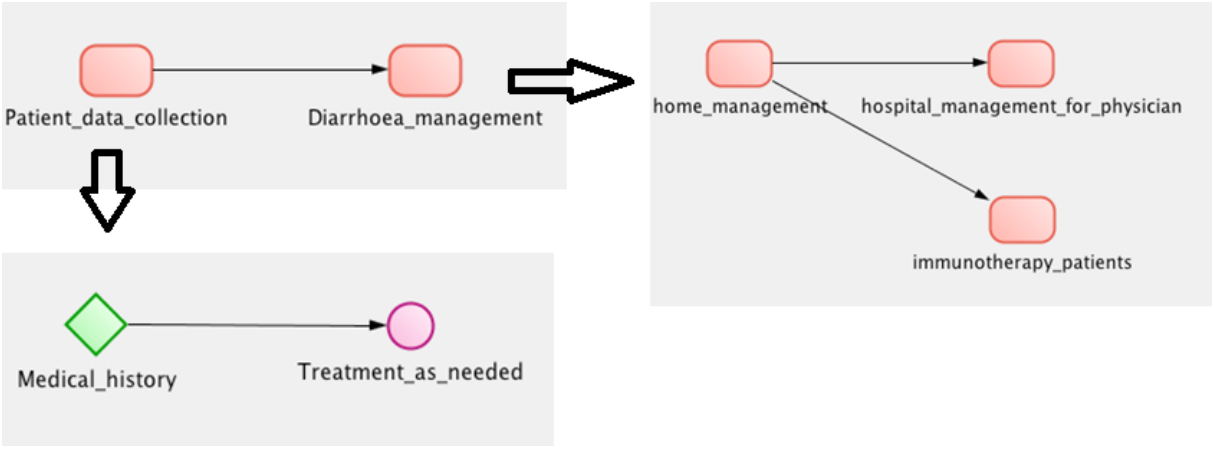


Figure 8 - Plan Editor of the ESMO_Diarrhoea guideline, with the 2 highest level plans and their second-level specification

In the Patient_data_collection there are two other related tasks, an inquiry task called Medical_history and a decision task called Treatment_as_needed. In the Medical history task the patient will be asked for a series of personal information useful for managing the diarrhoea symptom: The complete list is shown in Figure 9.

Figure 9 - Data for the task Medical History

The treatment as needed task has the preconditon Therapy_induced_diarrhoea, which is a dynamic data exploiting the function Aggressive_therapy. If the cancer therapy contains at least one of the drugs in the Aggressive_therapy_list, then the task Treatment_as_needed will be executed, producing the recommendation 'Prescribe Loperamide as needed'. This is the only candidate of the decision task, and if the physician complies with it, the postcondition Loperamide_as_needed=Yes will be asserted.

The diarrhoea management plan is a cyclic one, which is repeated until the symptom is resolved. Figure 10 summarizes the plan and gives some examples of the implemented rules.

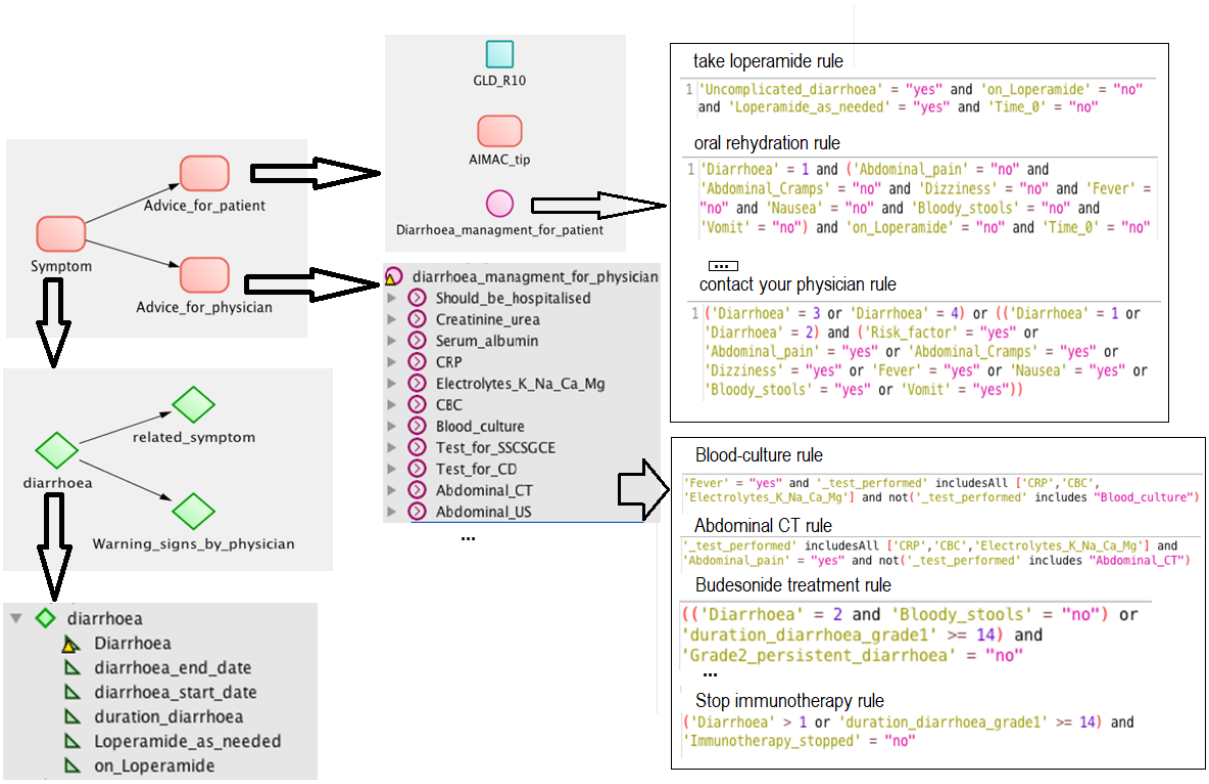


Figure 10 - The diarrhoea management plan, that is repeated until the symptom is resolved. Note the reported rules are only a few examples of many rules actually implemented

6.2 Mucositis guideline

For the Mucositis guideline we will illustrate some of the formalization steps.

According to the purpose, for semi-formal representations, tables or flowcharts have been used. Table 2 shows an example of a semi-formal knowledge representation. Here the effort has been to extract recommendations from the guideline text, and classify each recommendation according to some "interesting" attributes, such as the type (if it is an

alert - yellow, a treatment-green, a prevention action -red, etc), the target user, the evidence level, and if it is related to a drug. These characteristics are important to assess the modality of the recommendation delivery to the users (through different GUIs). For example, if a recommendation is for a drug treatment, the user is prompted, in case of adherence to the recommendation itself, to a page for the drug prescription. If it is an alert, it will be visible in the home page in such a way the doctor will see it as soon as he logs-in.

Table 2 - Characterization of guideline recommendations (excerpt of the full table)

Recommendation type	Target user of the recommendation	RULE (Recommendation)	Scientific evidence GRADE	Drug involvment
Alert	Physician	IF (H&N radiotherapy 60-70 Gy): THEN 85% of patients show oral mucositis with ulcers and require liquid diet		no
Treatment	Physician	IF (mucositis CTCAE grade>2): THEN Enteral nutrition support OR opioids		no
Treatment	Physician	IF (mucositis AND swallowing difficulty): THEN Early enteral nutrition		no
Prevention	Physician	IF (bone marrow transplant): THEN Do not use pentoxifiline	III	yes
Treatment	Physician	IF (ChT AND oral mucositis and oral pain): THEN Transdermic Fentanil	III	yes
Prevention	Physician	IF (Stem cell transplantation): THEN Do not prescribe systemic Pilocarpine		yes

As already mentioned, each recommendation is then analysed in order to detect the variables present in its premise and its conclusion. Table 3 shows such an analysis for the mucositis guideline. Among the attributes, also the person who entered the data item is very important, because some of the data may be entered by both patients and doctors, and different values of the same variables may be stored over time. Both the date and the user are important to select which is the last, more reliable value to be considered in the rules. For example, a patient may enter sign x indicating a certain level of severity y. After a few days, the patient goes for a control visit and his doctor makes a different evaluation about the severity level of x, updating it from y to z. If the severity is objectively detectable, it is clear that the evaluation of the doctor must be considered more reliable (this could be more debatable for subjective symptoms). Of course, also the patient may update the severity of his symptom or sign over time. That's why most of the rules consider both data items and their timestamps and authors.

Table 3 - The variables needed to represent premises and conclusions of the production rules (excerpt of the full table)

*CTCAE=Common Terminology Criteria for Adverse Events

Item	Reported by	Type and domain	Raw/Abstractions	Definition
Mucositis	patient/doctor	Set of integers (1/2/3/4)	Raw	CTCAE* grade
Oral pain	patient/doctor	Set of integers (1/2/3/4)	Raw	CTCAE grade
Date of anal hemorrhage	patient/doctor	DateTime	Raw	date
Oncologic therapy	doctor	Set of text (Bone marrow transplant/Stem cell transplantation/RT/ChT)	raw/Abstraction	ChT is inferred if one of the possible chemotherapeutical drugs has been prescribed
RT level gray	doctor	Integer		
ChT level	doctor	Set of text (ChT low doses/ChT moderate doses/ChT high doses)	Abstraction	the level is computed according to pre-defined levels for each ChT drug
Transdermal fentanyl	doctor	Boolean (present/absent)	Raw	

Another type of table is useful to check for actions that are recommended versus actions that are not recommended. The latter are very important, because if a guideline reports against some actions, it means that those actions are probably still performed by some professionals that did not update their knowledge according to the latest evidence. An example is reported in Table 4.

Table 4 - Prevention and treatment of mucositis in Head&Neck cancer patients: recommendation in favor and against

Mucositis Prevention:

If cancer treatment is:	Recommended	Suggested	Recommendation against	Suggestion against
Moderate dose radiation therapy (<=50Gy) without concomitant chemotherapy	Benzyamine mouthwash			
Radiation therapy			PTA and BcoG antimicrobial lozenges	Chlorhexidine mouthwash Misoprostol mouthwash Sistemic oral pilocarpine
Radiotherapy with no concomitant chemotherapy		Low-level laser therapy		
Radiation therapy or concomitant chemoradiation			Iseganan antimicrobial moutwash Sucralfate moutwash	

Mucositis Teatment:

If cancer treatment is:	Recommended	Suggested	Recommendation against	Suggestion against
Chemoradiation		0.2% morphine mouthwash for oral pain		
Conventional				
Radiation Therapy			Sucralfate moutwash	

Another useful formalism is the flowchart that, differently from tables, can represent sequences of actions, with decision points, parallel and sequential routings, and start and stop conditions. Flowcharts may be designed at different levels, in order to show the overall process at a glance (highest level), and progressively drilling down into the various details. Figure 11 shows the highest level flowchart for the mucositis guideline, while Figure 12 shows the detailed flowchart for the mucositis management in head&neck cancer patients, which varies according to the cancer treatment received.

Figure 11 - Highest-level flowchart of mucositis guideline

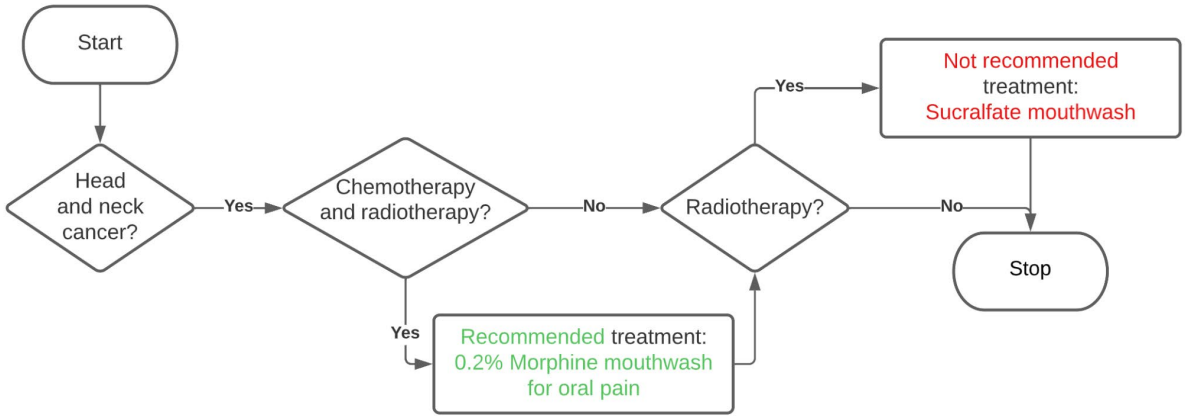


Figure 12 - A low-level flowchart of mucositis guideline referring to the management of the symptom in case of head&neck cancer patients

The Composer-based full specification of the mucositis guideline is available in the GIT repository of the project.

6.3 Skin toxicity guideline

To illustrate the skin toxicity guideline representation, we first show the flowcharts related to the management of specific symptoms, namely Tightness (Figure 13), Burning skin (Figure 14), Rash (Figure 15 and Figure 16) and Pruritus (Figure 17 and Figure 18).

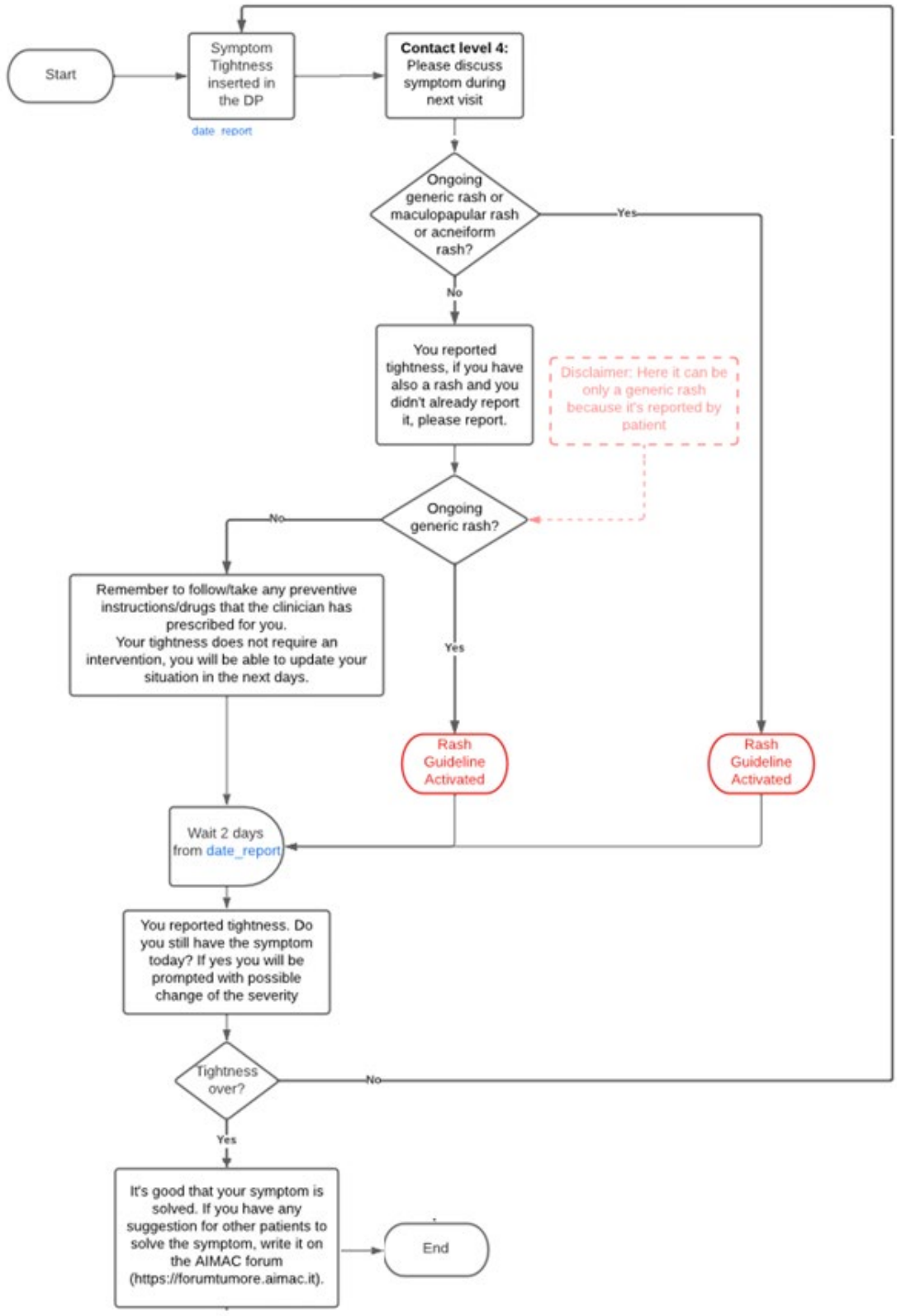


Figure 13 - The flowchart for the management of tightness

As usual, they have been developed by careful reading of the guideline text, and finalised through iterations with doctors to resolve all the uncertainties.

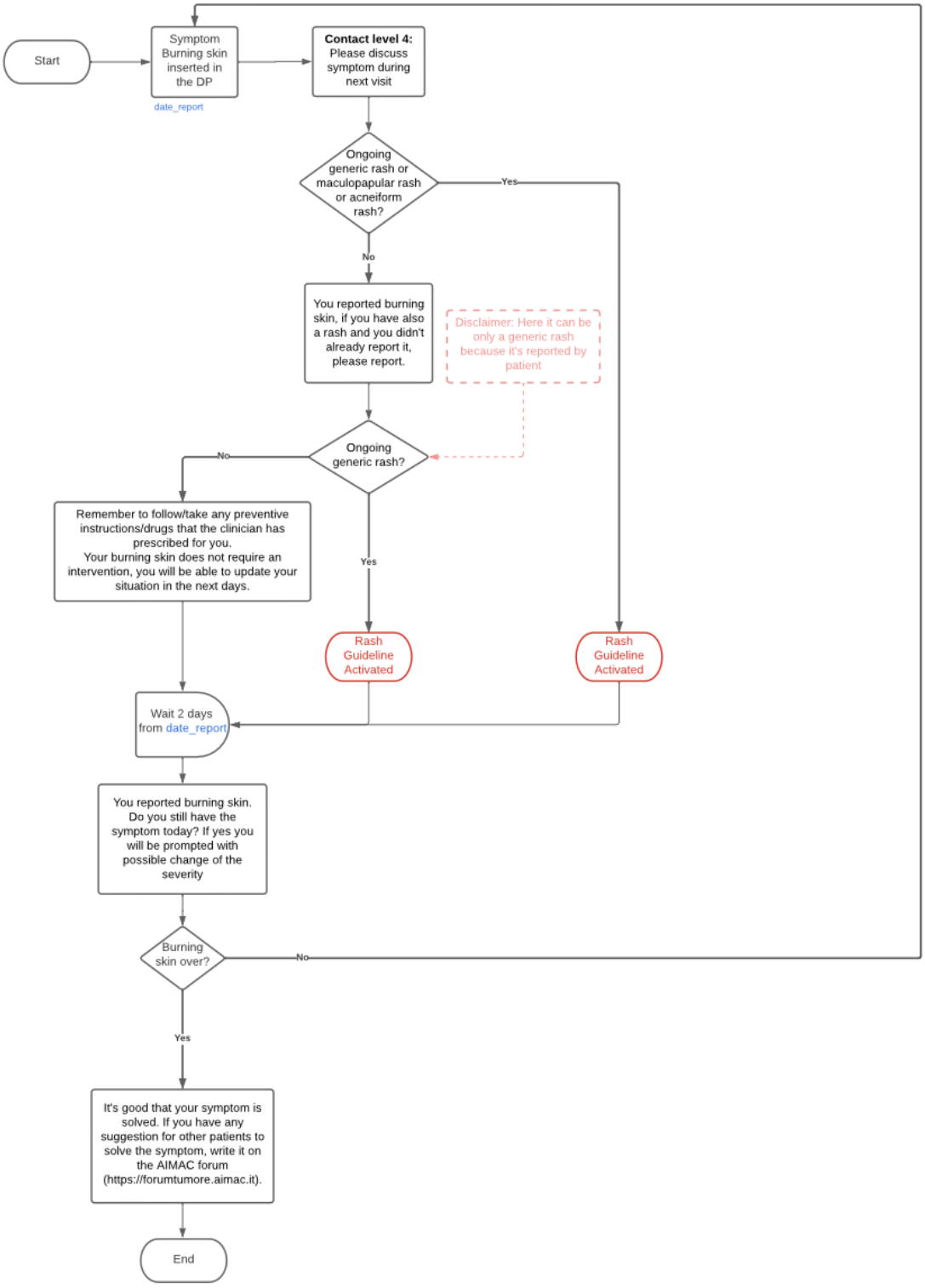


Figure 14 - The flowchart for the management of burning skin

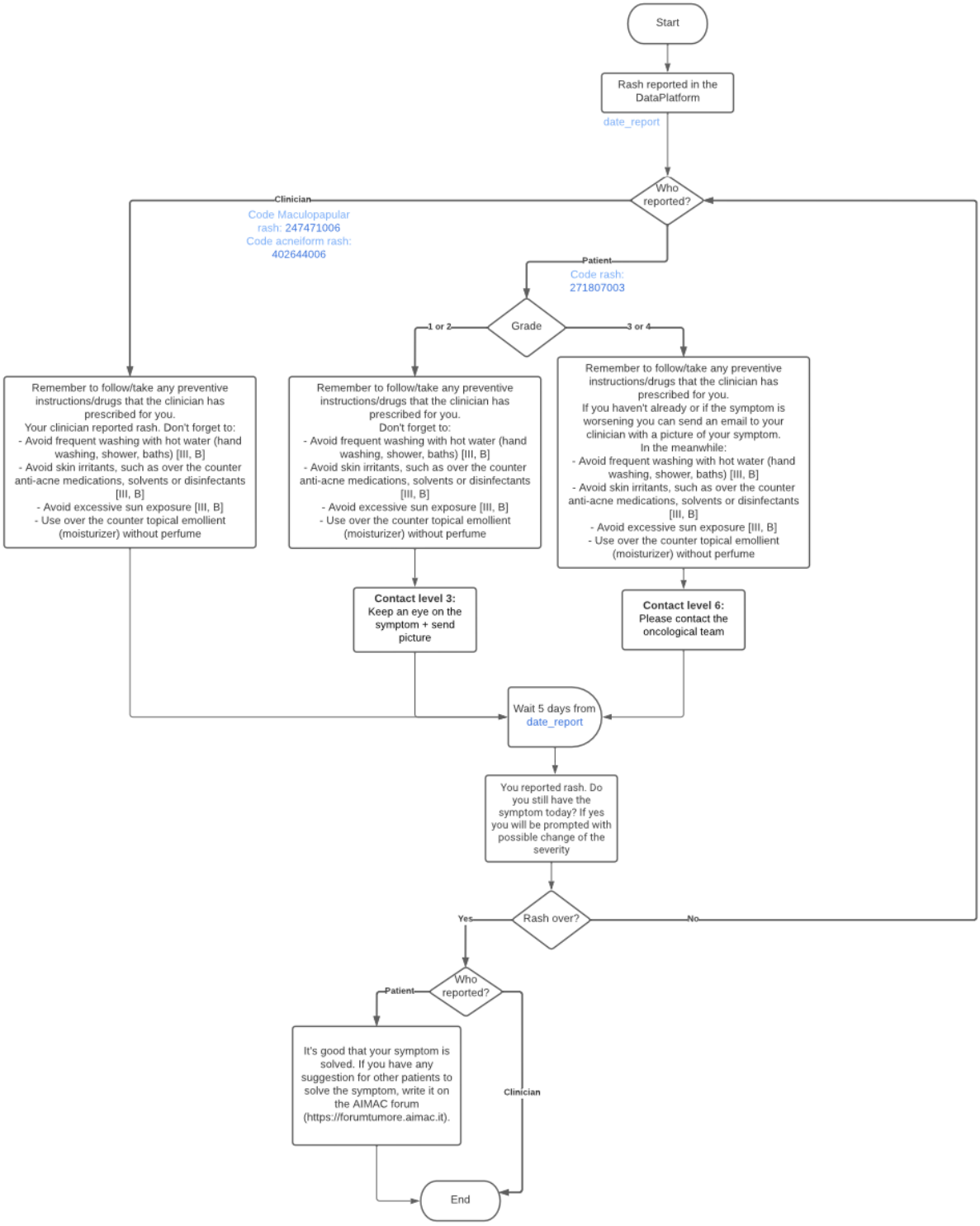


Figure 15 - The flowchart for the management of rash. Note that the recommendations to be delivered to the patient depend on who entered the symptom.

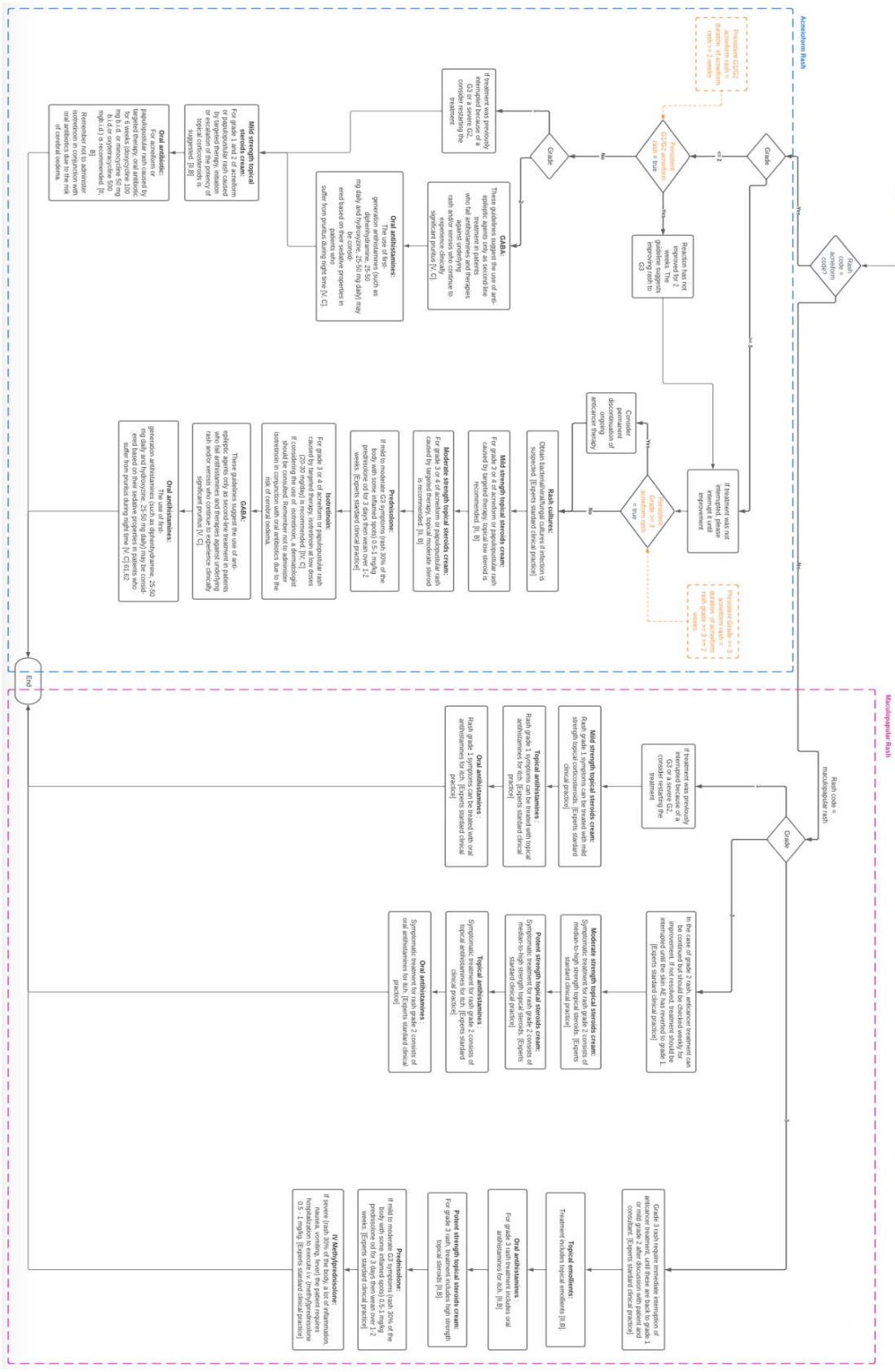


Figure 16 - The flowchart for the management of rash. It shows the recommendations for the oncologist

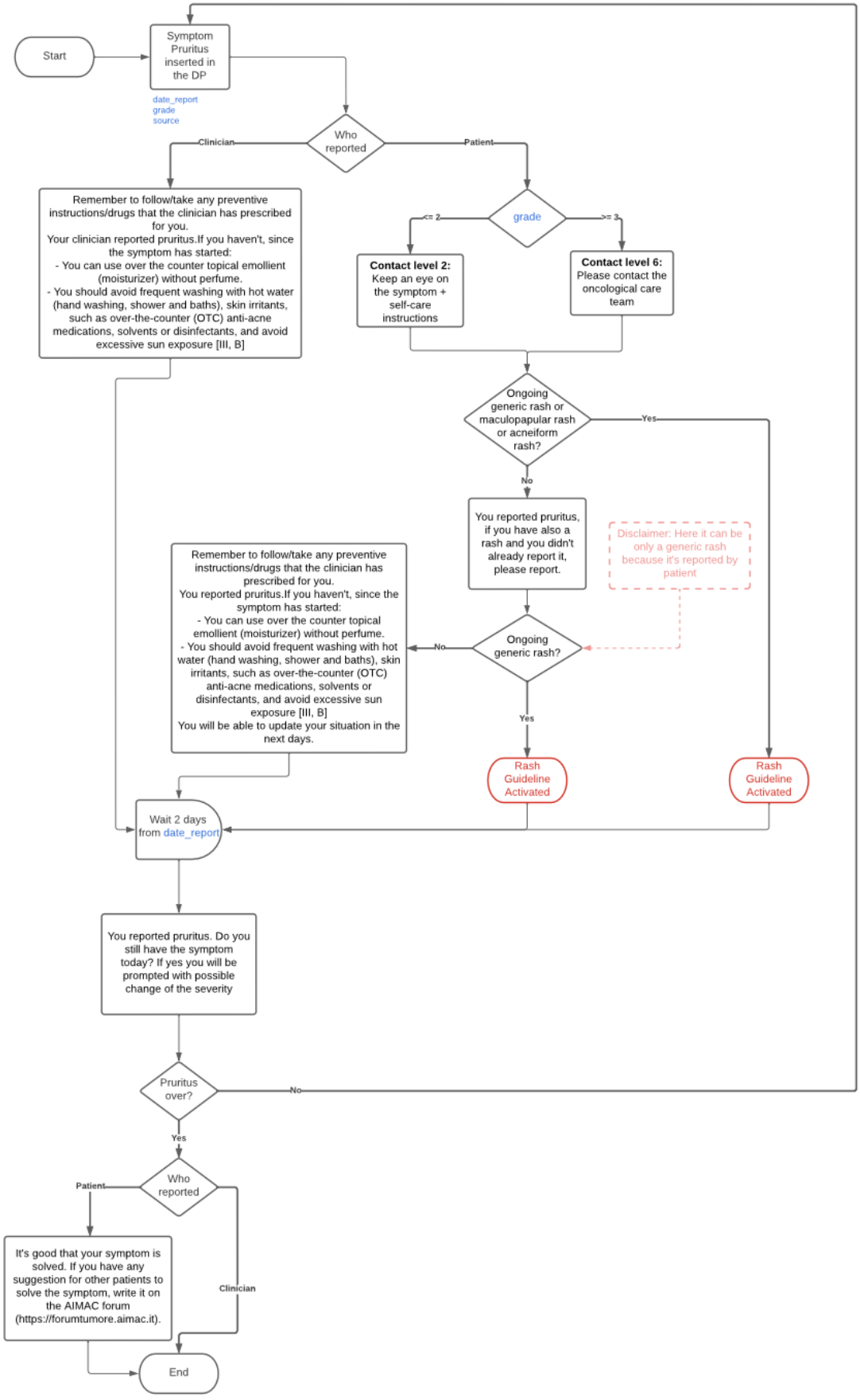


Figure 17 - The flowchart for the management of pruritus. In this flowchart suggestions for the patient are shown

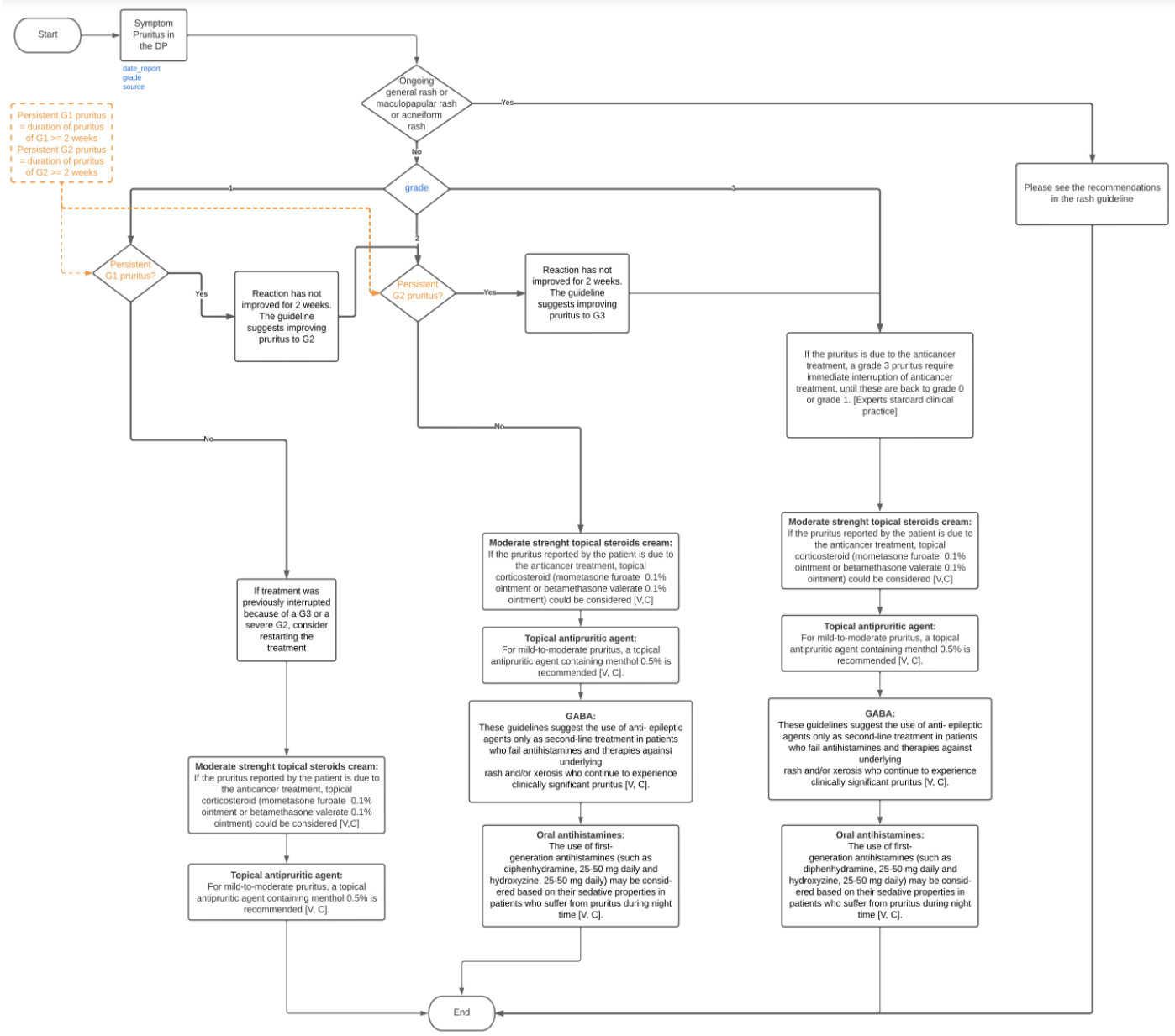


Figure 18 - The flowchart for the management of pruritus. In this flowchart suggestions for the oncologist are shown

6.4 Fatigue guideline

This section deals with the formalization of the data and abstractions of the ESMO guideline about Fatigue.

The modeling was carried out by following all the steps set out in previous sections.

Therefore, as with the previous guidelines, all extracted data and abstractions were reported in an Excel table, highlighting the data and abstractions, with the last column highlighting information that can in principle be monitored by sensors (Table 5).

Table 5 - the data and abstractions for the Fatigue guideline

Data Item	Type	Phase	Comments	Data monitoring by sensor
Age	Integer	Screening		
increased need to rest	Boolean		The symptoms must have persisted for or recurred during a defined period of time and caused significant distress or impaired social, occupational or other important areas of functioning.	
diminished energy	Boolean			
related symptoms across physical, emotional and cognitive domains	Set of Text			
NRS(Numerical rating scale)	Integer		Range: 0-10 1-3= mild 4-6= moderate 7-10= severe from the point of diagnosis onward, at regular intervals during therapy and aftercare and if clinically indicated	

Patient with cancer-related fatigue	Boolean		Abstraction TRUE if: NRS > 3 or (increased need to rest == true and diminished energy == true and related symptoms across physical, emotional and cognitive domains == true)	
Type of disease	String	Clinical history(Diagnosis)		
Stage of disease	String			
Recurrence or disease progression	Boolean			
Presence of metastasis	Boolean			
Time from diagnosis(days)	Integer			
Length of treatment(days)	Integer			
ongoing cancer medication list	Set of Text			
Onset	Date Time	Fatigue assessment(Diagnosis)		
Duration(days)	Integer			
Alleviating and worsening elements	Boolean			
Grade of interference with activities(daily life and recreational activities)				
Nausea	CTCAE	Associated elements(Diagnosis)		
Pain	CTCAE			

Other physical symptoms	Boolean		Abstraction TRUE if: Nausea == true or Pain == true	
Depression	Boolean			
Anxiety	Boolean			
Emotional distress	Boolean		Abstraction TRUE if: Depression == true or Anxiety == true	
Neurological symptoms	Boolean			
Cognitive symptoms	Boolean			
Sleep disturbances	Boolean			
Nutritional imbalance	Boolean			
Urinalysis for protein, blood and glucose				
full blood count				
urea				
electrolytes				
liver function				
thyroid function				
erythrocyte sedimentation rate				
C-reactive protein				
blood glucose				
serum creatinine				

Heart failure	Boolean	Comorbidities(Diagnosis)		Heart rate
Anemia	Boolean			
Pulmonary disease	Boolean			oxygen saturation
Hypothyroidism	Boolean		Especially in patients receiving immunotherapy	
Hypogonadism	Boolean			
adrenal insufficiency	Boolean			
hypopituitarism	Boolean			
Endocrine dysfunctions	Boolean		Abstraction TRUE if: Hypothyroidism == true or Hypogonadism == true or adrenal insufficiency == true or hypopituitarism == true	
Hepatic/kidney/neurologic dysfunction	Boolean			
Multiorgan failure	Boolean			
Infection	Boolean			
Alcohol/substance abuse	Boolean			
Presence of caregiver/social support	Boolean			

Ongoing no cancer medication list	Set of Text		Especially in elderly patients	
On_immunotherapy	Boolean		Abstraction TRUE if: Ongoing cancer medication list includes drug_Immunotherapy	
On_Chemotherapy	Boolean		Abstraction TRUE if: Ongoing cancer medication list includes drug_ChT	
dexamethasone_prescribed	Boolean			
methylprednisolone_prescribed	Boolean			

Two of the most important information for this guideline are:

• NRS: integer value that can vary from 0 to 10, with which the patient gives his personal feeling of fatigue. The guideline considers the values from: 1-3 mild fatigue, 4-6 moderate fatigue and 7-10 severe fatigue. However, to avoid double input for patients, instead of administering NRS, we relied on the CTCAE grade that patients provide, through the fatigue *level*, when they report the symptom, and that allows a reliable match with the NRS relevant ranges.

• Patient with cancer related fatigue: this is an abstraction that becomes true if NRS > 3 or if there is an increased need for rest, decreased energy and other related symptoms in the physical, emotional or cognitive domain. The NRS proxy is specified by the patient while the other 3 data are diagnosed by the doctor as it is not sufficient that they are present but must persist over time and create significant disruption in the patient's social or work life.

The fatigue guideline, unlike the diarrhoea guideline, is not triggered by any event but is always active. The flowchart in Figure 19 shows its workflow.

The screening phase is represented in orange, the diagnosis phase in blue and the treatment phase in green. The shaded area in light blue is the area dedicated to the patient, while the one in orange is aimed at the doctor.

At regular intervals (1 month for the CAPABLE project) the patient is invited to enter fatigue, if any. Subsequently we move on to the diagnosis phase which aims to understand what the possible cause of the fatigue is in order to be able to intervene in a targeted manner. Then, his previous medical condition, underlying cancer are investigated, other tests are done to try to understand the fatigue phenotype, and other comorbidities are also

investigated. The diagnosis phase is carried out through a medical examination in which the doctor will have to collect a series of information which is divided into 4 main blocks:

- Clinical history;
- Fatigue assessment;
- Associated elements;
- Comorbidities.

Once the diagnosis phase is completed, we move on to the treatment of the fatigue symptom which is foreseen in 4 key points:

1. Physical activity: aerobic training (walking, running, swimming, cycling) according to the patient's preferences combined with resistance training;

2. Education and information for the patient and his family: inform the patient and his family about the fatigue symptom and give advice on how to relieve it and how to behave in life;

3. Psychosocial interventions: recommend doing yoga or CBT (Cognitive behavioral therapy);

4. Pharmacological interventions: they are implemented only if the patient is under 65 years old. Only 2 drugs are recommended by the guideline which are Dexamethasone and Methylprednisolone.

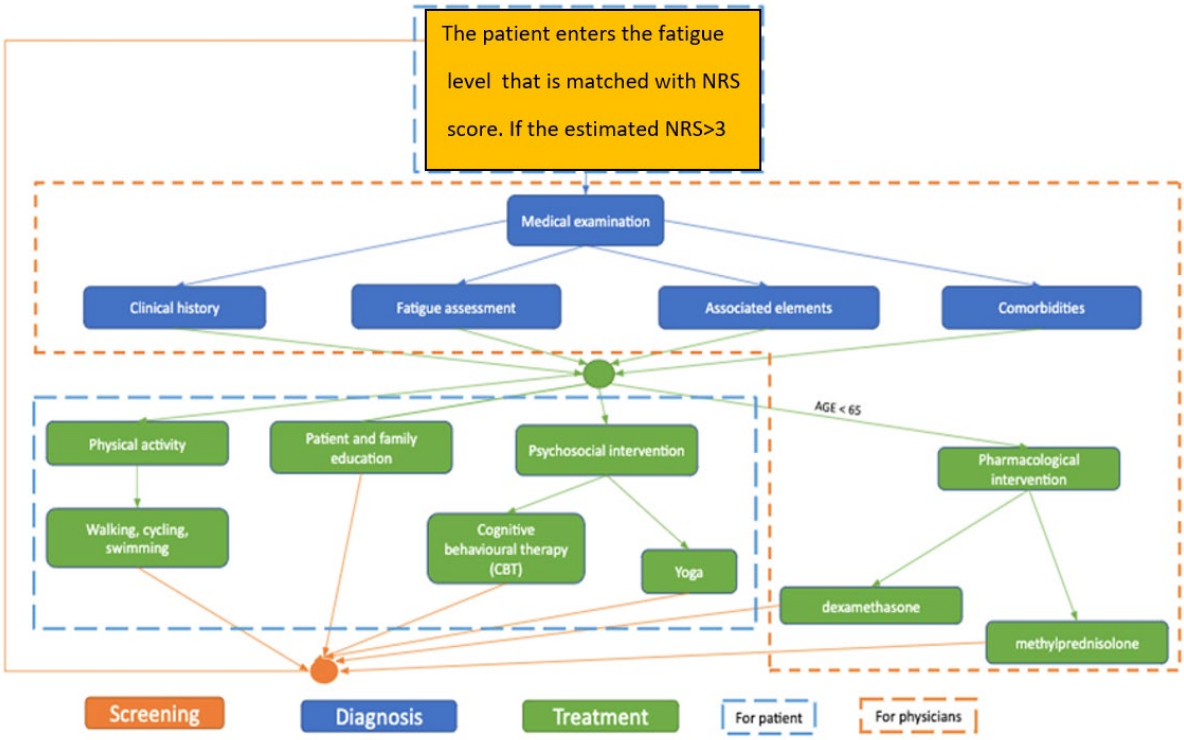
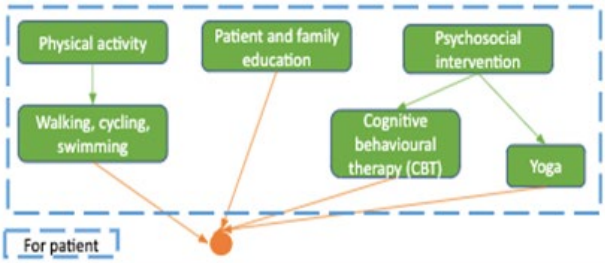


Figure 19 - The flowchart for the management of fatigue.

To complement these recommendations, as with the diarrhoea guideline, we extracted a set of recommendations from the AIMAC fatigue booklet.

These recommendations give advice on various aspects related to quality of life. This is shown in Figure 20.



Extension with AIMAC tips (from AIMAC booklet on fatigue, https://www.aimac.it/libretti-tumore/fatigue)

AIMAC TIP

- Nutrition tips
  - Small meals distributed throughout the day
  - Drink a lot
  - Taste new foods or eat the ones you like best especially if the taste changes
  - Adopt adequate oral hygiene
- Sleep tips
  - Getting enough sleep: never sleep more than necessary, but only enough to recover your strength. The less time you spend in bed, the better the quality of sleep
  - Waking up every morning at the same time: helps to achieve a good sleep-wake rhythm and facilitates the regular onset of sleep
  - Avoid the consumption of exciting substances: people suffering from insomnia should not consume coffee, strong tea and chocolate a few hours before bedtime
  - Carrying out mental exercises: mental exercises (for example thinking about something pleasant and trying to remember every detail, etc.) can be a good way to sleep
- Lifestyle tips
  - Relaxation
    - Consciousness of one's body: focus on every single part of the body
    - Check and release every muscle in the body
    - Perform breathing exercises
    - Perform imaginative skill exercises (e.g. writing a letter with thought)
    - Listen to recorded sounds (music, noises of nature such as birdsong, sea waves or the flow of a stream)

    These techniques offer maximum benefit if practiced for 5-15 minutes a day. Try, until you find the one that's right for you
  - Finding a balance between rest and activity during the days.
    This can be done by using diary techniques, including subjective rating of each activity in terms of the perceived level of fatigue. These techniques can be helpful to identify fatigue-promoting activities and develop specific strategies to avoid or modify these activities.
  - If you are unable to maintain normal work rates, talk to your superiors and inform them of your conditions and needs caused by illness and treatments

Figure 20 - Extension of the fatigue ESMO guideline with the tips from the AIMAC booklet

6.5 Immunotoxicity guideline

This guideline posed a particular challenge, because at the beginning of the project, we analysed and formalised the available version at that time, i.e the 2018 one. However, very recently [Haanen 2022] it has been revised, so we had to check for possible changes in the recommendations already developed. As an example, let's look at the diarrhoea management in Figure 21 (2018 version) and Figure 22 (2022 version).

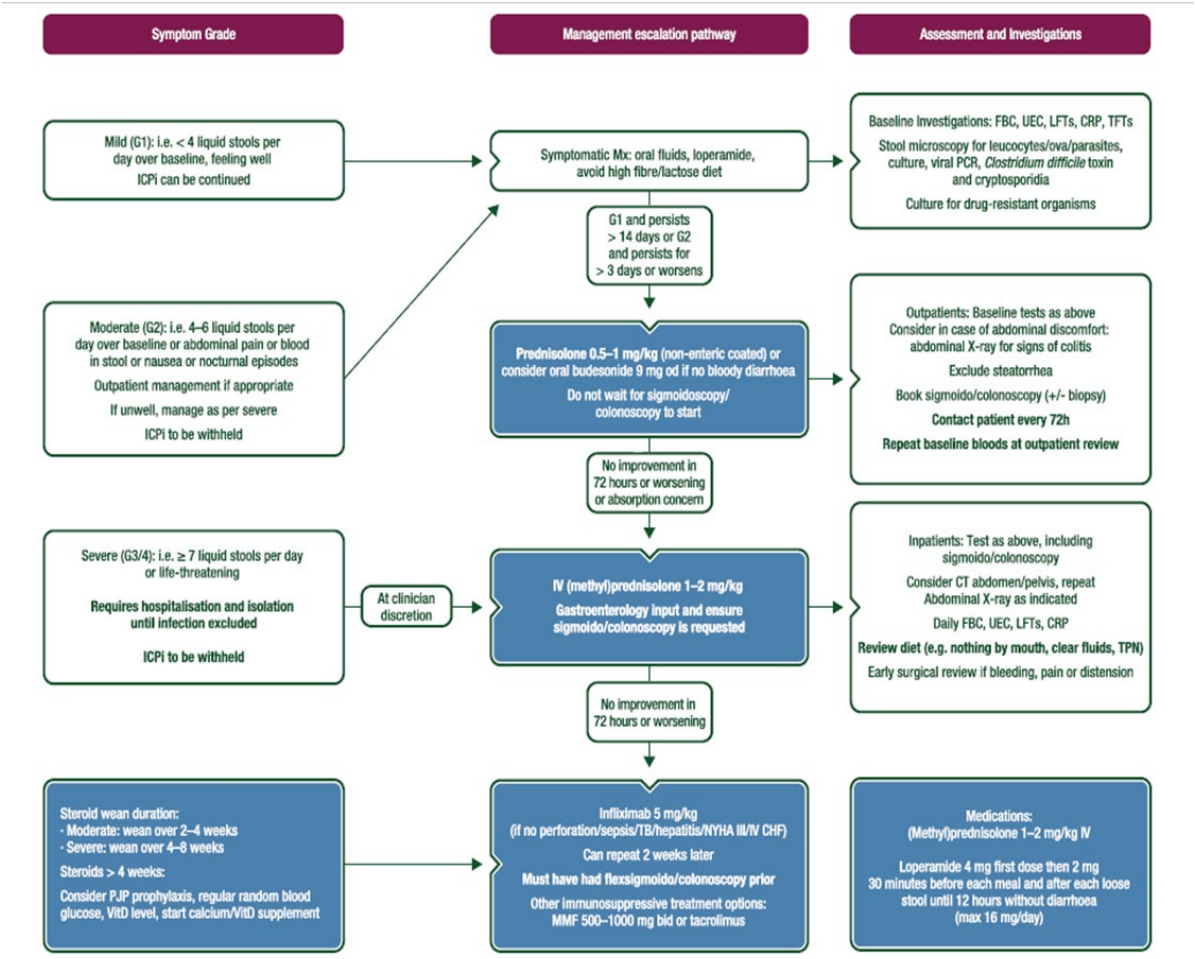


Figure 21 - The diarrhoea management in the immunotoxicity guideline version 2018 .

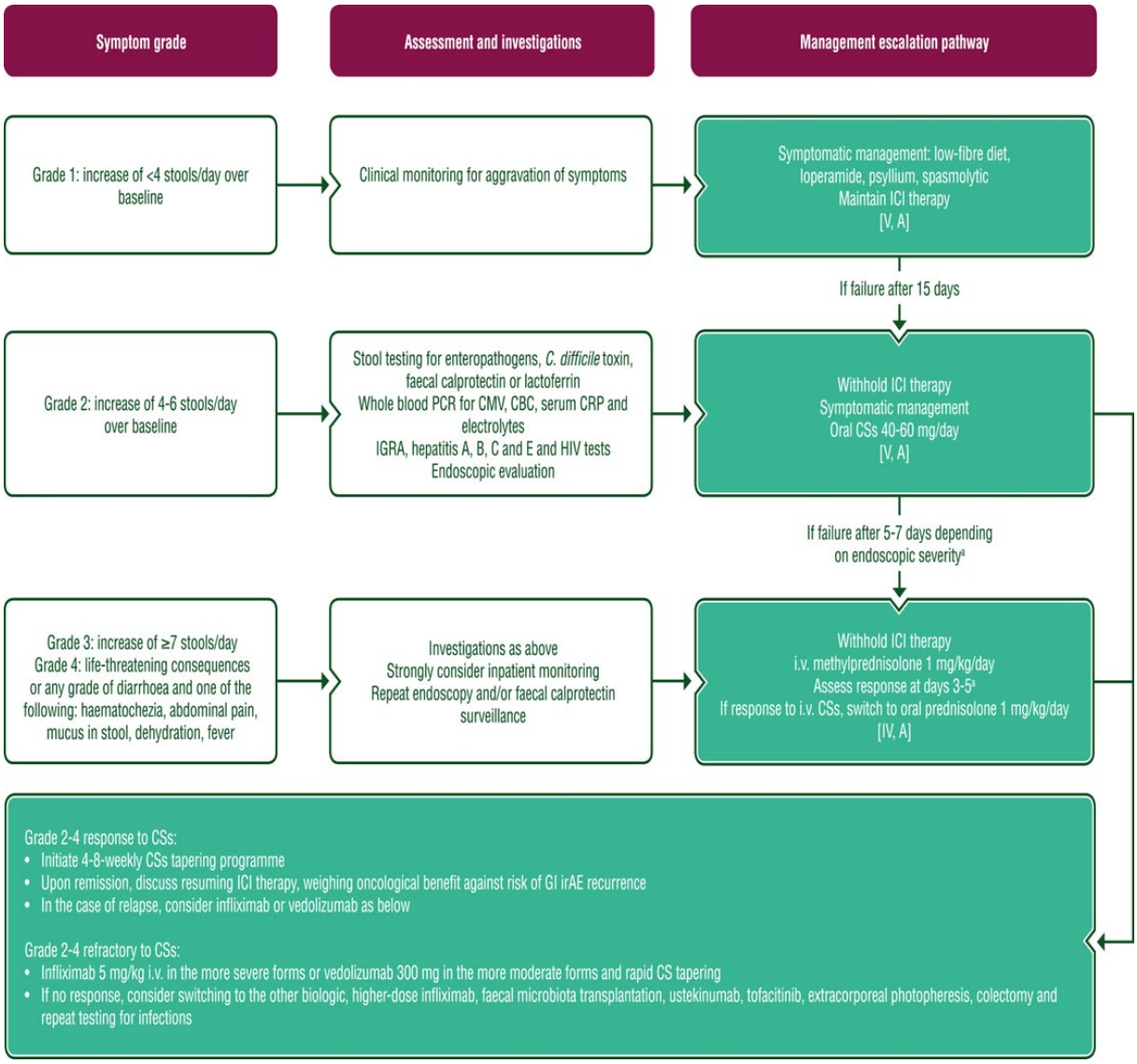


Figure 22 - The diarrhoea management in the immunotoxicity guideline updated version 2022 .

The comparison between the two versions led to some changes in the formalised guideline, the most important being:

- the lead time for defining a treatment failure has been increased, as well as the time for considering a possible hospitalisation of the patient;
- the baseline patient's assessment through blood examination and instrumental tests is now suggested starting from Grade 2 instead of Grade 1;
- budesonide for bloody diarrhoea is no more recommended
- racecadotril is no more recommended as an alternative to loperamide

As well, the skin toxicity guideline required some updates, which we do not show here for sake of space, but it is available at the following link:

https://drive.google.com/file/d/1SH1CIS_1aQnsUCwwnRCnMx0H-3yNyY3F/view?usp=sharing

The other toxicity that has been considered from this guideline is thyroid toxicity, and the flowchart is shown in Figure 23.

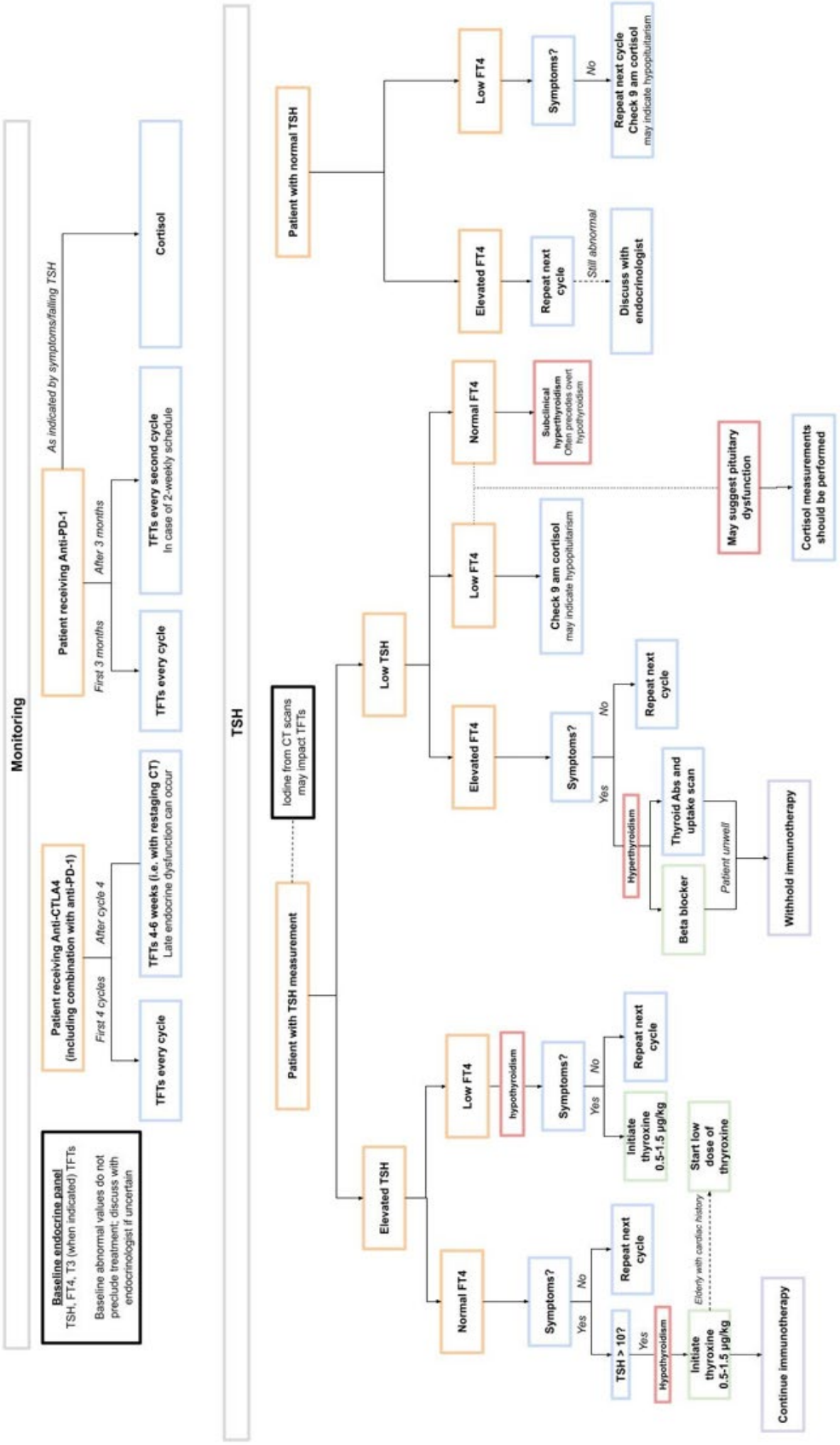


Figure 23 - The formalisation of the immunotherapy-induced thyroid toxicity management

7 Conclusions

In this deliverable we illustrated the process carried out to achieve a computer-interpretable representation of the five clinical practice guidelines implemented in CAPABLE. It's worth noting that each guideline led in fact to two versions, one for the clinicians, and the other one for the patients. At a technical level, the former are managed by the clinician DSS, and the latter by the patient Virtual Coach. The formalisms illustrated in this deliverable (tables, flowcharts, Composer visualizations), and simulation facilities offered by the Composer engine, have been used to validate the represented knowledge. Knowledge representation and its validation has been a joint effort among bioengineers and the multidisciplinary medical staff involved in the project.

8 Glossary

AI	Artificial Intelligence
AIMAC	Associazione Italiana Malati di Cancro
API	Application Programming Interface
ATC	Anatomical Therapeutic Chemical
CAPABLE	Cancer Patients Better Life Experience
CDM	Common Data Model
CIG	Computer-Interpretable Guideline
CTCAE	Common Terminology Criteria for Adverse Events
DSS	Decision Support System
EHR	Electronic Health Record
ESMO	European Society for Medical Oncology
FHIR	Fast Healthcare Interoperability Resources
GLD_R	Guideline diarrhoea Recommendation
GL	Guideline
GUI	Graphical User Interface
ICSM	Istituti Clinici Scientifici Maugeri
KDOM	Knowledge-Data Ontology Mapper
LOINC	Logical Observation Identifiers Names and Codes
NKI	Netherlands Cancer Institute
PRE	Patient Reported Experience
PRO	Patient Reported Outcome

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