Part 2: Features

Section A. Interactions among CPGs' advice

A1: Drug from a CPG has an effect on a comorbid condition
For example, low-dose Aspirin (Cardiovascular Disease CPG) affects Duodenal Ulcer (comorbid condition).

Implemented (Y/N): Y
The CMM implements that, in case DU caused by aspirin treatment is diagnosed, then aspirin treatment is suspended until the bleeding stops or after seven days, and then it is resumed, and finally long-term PPI therapy is added to the treatment.

To do this, first an enquiry asks if there is gastrointestinal bleeding, if the answer is yes, there is a plan with the actions to stop the bleeding. This has been implemented using a precondition. The plan includes the required stop and resume actions. For this purpose, a wait condition and cyclical properties are used in the tasks of this plan (see Case 1).

A2: Two or more drugs from different CPGs interact
For example, antibiotics such as Trimethoprim/Sulfamethoxazole impact the anticoagulant effect of Warfarin.

Implemented (Y/N): Y

This has been implemented in case 3. If a patient is being treated with warfarin and antibiotics are prescribed, the latter can influence the warfarin effects increasing the risk of bleeding. In this case, the warfarin dose is adjusted and the INR is measured every day making any adjustments accordingly.

There is a specific plan to solve the interaction between these medications, whose precondition is

is_completed(start_warfarin_therapy) AND
is_completed(start_TMP_SMX_antibiotic_therapy)

The plan has two incoming scheduling constraints. One arriving from the treatment with warfarin and another from the treatment with antibiotics.

Besides, since the INR has to be measured everyday, we use the repeat (cyclical) properties of the PROforma plans, running repeatedly every day until the INR arrives at an adequate value or the treatment with antibiotics finishes.

A3: Clinical goals from different CPGs conflict
For example, the goal of preventing thrombosis conflicts with the goal of preventing bleeding during surgery.

Implemented (Y/N): Y

This has been implemented but our approach does not have a specific mechanism for resolution of goal conflicts.

If a new problem is detected, the medication is changed according to the additional recommendations provided. Depending on the case, the medication will be suspended (possibly, resumed after certain conditions hold), or replaced with a new medication. We use preconditions and start/stop actions. In some cases, we also use wait conditions to resume medication when the risk disappears.

A4: Conflicting actions (e.g., drugs, procedures) from different CPGs

For example, one CPG recommends administration of Clopidogrel (Transient Ischemic Attack CPG) while another recommends suspending Clopidogrel (Coronary Artery Bypass Grafting CPG).
Implemented (Y/N): Y
By definition, the CMM itself cannot contain conflicts. If the conflict is described in the scenario, then a CMM should be modelled such that the conflicting recommendations are properly handled.

A5: Duplicate or redundant advice from different CPGs
For example, Calcium Channel Blockers are recommended in Hypertension and Cardiovascular Disease CPGs.

Implemented (Y/N): N
In our approach, this would require an adaptation of the PROforma CIGs containing redundant advice. Since we have focused on the CMMs alone, we consider that we do not support this feature.

A6: Temporal relationship between different CPGs
For example, take Cefpodoxime (Acute Otitis Media CPG) two hours after taking antacids (Gastroesophageal Reflux Disease CPG).

Implemented (Y/N): Y
Temporal relationships can be implemented using wait conditions. For example, in Case 1 the model checks if the gastrointestinal bleeding has ceased 3 days after the aspirin treatment has stopped.

A7: Multiple interactions from different CPGs interacting at the same time
For example, replacing low-dose Aspirin (Transient Ischemic Attack CPG) with Proton Pump Inhibitor to mitigate Duodenal Ulcer (Duodenal Ulcer CPG) impacts new comorbid condition of Osteoporosis (Osteoporosis CPG).

Implemented (Y/N): Y
Such interactions can be implemented in the PROforma CMM. In this example, if osteoporosis appears after adding PPI, there is a plan whose objective is to investigate if osteoporosis is due to PPI therapy.

Section B. Mitigation strategies when CPGs offer interacting advice

A mitigation strategy is an action taken to address one or many of the interactions that were identified above.

B1: Adding a drug to mitigate an adverse effect
For example, add a PPI to mitigate the Duodenal Ulcer due-to Aspirin.

Implemented (Y/N): Yes

It has been implemented in the PROforma CMM. If a duodenal ulcer due to aspirin is diagnosed, the CMM includes an action/plan to start the new treatment according to the additional recommendations provided. The existence of the adverse effect in question is checked by means of preconditions in the action/plan.

B2: Adjust drug dosage
For example, a reduction of 10% of warfarin dosage.

Implemented (Y/N): Y
In our CMMs we do not explicitly represent drug details such as dosage. Instead, we use a task naming that reflects such details. For example, reduce_dose_of_warfarin_by_10percent or start_dual_anti_platelet_therapy_for_12months.

Note that in PROforma it is possible to define variables for these drug details, and to modify them when necessary using task postconditions, although we have not used them.

In the corresponding CMM, we have an action named reduce_dose_of_warfarin_by_10percent that explicitly represents this reduction considering the INR value.

B3: Monitor the effect of a drug
For example, monitor progression of the Duodenal Ulcer during overlapping treatment with Aspirin.

Implemented (Y/N): Y
Regarding the above example, we have only considered stopping the treatment with aspirin until bleeding is solved, according to the additional recommendations provided.

In other cases, we monitor the effect of a drug using the cyclical properties of tasks. For example, we monitor the effect of antibiotics during the treatment with warfarin. Note that these monitoring actions are always encoded in specific cyclical tasks.

B4: Replacing a drug with a safer / non-interacting drug / more effective drug for comorbidity
For example, replace Aspirin with Clopidogrel for a patient with Duodenal Ulcer.

Implemented (Y/N):Y
This is implemented in the CMM. According to the additional recommendations provided, there is an action, whose name starts with the word “stop”, to stop aspirin treatment followed by an action, whose name begins with the word “start”, representing the clopidogrel treatment.

B5: Discard unsafe/interacting drug
For example, suspend ACE inhibitor when eGFR value drops by over 30% over 4 months.

Implemented (Y/N): N (not this particular case)

In this particular example, we have not implemented the part “over 4 months” because it is not included in the (additional) recommendations provided. If such recommendations were given, it would be possible to implement them using a cyclical task (with an “until” attribute). For other similar examples, we have implemented a solution (see Case 2, where PCB treatment is discarded for CKD patients).

B6: Delay a task to avoid a temporal overlap
For example, stop Dabigatran 4 days prior to surgery for a patient with high bleeding risk.

Implemented (Y/N): Y
We have asked to introduce the date of the surgery and, using a wait condition to avoid the temporal overlap. The wait condition is:
date_diff_days(now(), date_of_surgery)<5

B7: Add a task to ensure a temporal overlap
For example, for a patient with high risk of thromboembolism who is undergoing surgery with a high risk of bleeding, suspending Warfarin 5 days prior a surgery and resuming it one day after the surgery, introduces a 6-day period where the patient is at risk of bleeding; bridge with heparin starting on day 3 prior to surgery till the day of surgery to ensure overlap of the surgery context and the thromboembolism prevention context.

Implemented (Y/N): Y
The avoidance/enforcement of temporal overlaps has been implemented using wait conditions. Since the bridge treatment was described as an option, we have modelled it with an enquiry so that the user (clinician) can introduce the desired option. The bridge treatment has been modelled as a new action with the proper wait condition.

B8: Are there any other mitigation strategies for the multimorbidity CPG problem that you have implemented?

Implemented (Y/N): N
We have only implemented solutions when (additional) recommendations are provided.

Section C. Other features

C1: Patient preferences and/or patient burden
For example, choosing one drug over another due to lower price; or choosing DOACs over warfarin to avoid checking INR on regular basis.

Implemented (Y/N): Y
Patient (and clinician) preferences have been implemented by using enquiry tasks to introduce the desired option among the proposed alternatives.

C2: Optimization of clinical resources
For example, grouping tests on the same day.

Implemented (Y/N): N
We have only implemented solutions when (additional) recommendations are provided.

C3: Explanation of the mitigation strategy(ies)
For example, why a given strategy was identified and what it entails.

Implemented (Y/N): N / Partly
Our solutions do not provide any explanation utility. However, CMMs are self-contained and self-explanatory, therefore the reasons behind the enactment of a particular action path can be found by the examination of the CMM.

C4: Alternative mitigation strategies for a single interaction
For example, if there are more than one possible mitigation strategies, are they identified and presented.

Implemented (Y/N): Y
For example, in Case 1 there are 3 possible treatment alternatives that have been modelled in the CMM. The clinician (possibly, the patient) has the option to choose the most convenient one.