An Approach to Decision Support in Heart Failure

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Abstract. Chronic heart failure is a severe clinical syndrome among the most remarkable for prevalence and morbidity in the developed western countries. The European STREP project HEARTFAID aims at realizing an innovative platform of services which will improve the processes of diagnosis, prognosis and therapy provision in the heart failure domain. The core of the platform intelligence is a Clinical Decision Support System, designed by integrating innovative knowledge representation techniques and hybrid reasoning methods, and including advanced tools for the analysis of diagnostic data. In this paper we discuss how we are using semantic web technologies for implementing a real, significant clinical scenario, covering the clinical course of a heart failure patient.

Keywords: Decision Support Systems, Ontologies, Reasoning.

1 Introduction

Heart Failure (HF) is a complex clinical syndrome resulting from any structural or functional cardiac disorder and which impairs the ability of the ventricle to fill with or eject blood. In its chronic form, HF is one of the most remarkable health problems for prevalence and morbidity, especially in the developed western countries, with a strong impact in terms of social and economic effects [1].

The European STREP project HEARTFAID ("A knowledge based platform of services for supporting medical-clinical management of the heart failure within the elderly population") aims at defining efficient and effective health care delivery organization and management models for the "optimal" management of HF care.

The HEARTFAID platform (HFP) has been conceived as an integrated and interoperable system, able to guarantee an umbrella of services that range from the acquisition and management of raw data to the provision of effective diagnostic support to clinicians. Specifically, the core of HFP is the Clinical Decision Support

System (CDSS), which has been carefully designed by combining innovative knowledge representation formalisms, robust and reliable *reasoning* approaches, based on *learning* and *inference*, and innovative methods for diagnostic images and biomedical signals processing and analysis [2]. Semantic web technologies have been selected as the most advanced tools for knowledge formalization, re-using and sharing, for inferential reasoning, and for the integration and easy access to a number of services.

This paper aims at showing the approach based on semantic web technologies we have designed and at presenting and discussing the current results of the implementation activity, which will be finalized in 2009.

We will start by briefly reviewing the use of semantic web technologies for decision support, and then introduce the HEARTFAID approach, by describing CDSS peculiarities and main functionalities. Current results obtained on a real scenario are finally presented and discussed.

2 Clinical Decision Support and Semantic Web Technologies

The development of computerized applications for supporting health care givers is an old but still alive quest, started more than 45 years ago, in the early 1960s, and with ascending and descending periods of interest and growth. In their daily activity, health care practitioners have to continually face a wide range of challenges, ranging from making difficult diagnoses, to improve patients' quality of life, to saving money, which can benefit from effective support of computerized applications [3].

A number of systems have evolved for supporting medical decision by supplying a variety of services, from information retrieval and reporting, scheduling and communications, to cost-effectiveness, error prevention, safety, and improvement of health care quality. The most common realizations include electronic medical records [4], computerized alerts and reminders [5], clinical guidelines formalizations [6], provider order entries [7], diagnostic support [8].

The key element of all CDSS typologies is the corpus of *knowledge* meant as the necessary expertise and know-how for bringing health care to effect. Representing knowledge is then the primary task of CDSS development and concerns understanding, designing, and implementing ways of formally coding the knowledge necessary for deriving other knowledge, planning future activities, and solving problems that normally require human expertise. Suitable *languages* or *formalisms* are used for knowledge representation and result into a *Knowledge Base* (KB) of the clinical expertise. Usually, the formalism is *symbolic* and the KB contains *statements* or *expressions* of one of the following formalisms: (i) rule based; (ii) frame based; (iii) network based; and (iv) logic based [9]. Workflow based representation is also becoming well-known, especially for modeling guidelines [10], [11]. Moreover, in recent years ontologies are emerging as a powerful knowledge representation formalism which is conceptually equivalent to the frame based and to first order logic approach [12], [13].

The KB is exploited by a *reasoning engine* which processes available information for formulating new conclusions and answering questions. *Inferential* reasoning is employed for inferring new knowledge from the KB by deduction, induction or abduction.

Semantic Web Technologies (SWT) are gathering more and more attention within the sphere of clinical decision support, thanks also to the always wider computerization of clinical systems and to the increasing availability of internet connections. More significantly, they represent instruments for viable solutions to the key problems of CDSS development, such as data integration, knowledge representation, reasoning and intelligent agents. Such significance is testified, first of all, by the rise of several ontology-like formalizations of medical domain, e.g. the Systematized Nomenclature of Medicine (SNOMED) [14], the Unified Medical Language System (UMLS) [15] or the Medical Subject Heading (MeSH) [16], to name a few. Moreover, a number of systems have been developed by using SWT, e.g. for assisting decision support in breast cancer management [17], or for modelling clinical practice guidelines [18].

The W3C has issued several recommendations about SWT, trying to establish format standards. Worthy of mention is the *Semantic Web Technology Stack* [19] which suggests a list of instruments such as the Web Ontology Language, OWL [20], for defining ontologies, as the actual de-facto standard semantic markup language for this task, and SPARQL as a language for querying ontologies [21]. Moreover, it recognizes the importance of rules for filling representation lacks of ontologies and in this context a new standard is under development, i.e. the Rule Interchange Format (RIF) [22], which will allows rules to be translated between different rule languages and thus transferred between rule systems. As an evidence of the use of SWT, the RIF working group debated a use case within the medical field.

It is important to underline that, although being powerful knowledge representation and management instruments, SWT are unsufficient to solve important problems such as handling time events and constraints, and uncertainty. So far, ad hoc strategy are usually developed when needed.

3 The HEARTFAID Case: a Semantic Web Approach to Support Decision in Heart Failure

HEARTFAID aims at deploying an effective platform of services to support HF routine practice. All the functionalities and services supplied by the entire HFP fall into three macro “contexts”: (i) *biomedical data collection and management*, devoted to the acquisition and storage of continuous flows of information within healthcare structures, during patient hospitalization and outpatient visits, from analysis laboratories, and within a homecare program by *telemonitoring* patients’ conditions; (ii) *knowledge-based decision support*, whose main goal is supporting, at decisional level, the HF health care operators, by making more effective and efficient all the processes related to diagnosis, prognosis, therapy and health care personalization of the HF patients; and (iii) *end-user applications*, which provide the doorway to a multitude of end-user utilities and services, such as accessing an electronic health record (EHR), querying the CDSS, applying advanced models and methods for the extraction of new knowledge, and so forth.

Our focus is on CDSS which is meant for an overall support of HF management. A careful investigation about the needs of HF practitioners and the effective benefits assured by decision support was performed: four problems have been identified as highly beneficial of HEARTFAID CDSS point-of-care intervention, i.e. diagnosis, prognosis, therapy and follow-up. An accurate analysis of the corpus of knowledge highlighted these problems mainly relied to the domain know-how and the clinical guidelines. Nevertheless, the solution of some of them seemed still debated in the medical community, due to the lack of validated and assessed evidences, e.g. prognosis. In such cases, making a decision requires an investigation on the hidden, complex, often non-linear correlations among data, together with high-level analytical processing functions. The knowledge needed for the solution should, then, be acquired directly from data (*inductive knowledge*) and stored in a model (e.g. *Artificial Neural Networks*, *Support Vectors Machines*), able to induce *sub-symbolic* knowledge from a data-driven processing [23].

HEARTFAID CDSS was then designed for incorporating different reasoning models and according to a multilevel conceptualization scheme for distinguishing among (i) the *knowledge level*, corresponding to all the information needed by the system for performing tasks, e.g. data, domain knowledge, computational decision models; (ii) the *processing level*, consisting of the system components that are responsible of tasks accomplishment by using the knowledge level; (iii) the *end-user application level*, including the system components whose functionalities are specifically defined for interacting with the user. This separation assures a high level of flexibility, since any change of the formalized knowledge will not affect the processing level.

Moreover, the knowledge level was modeled by integrating a formalization of symbolic knowledge and computational reasoning models required by those difficult HF decision problems, such as prognosis assessment and early detection of patient's *decompensation*.

In detail, the CDSS architecture consists of the following components (Fig. 1):

- *Domain Knowledge Base*, consisting of the domain knowledge, formalized from the european guidelines for the diagnosis and treatment of chronic HF and the clinicians' know-how;
- *Model Base*, containing the computational decision models, signals and images processing methods and pattern searching procedures;
- *Meta Knowledge Base,* composed by the strategy knowledge about the organization of CDSS tasks.
- *Brain*, the system component endowed with the reasoning capability;
- *Explanation Facility*, providing means to explain conclusions taken.

The Brain was modeled by functionally separating a *meta level*, devoted to task accomplishment and organization, and an *object level*, responsible of actually performing tasks, by reasoning on the computational and domain knowledge. A *Strategy Controller* was inserted for performing the meta level functionalities, by orchestrating the two components of the object level, i.e. the *Inference Engine* and the *Model Manager*.

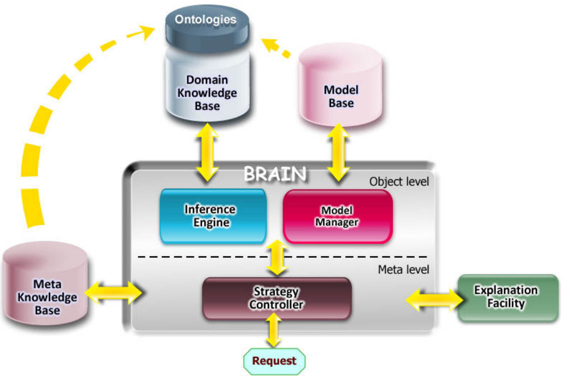


Fig. 1. The general view of the HEARTFAID CDSS architecture – dashed arrows correspond to reference to the ontologies, while the others denote a direct communication.

For modeling the Domain Knowledge Base, ontologies combined with rules were chosen as representation formalism since also assures easy re-use and sharing of knowledge. After a preliminary ontology, mainly corresponding to a structured terminology of the domain, we began to develop a new ontology by inserting relevant properties, classes and relations for a coherent and comprehensive formalization, also in accordance to standard medical ontologies, such as UMLS. To have a modular, less complicated developing, and more performing system we are developing some core and upper level ontologies. This was worthwhile and possible because in most cases the decisional support does not require the reasoner to take into account all about the patients and domain information (examples of core ontologies are *Therapy*, *MinnesotaQuestionnaire*, *Ecocardiocram* and example of upper ontologies are *DiagnosticProcedure*, *Suggestion*). A fragment of this ontology is shown in Fig. 2.

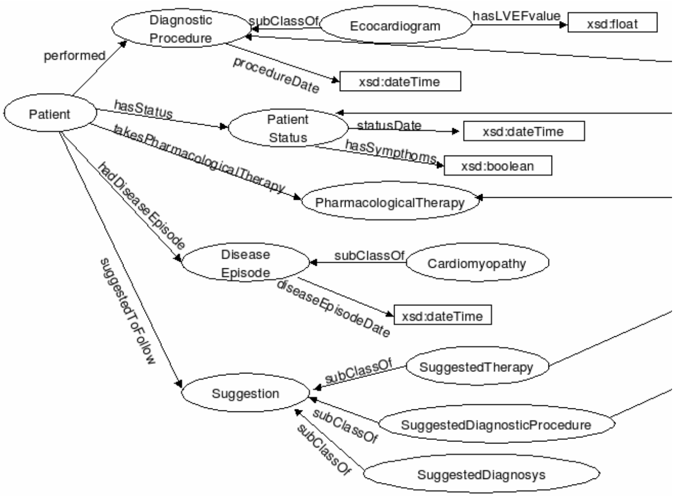


Fig. 2. Some relevant classes and properties of the ontology

Rules were used to fill the logical lacks of ontologies axioms and were elicited from the ESC guidelines and with a strong interaction with the clinicians. An example rule for therapy suggestion, elicited in a natural language implication format: "*If a patient has Left Ventricle Ejection Fraction <= 40% and he is asymptomatic and is assuming ACE Inhibitors or ARB) and he had a myocardial infarction then a suggestion for the doctor is to give the patient Betablockers*". Of course this first set of rules was incomplete caused by logic jumps so now we are revising the entire flow of reasoning by refining rules and ontologies when not rewriting them.

An inference engine was devised for the corresponding inferential reasoning processes, by induction and deduction on the formalized knowledge for assessing patients' status, formulating diagnosis and prognosis, assisting therapy planning, and patients' monitoring. Instruments selected for development are discussed in the successive section.

HFP was devised for supplying a number of services and conceived for consciously distributing the work load among the various components. This means that, to avoid burdening the CDSS, other components were inserted for aiding the effectiveness of the support services. Their development was distributed among the partners of the project. A sketch of the platform with the components interacting with the CDSS is shown in Fig. 3. An EHR module was inserted for suitably organizing, visualizing and managing patients' data, stored into the platform Repository. In particular, a dedicated repository for storing examination images was conceived in accordance to the DICOM standard. An Agenda module was included for managing patients' care planning, e.g., scheduling new visits, prescribing new examinations and so forth. The User Interface was designed as a fundamental component, responsible for all the interactions and communications with the users.

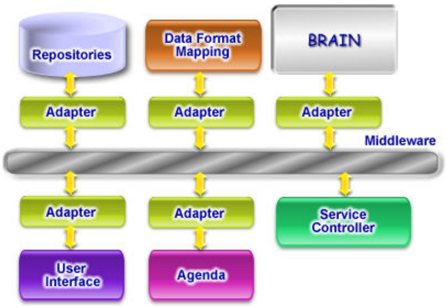


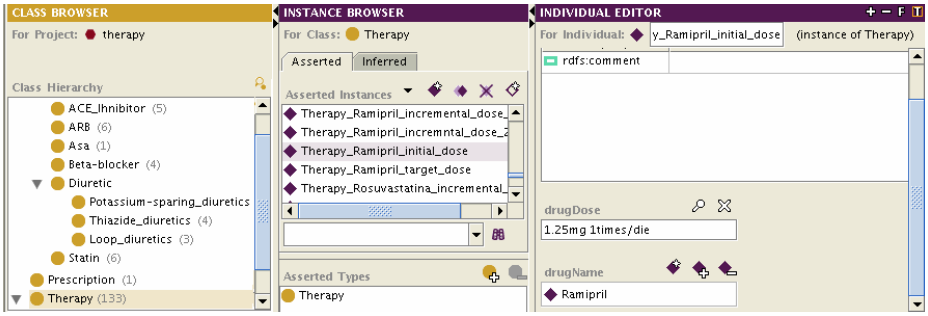
Fig. 3. A sketch of HFP with the components that interact with the CDSS.

The different components of the platform were seen as *resources*, by *virtualizing* the operations required for their management. When involved, the different components are dynamically integrated for supplying sophisticated but much flexible applications. The responsible of guaranteeing integration and interoperability among all the HFP components was defined as the platform Middleware, which includes all the adapters necessary for the virtualization. For simplifying the provision of different services, a Service Controller was comprised for managing platform events and invoking the other components. In this perspective, the CDSS component was designed as a resource able to offer a number of functionalities and to interact with the other resources for performing its tasks. Each decision-making problem has to be translated into a *request* or a *class of requests* committed to the CDSS, which is then activated *on-demand*. The system handles every request according to a specific policy encoded in the Meta KB, and interacting, when needed, with the other platform components.

4 Summary of Results on a Real Scenario

In accordance to W3C recommendations, we selected OWL for defining the ontologies and Protégé and Swoop as editors. For defining the rules of the knowledge base, we chose SWRL [24], the Semantic Web Rule Language combining OWL and RuleML [25], which is a submission to W3C that extends the set of OWL axioms to include Horn-like rules. For realizing the reasoning component, Jena [26] was selected as a Java programming environment that uses OWL, SPARQL and includes a rule-based inference engine. To improve the reasoning capability of the latter and also to use SWRL we also used Bossam [27] and Pellet [28] depending on the SWRL builtins offered.

A use case scenario was chosen in order to simulate a real case that is partial if related to the entire problem but it let us understand better the work and the rules to be implemented. According to what stated in the previous section, we developed several core ontologies: Fig. 4 shows a fragment of the Therapy core ontology.



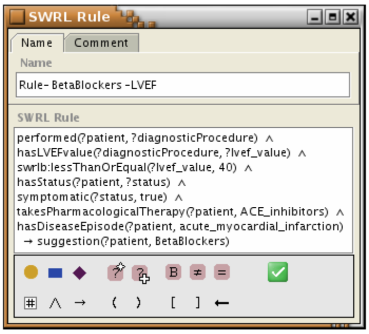
For Individual: y_Ramipril_initial_dose (instance of Therapy)

drugDose: 1.25mg 1times/die

drugName: Ramipril

Fig. 4. A Fragment from the therapy core ontology

The set of rules elicited using a logic implication format in natural language has been simply transformed into a set of SWRL rules. An example rule is shown in Fig. 5 as it has been defined in Protégé.



Name: Rule- BetaBlockers -LVEF

SWRL Rule:

```
performed(?patient, ?diagnosticProcedure) ∧
hasLVEFvalue(?diagnosticProcedure, ?lvef_value) ∧
swrlb:lessThanOrEqual(?lvef_value, 40) ∧
hasStatus(?patient, ?status) ∧
symptomatic(?status, true) ∧
takesPharmacologicalTherapy(?patient, ACE_inhibitors) ∧
hasDiseaseEpisode(?patient, acute_myocardial_infarction)
 → suggestion(?patient, BetaBlockers)
```

Fig. 5. A rule developed in SWRL.

Strongly typed data are stored into heterogeneous (relational and XML) and distributed databases by clinicians, patients and devices. Instead of using sets of rules codified into a programming language for transforming data into ontological format, we preferred to maintain the typed data and transform them into OWL using XML mapping files (D2R and XQuery). This allowed us to maintain independence of ontologies and rules from programming and from the inference engine choice using standards.

Currently the meta-level is only devoted to task accomplishment and sub-tasks organization, and for managing the requests from and towards the other HFP components. After all the object models completion, the strategy level will be used to foresee prognosis by merging the results coming from the inference and the other models (Support Vector Machines, Bayesian and Neural Networks).

Let us now consider the use case and how it is being developed. We consider a 65 years old patient, former smoker, suffering from hypertension from several years. The patient is enrolled in the HFP and, in particular, the telemonitoring services offered by the platform are activated. Information about the patient's status are sent to the HFP through the use of devices (blood pressure, oxygen saturation,...) and by web forms filling. For example the patient periodically answers a questionnaire through his web-based user interface and sends the information to the HFP interface that checks missing values. Then the Service Controller stores this information into the repository, gets historical data and opportunely invokes the specific CDSS service responsible of handling the request. The CDSS analyzes data and answers supplying the current patient's status, e.g. worsening of symptoms, and a set of suggested actions the clinician should undertake, e.g. schedule a new visit, change the New York Heart Association (NYHA) class, and change the therapy and so forth.

Then the Service Controller stores results into the repository and, according to the CDSS conclusions, if patient situation is worsening alert the clinician on duty, sending a sms or an email on the base of severity, for example suggesting to perform a visit.

When the doctor on duty logs in the HFP, the list of patients is displayed ordered by their severity status and the timestamp of the last related event (Fig. 6 - left).
Then he chooses to analyze the patient's situation and the change in his status is shown along with the list of suggested actions, for instance as a list of operations that can be selected. He then approves the schedule of the visit and the Service Controller forwards the request to the Agenda that opportunely records it and informs the patient. At the hospital, during the visit, the physician inserts his observations into the patient's record and decides to approve the change of the NYHA class (Fig. 6 - right): he selects the corresponding action within the list and the Service Controller takes care of registering the change in the patient's record. An ECG is then performed for further investigations. Once the information obtained by the ECG have been recorded, a request for its interpretation is sent by the Service Controller to the CDSS, which suggests performing an echocardiography as displayed in the recommended actions list. A change of therapeutic strategy is decided by the clinician supported by the CDSS (Fig. 7).

Future activities will consist in finalizing the platform implementation by concluding the realization of the Domain Knowledge Base, the algorithms contained in the Model Base and the Brain, in particular of its meta level in order to integrate all the object models and the interface.

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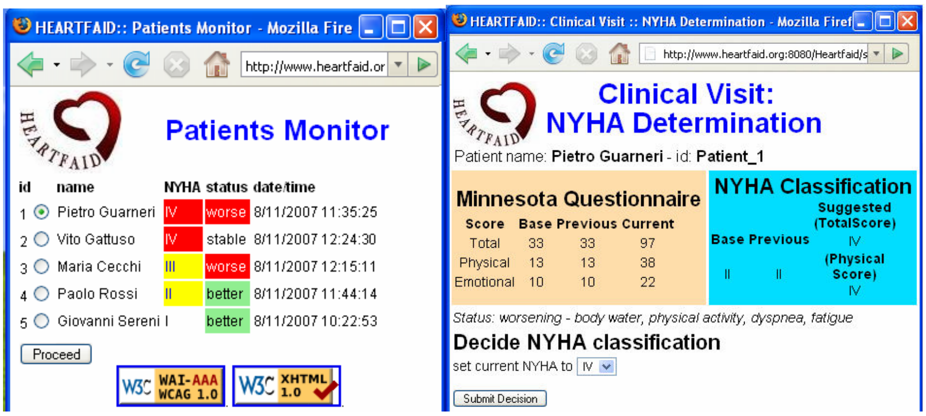


Patients Monitor

id		name	NYHA	status	date/time
1	●	Pietro Guarneri	IV	worse	8/11/2007 11:35:25
2	○	Vito Gattuso	IV	stable	8/11/2007 12:24:30
3	○	Maria Cecchi	III	worse	8/11/2007 12:15:11
4	○	Paolo Rossi	II	better	8/11/2007 11:44:14
5	○	Giovanni Sereni	I	better	8/11/2007 10:22:53

Clinical Visit:
NYHA Determination

Patient name: **Pietro Guarneri** - id: **Patient_1**

Minnesota Questionnaire

Score	Base	Previous	Current
Total	33	33	97
Physical	13	13	38
Emotional	10	10	22

NYHA Classification

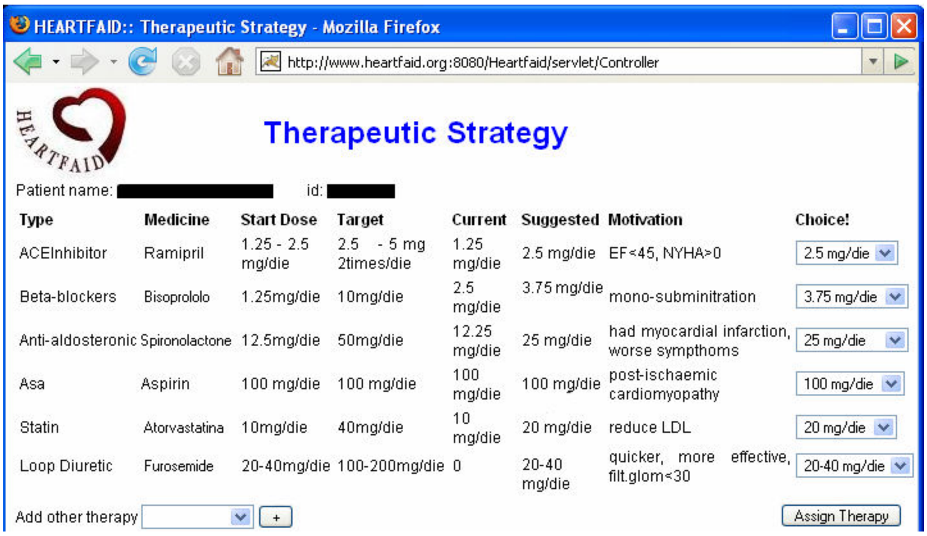
Base	Previous	Suggested (TotalScore)
		IV
II	II	(Physical Score) IV

Status: worsening - body water, physical activity, dyspnea, fatigue

Decide NYHA classification

set current NYHA to IV

Fig. 6. On the left, the patients monitor; on the right, the NYHA determination



Therapeutic Strategy

Patient name: [redacted] id: [redacted]

Type	Medicine	Start Dose	Target	Current	Suggested	Motivation	Choice!
ACEInhibitor	Ramipril	1.25 - 2.5 mg/die	2.5 - 5 mg 2times/die	1.25 mg/die	2.5 mg/die	EF<45, NYHA>0	2.5 mg/die
Beta-blockers	Bisoprololo	1.25mg/die	10mg/die	2.5 mg/die	3.75 mg/die	mono-subminitration	3.75 mg/die
Anti-aldosteronic	Spironolactone	12.5mg/die	50mg/die	12.25 mg/die	25 mg/die	had myocardial infarction, worse sympthoms	25 mg/die
Asa	Aspirin	100 mg/die	100 mg/die	100 mg/die	100 mg/die	post-ischaemic cardiomyopathy	100 mg/die
Statin	Atorvastatina	10mg/die	40mg/die	10 mg/die	20 mg/die	reduce LDL	20 mg/die
Loop Diuretic	Furosemide	20-40mg/die	100-200mg/die	0	20-40 mg/die	quicker, more effective, filt.glom<30	20-40 mg/die

Add other therapy

Fig. 7. CDSS suggestion for changing the patient's therapeutic strategy

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