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DESIGN AND DEVELOPMENT OF A CLINICAL DECISION SUPPORT SYSTEM FOR THE MANAGEMENT OF CHRONIC PATIENTS

Technical Report

Sara Colantonio, Massimo Martinelli

March, 2021

Table of Contents

| | | |
|----------|---|-----------|
| 1 | INTRODUCTION | 3 |
| 2 | CHRONIOUS GUIDELINES FRAMEWORK | 8 |
| 2.1 | AIMS AND CHARACTERISTICS..... | 8 |
| 2.2 | GENERAL STRUCTURE OF CHRONIOUS CLINICAL GUIDELINES | 10 |
| 3 | CHRONIOUS CORE DEVELOPMENT: THE CENTRAL CLINICAL DECISION SUPPORT SYSTEM | 28 |
| 3.1 | FUNCTIONALITIES..... | 29 |
| 3.2 | SOFTWARE ARCHITECTURE AND DESIGN | 40 |
| 3.3 | THE CENTRAL KNOWLEDGE BASE | 45 |
| 4 | REFERENCES AND MAIN BIBLIOGRAPHY | 65 |
| 5 | LIST OF ABBREVIATIONS | 67 |

1 INTRODUCTION

This report summarizes a part of the activities carried out within the EU FP7-IP-Project CHRONIOUS, *An Open, Ubiquitous and Adaptive Chronic Disease Management Platform for COPD and Renal Insufficiency* (GA 216461), more precisely within Work Package 6.

As stated in the Description of Work, “CHRONIOUS primary goal is to define a European framework for a generic health status monitoring platform schema, addressing people at risk or with chronic health conditions. This will be achieved by developing a multidisciplinary, sophisticated, and adaptive chronic disease platform that integrates state of the art sensors and services in order to cover both patients and healthcare professional’s needs”.

In order to accomplish this goal, the CHRONIOUS system has been designed as a set of components interacting in order to provide all the services needed [ROSSO10].

One of the key components of the platform is the CHRONIOUS Guidelines Framework. It is aimed at offering all the Decision Support services for professionals involved in the Chronic Disease Monitoring and Management Process. This module contains all the decision support functionalities needed for providing the possible diagnoses and treatments according to the medical category of the patient and the patient’s specific data available. This report addresses the work done on modelling the guidelines for **Chronic Obstructive Pulmonary Disease** (COPD).

The main component of the Guidelines Framework is the CHRONIOUS Decision Support System (DSS), which has been designed and developed in order to satisfy important features for the project, i.e. to be:

- structured and distributed
- reliable and effective
- dynamic and upgradable.

The module has been implemented according to the approach followed within another EU Project, i.e., the 6th FP STREP project HEARTFAID (IST-2005-027107), 2006-2009 [CHIARUGI10; COLANTONIO08a; COLANTONIO08b; COLANTONIO08c; COLANTONIO07], which had goals similar to those of CHRONIOUS as it was devoted to the management and monitoring of heart failure patients. Within HEARTFAID, once having analyzed a number of alternatives, such as guidelines representation systems based on different approaches (e.g., PROFORMA, SAGE and so on), knowledge-based systems based on different formalization paradigms (e.g., *network based*, *logic based*, and so on), and computational methods (e.g., *case-based reasoning*, *Bayesian Networks*, and so on), the solution, adopted, since more feasible and reliable, was based on a combination of computational reasoning methods and knowledge-based methods developed with ontologies and rules. After intense and in-depth discussions with clinicians, a similar solution appeared the most suitable for both the reasoning processes and the interactions that clinicians should have with the system. In addition, within CHRONIOUS, there appeared the need for a distribution of the functionalities and the components of the system, with a consequent partition of the manipulated information.

More in detail, the DSS is devoted at aiding clinicians in *monitoring* chronic patients in long-time (home or on the move) settings. Working in this domain, namely chronic patients' monitoring, implies a number of issues that should be taken into account:

- *Identification of exacerbation events through data collection and interpretation*: there is the necessity of detecting the incoming or the occurring of acute events by acquiring, via a suitable sensor infrastructure, a number of data about patients' disease signs, behaviour, activity, and contextual situations, and combining these with patients' clinical data. However, the mere collection of these data and their presentation to clinicians, without any type of pre-processing, can be useless, overwhelm clinicians and have a counter effect on their activity, by making the decisional processes even more difficult. Hence, to be really effective and useful, a support system should be able to interpret acquired data, combine them with patients' clinical information, issue possible alarms and supply motivated suggestions. Clinicians involved in the projects were strongly convinced of this issue and confirmed that a system like this can ease their activity in an effective way.

- *Absence of clinical guidelines*: clinical guidelines provide clinicians with general instructions for disease diagnosis and treatment within the daily practice in clinical environment. They do not contain any information about which parameters should be acquired for monitoring patients in their daily life, how these should be interpreted and how an exacerbation event could be identified. So far, only few medical studies, carried out in home settings, have dealt with the interpretation of continuously acquired patients' data and the correlation of specific signs and conditions to acute disease events. The knowledge coming from them is still not well-assessed and no universal protocols are currently applied. Two approaches can be followed for facing this issue: i) to elicit knowledge from clinicians that have specific experience in patients' monitoring; ii) to develop data driven algorithms able to extract directly from data the relevant knowledge.
- *Knowledge evolution*: the previous issue implies that knowledge about patients' monitoring is continuously evolving; new information and procedures can come from and during the CHRONIOUS experience, for instance, as well as from other studies that are being carried out. Hence, the support system should be upgradable, maintainable and easy to be changed.

CHRONIOUS DSS properly faces all of these issues:

- It is mainly committed to the analysis of collected patients' sensor data for diagnosing patients' current status and the identification of worrying conditions; to the alert of caregivers when an acute event is happening; and to the combination of patients' information for providing suggestions on possible changes of the therapeutic plans.
- Both the knowledge and data driven approaches were followed for its development. In particular, for a suitable, feasible and effective solution, CHRONIOUS DSS was developed as a structured and distributed decision support system, organized in two cooperating *layers*:
 - o a first layer of intelligence is located on the *Smart Personal Digital Assistance device* (PDA) and is devoted to data analysis and identification of worsening conditions by means of *computational reasoning methods* (e.g., *Artificial Neural Networks*, *Bayesian Networks*, and so on);

- a second layer of intelligence, the *Central Clinical Decision Support System* located on CHRONIOUS central system, is a knowledge based system developed by formalizing the know-how of clinicians expert in patients' monitoring, and also the clinical guidelines. This system is capable of supplying suitable suggestions by analyzing and correlating a wider amount of information, i.e., sensors collected data plus all the patients' clinical data. The encoding formalism was selected pursuing flexibility, simplicity, functionality and interoperability requirements. In particular, the formalization consists of an ontological model and a base of rules built on the same model. The use of an ontology, developed according to W3C standards, assures the definition of a clear structure of the encoded knowledge and its interoperability and easy integration with other possible implementations. Moreover, the adoption of ontologies and rules made it easier the cooperation with clinicians and the elicitation of their know-how, since such a formalism is easier to understand than others for them and more similar to their way of thinking. Actually, the knowledge elicited from clinicians about patients' monitoring came exactly in the form of rules.
- The corpus of knowledge used by the system is upgradable: clinicians have the possibility of building and modifying the encoded knowledge base, through a knowledge base editor equipped with the enhanced capability of verifying the rule consistency with respect to the knowledge already encoded. In this context, the formalism based on ontology and rules shown to strengthen the use of the system since it allows direct understanding and manipulation of information and knowledge. This service has been detailed in the paper [COLANTONIO12a].

Finally, it is worth noting that the success of a system such as CHRONIOUS DSS cannot be obtained without constant and continuous cooperation and exchange among technicians and clinicians. The different languages and mindset required a considerable effort in terms of time and testing activity to allow, from one side, technicians understanding which were the data, information and interactions involved, and, from the other side, clinicians comprehending the technological constraints of the development of the system.

This report describes the design of the DSS and of all the modules needed to implement the Guidelines Framework functionalities.

In particular,

- 1) after a quick overview of the guidelines framework, the different components are presented in details by defining the specific clinical guidelines for the clinical management of COPD patients during their everyday life is presented in chapter 2;

2) the CHRONIOUS clinical decision support system design and development is presented in chapter 3.

The work has been presented in several works published in international conferences and journals, please refer to them for citing this research [COLANTONIO14; COLANTONIO12b; COLANTONIO11].

2 CHRONIOUS GUIDELINES FRAMEWORK

2.1 AIMS AND CHARACTERISTICS

The CHRONIOUS Guidelines Framework contains all the decision support functionalities needed to provide the continuous clinical evaluation of patient's current status with the aim of early detecting patients worsening according to the medical category of the patient and the patient specific data available. Furthermore, it will offer Decision Support Tools for Professionals involved in the Chronic Disease Monitoring and Management Process which will indicate and suggest the possible need of adjusting of the treatments.

In order to offer these services, the CHRONIOUS Guidelines Framework needs the following components:

1) Clinical Guidelines and Templates for Chronic Diseases

The existing clinical guidelines and clinicians' know-how in the management of the disease need to be formalized into a Knowledge Based Decision Support System to provide services aimed at aiding clinical professionals in managing chronic patients on a daily basis.

As the clinical knowledge on chronic diseases is continuously improving, the CHRONIOUS Knowledge Base must be able to continuously incorporate and to be updated with the new knowledge developed by the scientific community.

This feature is provided by the Knowledge-Based Editor & Template management tool, that will be used in a background process of the CHRONIOUS Engine and whose main functionality is to assist the end user in transforming the clinical guidelines available on textual format as well as clinician's clinical experience to a form that can be interpreted and executed by the CHRONIOUS Guideline Framework. In order to achieve this transformation effectively this editor must enable the user to capture and model the clinical guidelines.

The CHRONIOUS system will be validated by applying it to two pathologies, the Chronic Obstructive Pulmonary Disease and Chronic Kidney Disease. For this reason, the process of building-up the knowledge base from existing clinical guidelines and clinician's know how has been implemented for these two diseases.

2) CHRONIOUS Core

The CHRONIOUS Core is constituted by the *Central Clinical Decision Support System* and is responsible for providing the continuous evaluation of patient's current conditions and the suggestions of possible adjustments in treatments accordingly to the medical category of the patient and the patient specific data available. The outcome of this process is based on the clinical guidelines that are formulated and stored in the CHRONIOUS clinical knowledge base, by the Clinical Guidelines and Template for Chronic Diseases.

3) CHRONIOUS Services

The CHRONIOUS Services are all the modules needed to enable the CHRONIOUS Core to provide all functionalities indicated in the CHRONIOUS Guideline Framework functional requirements. In particular, a Knowledge Base Editor allows the updates and modification of the clinical knowledge base with a simple and easy-to-use user interface. In order to operate properly, an appropriate template to model clinical knowledge has been defined and a Consistency Checker has been designed and developed in order to assure that all requested changes to the knowledge base are consistent with the rules already incorporated.

4) Interoperability and Intercommunication

The Interoperability Modules implement the interoperability architecture that bridges the communication among the CHRONIOUS system and the external medical repositories. It is responsible for providing an interoperability framework through which EHR are accessed and exchanged between the different modules of the CHRONIOUS Guideline Framework. In order to warranty the interoperability with other EHR systems used by the different clinical sites, all medical data are communicated with standard formats.

2.2 GENERAL STRUCTURE OF CHRONIOUS CLINICAL GUIDELINES

As already identified by the analysis of the requirements of CHRONIOUS system, the COPD clinical guidelines are defined by considering two different set of rules. The first will comprise all the rules, which do not require a specific and comprehensive knowledge of the clinical phenotype, and condition of the patient and that can be managed by the intelligence on the CHRONIOUS patient's framework, the second will comprise all other clinical rules. Because of these criteria, the rules of the first set will be devoted to manage either emergency situations or to identify situation which may raise suspects of possible problems and will require a quick further analysis which needs more information of the ones available at the patient side.

Clinical Guidelines for the Patients Sensing Framework

These rules must be defined by considering only simple logical functions (such as applying thresholds) on the variables acquired by the sensors. There are two different levels of actions, one is devoted to identify patient's critical conditions that must activate a request for an immediate reaction from the caregiver, the other is used to identify possible worsening conditions, which have to be confirmed by more extensive analysis that has to be carried on by the CHRONIOUS core. In this second case, the rules activate the immediate transmission of the data from the Patient Sensing Framework to the central system and request the activation of the CDSS for the proper and comprehensive evaluation of the patient's condition.

Clinical Guidelines for the CHRONIOUS core

These clinical guidelines represent the whole knowledge about the disease and its management, which is coded into the Knowledge Base. These rules can refer to both data recorded by the patients sensing framework and the information acquired by the intercommunication module from the EHR which comprises, for example, the results of laboratory exams. Moreover, the rules can be more complex if compared to the ones for the Patient Sensing Framework in order to adequately model the knowledge needed to describe a very complex task such as the management of the disease.

In this chapter, the description of possible guidelines for managing COPD are reported. Given the very different characteristics of the two diseases, the approach used to define the sets of guidelines is also different.

COPD guidelines have been designed thanks to a close collaboration and interaction between biomedical engineers from the MIP – Biomedical Engineering Department of the Politecnico di Milano and a team of physicians with specific experience in telemedicine programs for COPD patients. In particular, the CHRONIOUS COPD Clinical Guidelines have been designed with a relevant contribution especially from Dr. Michele Vitacca, who is one of the scientific responsible of Telemaco Project, a project sponsored by the local government of Regione Lombardia, Italy, which involved, up to now, more than 300 COPD patients and constitutes, to our knowledge, the widest trial on telemedicine in COPD ever done.

2.2.1 COPD CLINICAL GUIDELINES

As already identified in D2.2, all available COPD clinical guidelines are not designed taking account the availability of continuous or frequent monitoring of several physiological variables and clinical parameters as it will happen in CHRONIOUS. For this reason, they are not highly specific in the definition of the appropriate interventions and on how to optimise the therapies on a given patient, leaving most of this task to the experience of the physician in care of the patient.

After a further deep search in several scientific article databases and discussion and contacts with chest physicians highly experienced in the clinical management of COPD, we identified and designed the CHRONIOUS COPD clinical guideline by considering the following aspects:

- 1) The most important aim of CHRONIOUS COPD clinical guidelines is the early detection of changes in the clinical condition of the patient.

This consideration results from the analysis of the scientific literature on clinical management of COPD. Published data offer several different follow-up models of home care in COPD patients. Reduction in hospitalization (Lancet 1992, 339: 1517–20) and use of other acute healthcare services (Arch Intern Med 2007; 167: 551–61; Chest 1991; 100: 607–12), reduction in mortality rate, improvement in the sickness impact profile scores and patient satisfaction (Thorax 1991; 46: 559–64; BMJ 1987; 294: 225–8) have all been reported with programs providing chronic home care interventions and patient education. These programs were based on strict adherence to interventions enhancing symptoms self-monitored by patients and their caregivers and increasing their understanding of drug therapy, symptom and treatment monitoring, as well as acting as a liaison between primary care providers and hospital services. Even if telemedicine resulted in a reduction in hospitalization and use of other acute health care services, there is still not enough evidence that this approach is cost-effective.

Only recently it has been shown that, if the telemedicine approach is applied to COPD patients with the aim of early detecting patient worsening and of promptly beginning the treatment of exacerbations, the cost-effectiveness of teleassistance can be demonstrated. To date, there are still very limited studies available, also because of the lack of availability of technological platforms able to continuously monitor the relevant physiological parameters at the patient's home. Nevertheless, it has been recently shown that in patients with severe chronic respiratory failure (CRF) needing home oxygen therapy and/or home mechanical ventilation, the integration of home monitoring and care with the aid of ICT can reduce the rate of hospitalizations by about 36%, General Practitioner (GP) urgent calls by 65%, home relapses by 71%, even in more severe patients. The results highlighted also that patients with COPD seem to take greater advantage of this kind of teleassistance compared to other pathologies [VITACCA09]. Because of these considerations, CHRONIOUS COPD Clinical Guidelines have been designed with the specific aim of early detecting symptoms worsening, in order to promptly alert care providers and to allow the physician to identify and prescribe the appropriate treatment for a given patient.

2) The lack of availability of devices and ICT platform able to acquire a large variety of physiological parameters provided by wearable sensors and/or home monitoring systems prevented the scientific community to identify the best set of variables and rules to be used as clinical guidelines for tele-care of COPD. For this reason, the CHRONIOUS COPD clinical guidelines module has to be defined by combining established medical knowledge with the knowledge obtained from experienced physicians in order to define an initial set of rules to be used for the first validation study. Considering that CHRONIOUS platform will fill up the lack of data mentioned here above, it is very likely that the first set of clinical guidelines will be soon expanded and integrated while new knowledge will be derived from the data coming from the clinical trials. For this reason, the first set of rules of CHRONIOUS Clinical Guidelines should follow a simple structure in order to be easily expanded and tuned during the first clinical studies.

COPD clinical guidelines for the Patient Sensing Framework

These rules were defined on the basis of general clinical guidelines by considering physiologically acceptable parameters and by introducing some more restrictive parameters specific for COPD.

Since COPD, like most of chronic diseases diffused in elderly patients, is often characterised by the presence of co-morbidities, at the Patient Sensing Framework level only general threshold values are suggested. More specific reasoning is performed at the level of the CDSS, allowing different sensitivity to change in some of the parameters depending on patient's phenotype.

The values suggested for the CHRONIOUS COPD Clinical Guidelines for the Patient Sensing Framework are reported in the table here below.

| | Alarm - immediate action | Send data to CDSS |
|--|---|--|
| Body temperature (T) | T > 38°C | T > 37.5°C during 4 consecutive hours |
| Weight | > 2kg in 24 ore | (every 24h) |
| Heart Rate (HR) | HR > 120 BPM | HR > 100 BPM, with patient at rest |
| ECG | atrial fibrillation, atrial flutter, tachycardia supraventricular | |
| Arterial Pressure | Diastolic > 100 mmHg, systolic > 150 mmHg | Diastolic > 85 mmHg, systolic > 130 mmHg (hypertensive therapies?) |
| SpO2 | SpO2 < 91% (oxygen therapy?) | 91% < SpO2 < 94% |
| Respiratory Frequency (f) | f > 20 BPM | f > 15 BPM |
| Inspiratory Time (Ti) | Ti < 1 sec | |
| Expiratory Time (Te) | Te > 5 sec | |
| Respiration Asinchrony (n/min) | | (every 24h) |
| (Resp. Freq.)/(tidal volume) = f/Vt | f/Vt > 100 BPM/L | 60 < f/Vt < 100 BPM/L |
| Minute Ventilation (Ve) | >10L | |
| Patient Activity | | (every 24h) |
| Coughs Counter | > 60-70 per hour | |
| Ambient Temperature and Humidity | | (every 24h) |
| Mental Solicitation Indicator | | |
| Home Pollution | | (every 24h) |
| Patient Position | | (every 24h) |
| Sleep Quality | | Apnoeas, Position |
| Symptoms self evaluation (questionnaires: bcss, respicard...) | Dyspnoea at rest (borg, vas scale + check on respiratory frequency) | (every 24h) |
| Social context, environment (microphone for sounds) | | |

COPD clinical guidelines for the CHRONIOUS Core

COPD is a complex and heterogeneous disease whose definition comprises very different manifestations, or *phenotypes*. In order to define the appropriate rules to evaluate patient's conditions, it is mandatory to consider which phenotype he/she belongs to.

Several studies have been addressed to this issue, but COPD phenotyping is still an open question and it is nowadays considered a hot topic by the scientific community.

After an extensive review of the scientific literature and also thanks to the support and interaction with physicians and scientists internationally considered opinion leader in the field a CHRONIOUS COPD, a phenotyping schema was defined taking into account the field of application of CHRONIOUS.

In particular, CHRONIOUS COPD phenotypes are identified by considering the most valuable and predictive parameters for prognosis. One of the first effective attempts to better characterise patients' condition is the study from [CELLI04]. published into the New England Journal of Medicine in 2004, which introduced the BODE index, derived by a retro prospective analysis of a large cohort of COPD patients.

As CHRONIOUS COPD Clinical Guidelines are aimed at early detecting patient worsening, it has been decided to add some feature to the BODE index, in particular considering smoking habits, physical activity performed by the patient and the attitude of the patient to develop exacerbations.

Here below the CHRONIOUS phenotyping schema is described with the references to the relevant scientific literature.

Definition of CHRONIOUS phenotypes:

- BODE Index:
It has been used the classification of the COPD patients on the basis of the BODE index described in "Celli et al., *The Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index, in Chronic Obstructive Pulmonary Disease*, N Engl J Med 2004; 350: 1005-12". In this article are described eleven categories of COPD patients on the basis of four indexes which score the patient from 0 to 10. The categories are analyzed divided into four bigger groups that take into account a range of categories: first group 0-2, second group 3-4, third group 5-6, and fourth group 7-10. These bigger categories are the ones used for the BODE Index classification, thus allowing us to classify the patients into four groups.
- Smoker:
It has been proved that smoking is a determining factor for the progress of the disease in COPD patients.
"Lacasse Y, Maltais F, Goldstein RS J, *Smoking cessation in pulmonary rehabilitation: goal or prerequisite?*, *Cardiopulm Rehabil.* 2002 May-Jun;22(3):148-53.PMID: 12042681
"BOSE index. from ERS Congress 2008."
- Number of exacerbations per year:
For a COPD patient an exacerbation means a worsening of the disease, hospitalization, pharmacological therapy and, in some cases, death. Therefore, it is very important how many exacerbations the patient has per year. It has been chosen a value of two exacerbations per year as a threshold to classify COPD patients. A higher number of exacerbations means a major risk for the patient.
"Hurst JR, Donaldson GC, Quint JK, Goldring JJ, Baghai-Ravary R, Wedzicha JA, Temporal clustering

of exacerbations in chronic obstructive pulmonary disease, Am J Respir Crit Care Med. 2009 Mar 1;179(5):369-74”

“Seemungal TA, Hurst JR, Wedzicha JA, Exacerbation rate, health status and mortality in COPD--a review of potential interventions, Int J Chron Obstruct Pulmon Dis. 2009;4:203-23”

“Dusser et al., The effect of tiotropium on exacerbations and airflow in patients with COPD, ERJ 2006; 27:547-555”

- Activity, number of steps per day:

In COPD patients daily activity is an indicator of the progress of the disease, in fact activity is strongly related to the amount of available oxygen brought by the respiratory system. The more the patient is at severe stages of the disease the less oxygen is provided by the respiratory system to the whole body, thus limiting patient’s movements.

“Enfield K, Gammon S, Floyd J, Falt C, Patrie J, Platts-Mills TA, Truwit JD, Shim YM, *Six-minute walk distance in patients with severe end-stage COPD: association with survival after inpatient pulmonary rehabilitation*, J Cardiopulm Rehabil Prev. 2010 May-Jun;30(3):195-202”

By considering all references indicated above, we identified the following criteria to characterise COPD phenotypes:

Phenotypes Definition

| Criteria: | 1 | 2 | 3 | 4 |
|-------------------------|------|------|--|------|
| 1 BODE Index | 0-2 | 3-4 | 5-6 | 7-10 |
| 2 Smoker | yes | no | Bode 0-2 / 3-4 / 5-6 / 7-10 | |
| 3 exacerbatation per yr | ≥ 2 | <2 | smoker / not a smoker | |
| 4 steps per day | >500 | <500 | <2 exacerbatations per year / ≥ 2 exacerbatations per year | |
| | | | active / sedentary | |

It is important to underline that these phenotypes are defined with the specific aim of identifying different attitude in developing symptoms worsening and exacerbations, not with the aim of solving the still discussed issue of disease phenotyping.

These criteria defined 32 COPD phenotypes, which are summarized in the following table:

CHRONIOUS Phenotypes:

| | BODE | Smoker | exhacerb. | steps | = | Category name |
|----|-------------|---------------|------------------|--------------|----------|--|
| 1 | 0-2 | no | <2 | >500 | = | Bode 0-2, not a smoker, <2 exhacerbations per year, active |
| 2 | 0-2 | no | <2 | <500 | = | Bode 0-2, not a smoker, <2 exhacerbations per year, sedentary |
| 3 | 0-2 | no | ≥2 | >500 | = | Bode 0-2, not a smoker, ≥2 exhacerbations per year, active |
| 4 | 0-2 | no | ≥2 | <500 | = | Bode 0-2, not a smoker, ≥2 exhacerbations per year, sedentary |
| 5 | 0-2 | yes | <2 | >500 | = | Bode 0-2, smoker, <2 exhacerbations per year, active |
| 6 | 0-2 | yes | <2 | <500 | = | Bode 0-2, smoker, <2 exhacerbations per year, sedentary |
| 7 | 0-2 | yes | ≥2 | >500 | = | Bode 0-2, smoker, ≥2 exhacerbations per year, active |
| 8 | 0-2 | yes | ≥2 | <500 | = | Bode 0-2, smoker, ≥2 exhacerbations per year, sedentary |
| 9 | 3-4 | no | <2 | >500 | = | Bode 3-4, not a smoker, <2 exhacerbations per year, active |
| 10 | 3-4 | no | <2 | <500 | = | Bode 3-4, not a smoker, <2 exhacerbations per year, sedentary |
| 11 | 3-4 | no | ≥2 | >500 | = | Bode 3-4, not a smoker, ≥2 exhacerbations per year, active |
| 12 | 3-4 | no | ≥2 | <500 | = | Bode 3-4, not a smoker, ≥2 exhacerbations per year, sedentary |
| 13 | 3-4 | yes | <2 | >500 | = | Bode 3-4, smoker, <2 exhacerbations per year, active |
| 14 | 3-4 | yes | <2 | <500 | = | Bode 3-4, smoker, <2 exhacerbations per year, sedentary |
| 15 | 3-4 | yes | ≥2 | >500 | = | Bode 3-4, smoker, ≥2 exhacerbations per year, active |
| 16 | 3-4 | yes | ≥2 | <500 | = | Bode 3-4, smoker, ≥2 exhacerbations per year, sedentary |
| 17 | 5-6 | no | <2 | >500 | = | Bode 5-6, not a smoker, <2 exhacerbations per year, active |
| 18 | 5-6 | no | <2 | <500 | = | Bode 5-6, not a smoker, <2 exhacerbations per year, sedentary |
| 19 | 5-6 | no | ≥2 | >500 | = | Bode 5-6, not a smoker, ≥2 exhacerbations per year, active |
| 20 | 5-6 | no | ≥2 | <500 | = | Bode 5-6, not a smoker, ≥2 exhacerbations per year, sedentary |
| 21 | 5-6 | yes | <2 | >500 | = | Bode 5-6, smoker, <2 exhacerbations per year, active |
| 22 | 5-6 | yes | <2 | <500 | = | Bode 5-6, smoker, <2 exhacerbations per year, sedentary |
| 23 | 5-6 | yes | ≥2 | >500 | = | Bode 5-6, smoker, ≥2 exhacerbations per year, active |
| 24 | 5-6 | yes | ≥2 | <500 | = | Bode 5-6, smoker, ≥2 exhacerbations per year, sedentary |
| 25 | 7-10 | no | <2 | >500 | = | Bode 7-10, not a smoker, <2 exhacerbations per year, active |
| 26 | 7-10 | no | <2 | <500 | = | Bode 7-10, not a smoker, <2 exhacerbations per year, sedentary |
| 27 | 7-10 | no | ≥2 | >500 | = | Bode 7-10, not a smoker, ≥2 exhacerbations per year, active |
| 28 | 7-10 | no | ≥2 | <500 | = | Bode 7-10, not a smoker, ≥2 exhacerbations per year, sedentary |
| 29 | 7-10 | yes | <2 | >500 | = | Bode 7-10, smoker, <2 exhacerbations per year, active |
| 30 | 7-10 | yes | <2 | <500 | = | Bode 7-10, smoker, <2 exhacerbations per year, sedentary |
| 31 | 7-10 | yes | ≥2 | >500 | = | Bode 7-10, smoker, ≥2 exhacerbations per year, active |
| 32 | 7-10 | yes | ≥2 | <500 | = | Bode 7-10, smoker, ≥2 exhacerbations per year, sedentary |

Once phenotypes are defined, it is necessary to define an index of the condition of the patient aimed at early identifying changes in patient conditions potentially leading to the development of an exacerbation.

For the COPD clinical guidelines, it was decided to use, for the first set of clinical rules, an evolution of the scoring card used in the most relevant clinical trial of telemonitoring of COPD (the Telemaco Project) and proposed and validated in literature [VITACCA09].

This approach is based on the evaluation of several physiological variables measured by the CHRONIOUS Patients Sensing Framework. In particular, the following parameters have been considered on the basis of scientific literature and the experience of the collaborating physicians:

- Dyspnea
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Cough
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”

- Sputum
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Sputum color
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Wheeze
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Neurological status
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Ventilation interaction
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Walk
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Body temperature
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Weight
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Heart rate
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- ECG
The use of this parameter has been described, scored and discussed in the following book:
“*Harrison’s Principles of Internal Medicine*, Mc Graw HILL 1980”
- Arterial pressure (systolic)
The use of this parameter has been described, scored and discussed in the following book:
“*Harrison’s Principles of Internal Medicine*, Mc Graw HILL 1980”
- Arterial pressure (diastolic)
The use of this parameter has been described, scored and discussed in the following book:
“*Harrison’s Principles of Internal Medicine*, Mc Graw HILL 1980”
- SpO₂
The use of this parameter has been described, scored and discussed in the following article:
“Vitacca et al., *Tele assistance in chronic respiratory failure patients a randomised clinical trial*, Eur Respir J 2009; 33: 411–418”
- Respiratory frequency
The use of this parameter has been described, scored and discussed in the following books:
“*JB West Respiratory Physiology The essentials*, Baltimore USA 1977”

- “Murray JF, *Text book of respiratory Medicine*, 2nd ed, WB Saunders Co Phyladelphia 1994”
- “Martin J. Tobin, *Principles and practice of mechanical ventilation*, 2nd edition, McGraw-Hill, 2006”
- Inspiratory time
The use of this parameter has been described, scored and discussed in the following books:
“JB West *Respiratory Physiology The essentials*, Baltimora USA 1977”
- “Murray JF, *Text book of respiratory Medicine*, 2nd ed, WB Saunders Co Phyladelphia 1994”
“Martin J. Tobin, *Principles and practice of mechanical ventilation*, 2nd edition, McGraw-Hill, 2006”
- Expiratory time
The use of this parameter has been described, scored and discussed in the following books:
“JB West *Respiratory Physiology The essentials*, Baltimora USA 1977”
“Murray JF, *Text book of respiratory Medicine*, 2nd ed, WB Saunders Co Phyladelphia 1994”
“Martin J. Tobin, *Principles and practice of mechanical ventilation*, 2nd edition, McGraw-Hill, 2006”
- Respiration asynchrony
The use of this parameter has been described, scored and discussed in the following books:
“JB West *Respiratory Physiology The essentials*, Baltimora USA 1977”
“Murray JF, *Text book of respiratory Medicine*, 2nd ed, WB Saunders Co Phyladelphia 1994”
“Martin J. Tobin, *Principles and practice of mechanical ventilation*, 2nd edition, McGraw-Hill, 2006”
- Respiratory frequency / Tidal volume
The use of this parameter has been described, scored and discussed in the following books:
“JB West *Respiratory Physiology The essentials*, Baltimora USA 1977”
“Murray JF, *Text book of respiratory Medicine*, 2nd ed, WB Saunders Co Phyladelphia 1994”
“Martin J. Tobin, *Principles and practice of mechanical ventilation*, 2nd edition, McGraw-Hill, 2006”
- Minute ventilation
The use of this parameter has been described, scored and discussed in the following books:
“JB West *Respiratory Physiology The essentials*, Baltimora USA 1977”
“Murray JF, *Text book of respiratory Medicine*, 2nd ed, WB Saunders Co Phyladelphia 1994”
“Martin J. Tobin, *Principles and practice of mechanical ventilation*, 2nd edition, McGraw-Hill, 2006”
- Patient activity
The use of this parameter has been described, scored and discussed in the following articles:
“Connors et al, *Four predictors of survival in COPD*, AJRCCM 1996; 154: 959-967”
“F. Pitta et al, *Characteristics of physical activity in daily life in COPD*, Am J Respir Crit Care Med Vol 171. pp 972–977, 2005”
“C. Aymerich, *Inactivity and chronic diseases*, Thorax 2006”
- Depressive phenotype (HAD)
The use of this parameter has been described, scored and discussed in the following article:
“Burgel et al, *Clinical COPD phenotype: a novel approach using principal component and cluster analysis*, ERJ 2010; 36-531-539”
“G C Donaldson et al. Am J Respir Crit Care Med Vol 171. pp 446–452, 2005”
“Janssen DJ, Spruit MA, Leue C, Gijzen C, Hameleers H, Schols JM, Wouters EF, *Symptoms of anxiety and depression in COPD patients entering pulmonary rehabilitation*, Chron Respir Dis. 2010 Aug;7(3):147-57”

The following parameters are included in the guidelines because of the judgment of our clinical consultant. As soon as new scientific evidence of their importance will be available (also thanks to the CHRONIOUS validation studies), CHRONIOUS guidelines will be updated.

- Coughs
- Ambient temperature
- Ambient humidity
- Mental solicitation indication
- Home pollution

- Patient position
- Sleep quality (number of position changes)
- Sleep quality (questionnaire)
- Asthenia
- Social context, environment
- Age

These parameters are considered by assigning a score to each one on the basis of its value, as suggested by the RESPIcard introduced by Vitacca et al, ERJ 2009 [Vitacca09].

The values of the scores for the CHRONIOUS COPD card have been defined as follow:

| CHRONIOUS COPD CARD SCORES | 0 | 1 | 2 | 3 | 4 |
|---|---------------------------------------|---|---|--|--|
| Dyspnoea | Under strong activity | Speed walk or climb | Moderate activity with stops | Light activity, stop after few steps | At rest during daily activities |
| Cough | Spontaneous and strong | Weak, not productive | Strong but extremely productive | Weak, productive, frequent | No spontaneous cough; need for suction |
| Sputum | No need for sputum | Moderate | Copious | Very copious | Unbearable |
| Sputum Colour | No sputum | white | Yellow | Yellow/green | Green/brown or with blood |
| Wheeze | Never | Occasional | Under strong efforts | Under moderate efforts | At rest |
| Neurological Status | Normal, wakeful | Slow but answering | Confused, diurnal drowsiness | Difficult posture and verbal answer | No answer to manual stimulus |
| Ventilator Interaction | No troubles or no ventilator | Occasional alarms on ventilator | Alarms and need for suction, or mask discomfort | Alarms, occasional contrasts and dyspnoea under ventilator | Ventilator break; alarms and fighting against ventilator |
| Walk | Autonomous | Walk with stops, no dyspnoea | Walk with stick and dyspnoea | Assisted walk, few steps, armchair use | No deambulation, bedridden |
| Body temperature (T) | Normal | >37°C and <37.5°C without antipiretic | >37°C and <38°C with antipiretic | >38°C with antipiretic and antibiotic for 1 day | >38°C with antibiotic for 3 days |
| Weight | Stable weight, no ankle oedema | Increase of <2Kg in 2 days | 2-4Kg in 2 days | 2-4Kg in 1 day | >4Kg in 1 day |
| Heart Rate (HR) | <90 BPM | 90-100 BPM | 100-110 BPM | 110-120 BPM | >120 BPM |
| ECG | regular | extrasystols | atrial fibrillations | atrial flutter | ventricular arrhythmia |
| Arterial Pressure (systolic) | 120 | 120-140 | 140-160 | 140-160 | >190 |
| Arterial Pressure (dyastolic) | 70 | 70-90 | 90-100 | 100-110 | >110 |
| SpO₂ | >92% with room air and O ₂ | 91% with air and 90-92% with O ₂ | <90% with room air | <90% with O ₂ | <80% with O ₂ |
| Respiratory Frequency (f) | <14 | 14-16 | 16-20 | 20-25 | >25 |
| Inspiratory Time (Ti) | 1.6-1.8 | < 1.6 > 1.20 | < 1.2 > 1.0 | > 0.80 < 1.0 | <0.80 |
| Expiratory Time (Te) | 3.0-3.4 | < 3 > 2.5 | < 2.5 > 2.0 | < 2.0 > 1.60 | <1.60 |
| Respiration Asynchrony (LBI mean value in the last 30mins) | 1.0 | 1.2 | 1.4 | 1.6 | 1.8 |
| (Resp. Freq.)/(tidal volume) = f/Vt | <80 | 80-95 | 95-110 | 110-120 | > 120 |
| Minute Ventilation (Ve) | <12 > 10 | < 10 | < 8 | < 7 | < 6 |
| Patient Activity (steps num. per day) | >2000 | < 2000 > 1800 | < 1800 > 1000 | < 1000 > 500 | <500 |
| Coughs Counter (n/min) | 0 | <2 | <10 | <15 | >15 |
| Ambient Temperature | 22°C | 24-26°C | 26-28°C | 28-30°C | >30°C |
| Ambient Humidity | 50% | 40% or 60% | 30% or 70% | 20% or 80% | <20% or >80% |
| Mental Solicitation Indicator | | | | | |
| Home Pollution | | | | | |
| Patient Position (supine) h | < 8 | > 8 < 10 | > 10 < 15 | >15 <18 | > 18 |
| Sleep Quality (N° position changes/h) | <10 | > 10 < 15 | > 15 < 25 | 25-30 | > 30 |
| sleep quality (questionnaire) | optimal | good | sufficient | bad | very bad |
| Do you feel tired? (asthenia) | never | occasionally | after light activity | after heavy activity | for the most part of the day |
| Social context, environmet (microphone for sounds) | | | | | |
| Age | <55 | >55 and <60 | >60 and <70 | >70 and <75 | >75 |
| Depressive Phenotype (HAD) | never | sometimes | frequent | very frequent | pathological |

Once scores have been attributed to all the parameters, we decided to consider a subset of them with different weights depending of the patient's phenotype in order to compute a total score, which can be used to detect possible changes in patients' conditions.

The values of the weights presented in this chapter were defined in collaboration with experienced physicians, and in particular with Dr. Michele Vitacca, taking advantage of his specific knowledge and experience on the use of telemedicine in COPD patients.

However, the availability of new data provided by CHRONIOUS validation studies as well as by the data recorded during the use of CHRONIOUS on COPD patients will provide the possibility to update the values of the weights by tuning them on the basis of appropriate statistical analysis.

The equations defined for each phenotype are listed here below:

- Phenotype 1 = (ECG score)*0.1 + (arterial pressure score)*0.1
- Phenotype 2 = (walk score)*0.1 + (ECG score)*0.1 + (arterial pressure score)*0.1
- Phenotype 3 = (dyspnoea score)*0.1 + (cough score)*0.1 + (sputum score)*0.1 + (sputum color score)*0.1 + (wheeze score)*0.1 + (weight score)*0.1 + (neurological status score)*0.1 + (body temperature score)*0.1 + (heart rate score)*0.1 + (ECG score)*0.1 + (arterial pressure score)*0.1 + (respiratory frequency score)*0.1 + (inspiratory time score)*0.1 + (expiratory time score)*0.1 + (respiration asynchrony score)*0.1 + (resp. freq. / tidal vol. score)*0.1 + (patient activity score)*0.1 + (coughs counter score)*0.1 + (home pollution score)*0.1 + (patient position score)*0.1 + (sleep quality score)*0.1 + (asthenia score)*0.1 + (social context , environment score)*0.1 + (depressive phenotype score)*0.1
- Phenotype 4 = (dyspnoea score)*0.1 + (cough score)*0.1 + (sputum score)*0.1 + (sputum color score)*0.1 + (wheeze score)*0.1 + (weight score)*0.1 + (neurological status score)*0.1 + (walk score)*0.1 + (body temperature score)*0.1 + (heart rate score)*0.1 + (ECG score)*0.1 + (arterial pressure score)*0.1 + (respiratory frequency score)*0.1 + (inspiratory time score)*0.1 + (expiratory time score)*0.1 + (respiration asynchrony score)*0.1 + (resp. freq. / tidal vol. score)*0.1 + (patient activity score)*0.1 + (coughs counter score)*0.1 + (home pollution score)*0.1 + (patient position score)*0.1 + (sleep quality score)*0.1 + (asthenia score)*0.1 + (social context , environment score)*0.1 + (depressive phenotype score)*0.1
- Phenotype 5 = (ECG score)*0.1 + (arterial pressure score)*0.1
- Phenotype 6 = (walk score)*0.1 + (ECG score)*0.1 + (arterial pressure score)*0.1
- Phenotype 7 = (dyspnoea score)*0.2 + (cough score)*0.2 + (sputum score)*0.2 + (sputum color score)*0.2 + (wheeze score)*0.2 + (weight score)*0.2 + (neurological status score)*0.2 + (body temperature score)*0.2 + (heart rate score)*0.2 + (ECG score)*0.1 + (arterial pressure score)*0.1 + (SpO₂ score)*0.1 + (respiratory frequency score)*0.2 + (inspiratory time score)*0.2 + (expiratory time score)*0.2 + (respiration asynchrony score)*0.2 + (resp. freq. / tidal vol. score)*0.2 + (minute ventilation score)*0.1 + (patient activity score)*0.2 + (coughs counter score)*0.2 + (home pollution score)*0.2 + (patient position score)*0.2 + (sleep quality score)*0.2 + (asthenia score)*0.2 + (social context , environment score)*0.2 + (depressive

phenotype score)*0.2

- Phenotype 8 = (dyspnoea score)*0.2 + (cough score)*0.2 + (sputum score)*0.2 + (sputum color score)*0.2 + (wheeze score)*0.2 + (weight score)*0.2 + (neurological status score)*0.2 + (walk score)*0.1 + (body temperature score)*0.2 + (heart rate score)*0.2 + (ECG score)*0.1 + (arterial pressure score)*0.1 + (SpO₂ score)*0.1 + (respiratory frequency score)*0.2 + (inspiratory time score)*0.2 + (expiratory time score)*0.2 + (respiration asynchrony score)*0.2 + (resp. freq. / tidal vol. score)*0.2 + (minute ventilation score)*0.1 + (patient activity score)*0.2 + (coughs counter score)*0.2 + (home pollution score)*0.2 + (patient position score)*0.2 + (sleep quality score)*0.2 + (asthenia score)*0.2 + (social context , environment score)*0.2 + (depressive phenotype score)*0.2
- Phenotype 9 = (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.1 + (social context , environment score)*0.2 + (age score)*0.1
- Phenotype 10 = (walk score)*0.2 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.1 + (social context , environment score)*0.2 + (age score)*0.1
- Phenotype 11 = (dyspnoea score)*0.3 + (cough score)*0.3 + (sputum score)*0.3 + (sputum color score)*0.3 + (wheeze score)*0.3 + (weight score)*0.3 + (neurological status score)*0.3 + (ventilator interaction score)*0.1 + (walk score)*0.1 + (body temperature score)*0.3 + (heart rate score)*0.3 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.2 + (respiratory frequency score)*0.3 + (inspiratory time score)*0.3 + (expiratory time score)*0.3 + (respiration asynchrony score)*0.3 + (resp. freq. / tidal vol. score)*0.3 + (minute ventilation score)*0.1 + (patient activity score)*0.3 + (coughs counter score)*0.3 + (home pollution score)*0.3 + (patient position score)*0.3 + (sleep quality score)*0.3+ (asthenia score)*0.3 + (social context , environment score)*0.2 + (age score)*0.1 + (depressive phenotype score)*0.3
- Phenotype 12 = (dyspnoea score)*0.3 + (cough score)*0.3 + (sputum score)*0.3 + (sputum color score)*0.3 + (wheeze score)*0.3 + (weight score)*0.3 + (neurological status score)*0.3 + (ventilator interaction score)*0.1 + (walk score)*0.2 + (body temperature score)*0.3 + (heart rate score)*0.3 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.2 + (respiratory frequency score)*0.3 + (inspiratory time score)*0.3 + (expiratory time score)*0.3 + (respiration asynchrony score)*0.3 + (resp. freq. / tidal vol. score)*0.3 + (minute ventilation score)*0.1 + (patient activity score)*0.3 + (coughs counter score)*0.3 + (home pollution score)*0.3 + (patient position score)*0.3 + (sleep quality score)*0.3+ (asthenia score)*0.3 + (social context , environment score)*0.2 + (age score)*0.1 + (depressive phenotype score)*0.3
- Phenotype 13 = (ventilator interaction score)*0.1 + (walk score)*0.1 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.2 + (social context , environment score)*0.2 + (age score)*0.1
- Phenotype 14 = (ventilator interaction score)*0.1 + (walk score)*0.2 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.2 + (social context , environment score)*0.2 +

(age score)*0.1

- Phenotype 15 = (dyspnoea score)*0.4 + (cough score)*0.4 + (sputum score)*0.4 + (sputum color score)*0.4 + (wheeze score)*0.4 + (weight score)*0.4 + (neurological status score)*0.4 + (ventilator interaction score)*0.1 + (walk score)*0.1 + (body temperature score)*0.4 + (heart rate score)*0.4 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.3 + (respiratory frequency score)*0.4 + (inspiratory time score)*0.4 + (expiratory time score)*0.4 + (respiration asynchrony score)*0.4 + (resp. freq. / tidal vol. score)*0.4 + (minute ventilation score)*0.2 + (patient activity score)*0.4 + (coughs counter score)*0.4 + (home pollution score)*0.4 + (patient position score)*0.4 + (sleep quality score)*0.4+ (asthenia score)*0.4 + (social context , environment score)*0.3 + (age score)*0.2 + (depressive phenotype score)*0.4
- Phenotype 16 = (dyspnoea score)*0.4 + (cough score)*0.4 + (sputum score)*0.4 + (sputum color score)*0.4 + (wheeze score)*0.4 + (weight score)*0.4 + (neurological status score)*0.4 + (ventilator interaction score)*0.1 + (walk score)*0.2 + (body temperature score)*0.4 + (heart rate score)*0.4 + (ECG score)*0.2 + (arterial pressure score)*0.2 + (SpO₂ score)*0.3 + (respiratory frequency score)*0.4 + (inspiratory time score)*0.4 + (expiratory time score)*0.4 + (respiration asynchrony score)*0.4 + (resp. freq. / tidal vol. score)*0.4 + (minute ventilation score)*0.2 + (patient activity score)*0.4 + (coughs counter score)*0.4 + (home pollution score)*0.4 + (patient position score)*0.4 + (sleep quality score)*0.4+ (asthenia score)*0.4 + (social context , environment score)*0.3 + (age score)*0.2 + (depressive phenotype score)*0.4
- Phenotype 17 = (dyspnoea score)*0.4 + (cough score)*0.4 + (sputum score)*0.4 + (sputum color score)*0.4 + (wheeze score)*0.4 + (weight score)*0.4 + (neurological status score)*0.4 + (ventilator interaction score)*0.2 + (walk score)*0.3 + (body temperature score)*0.4 + (heart rate score)*0.4 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.3 + (respiratory frequency score)*0.4 + (inspiratory time score)*0.4 + (expiratory time score)*0.4 + (respiration asynchrony score)*0.4 + (resp. freq. / tidal vol. score)*0.4 + (minute ventilation score)*0.3 + (patient activity score)*0.4 + (coughs counter score)*0.4 + (home pollution score)*0.4 + (patient position score)*0.4 + (sleep quality score)*0.4+ (asthenia score)*0.4 + (social context , environment score)*0.3 + (age score)*0.2 + (depressive phenotype score)*0.4
- Phenotype 18 = (dyspnoea score)*0.4 + (cough score)*0.4 + (sputum score)*0.4 + (sputum color score)*0.4 + (wheeze score)*0.4 + (weight score)*0.4 + (neurological status score)*0.4 + (ventilator interaction score)*0.2 + (walk score)*0.4 + (body temperature score)*0.4 + (heart rate score)*0.4 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.3 + (respiratory frequency score)*0.4 + (inspiratory time score)*0.4 + (expiratory time score)*0.4 + (respiration asynchrony score)*0.4 + (resp. freq. / tidal vol. score)*0.4 + (minute ventilation score)*0.3 + (patient activity score)*0.4 + (coughs counter score)*0.4 + (home pollution score)*0.4 + (patient position score)*0.4 + (sleep quality score)*0.4+ (asthenia score)*0.4 + (social context , environment score)*0.3 + (age score)*0.2 + (depressive phenotype score)*0.4
- Phenotype 19 = (dyspnoea score)*0.5 + (cough score)*0.5 + (sputum score)*0.5 + (sputum color score)*0.5 + (wheeze score)*0.5 + (weight score)*0.5 + (neurological status score)*0.5 + (ventilator interaction score)*0.2 + (walk score)*0.3 + (body temperature score)*0.5 + (heart

rate score)*0.5 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.4 + (respiratory frequency score)*0.5 + (inspiratory time score)*0.5 + (expiratory time score)*0.5 + (respiration asynchrony score)*0.5 + (resp. freq. / tidal vol. score)*0.5 + (minute ventilation score)*0.4 + (patient activity score)*0.5 + (coughs counter score)*0.5 + (home pollution score)*0.5 + (patient position score)*0.5 + (sleep quality score)*0.5+ (asthenia score)*0.5 + (social context , environment score)*0.4 + (age score)*0.3 + (depressive phenotype score)*0.5

- Phenotype 20 = (dyspnoea score)*0.5 + (cough score)*0.5 + (sputum score)*0.5 + (sputum color score)*0.5 + (wheeze score)*0.5 + (weight score)*0.5 + (neurological status score)*0.5 + (ventilator interaction score)*0.2 + (walk score)*0.4 + (body temperature score)*0.5 + (heart rate score)*0.5 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.4 + (respiratory frequency score)*0.5 + (inspiratory time score)*0.5 + (expiratory time score)*0.5 + (respiration asynchrony score)*0.5 + (resp. freq. / tidal vol. score)*0.5 + (minute ventilation score)*0.4 + (patient activity score)*0.5 + (coughs counter score)*0.5 + (home pollution score)*0.5 + (patient position score)*0.5 + (sleep quality score)*0.5+ (asthenia score)*0.5 + (social context , environment score)*0.4 + (age score)*0.3 + (depressive phenotype score)*0.5
- Phenotype 21 = (dyspnoea score)*0.5 + (cough score)*0.5 + (sputum score)*0.5 + (sputum color score)*0.5 + (wheeze score)*0.5 + (weight score)*0.5 + (neurological status score)*0.5 + (ventilator interaction score)*0.2 + (walk score)*0.3 + (body temperature score)*0.5 + (heart rate score)*0.5 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.4 + (respiratory frequency score)*0.5 + (inspiratory time score)*0.5 + (expiratory time score)*0.5 + (respiration asynchrony score)*0.5 + (resp. freq. / tidal vol. score)*0.5 + (minute ventilation score)*0.5 + (patient activity score)*0.5 + (coughs counter score)*0.5 + (home pollution score)*0.5 + (patient position score)*0.5 + (sleep quality score)*0.5+ (asthenia score)*0.5 + (social context , environment score)*0.4 + (age score)*0.3 + (depressive phenotype score)*0.5
- Phenotype 22 = (dyspnoea score)*0.5 + (cough score)*0.5 + (sputum score)*0.5 + (sputum color score)*0.5 + (wheeze score)*0.5 + (weight score)*0.5 + (neurological status score)*0.5 + (ventilator interaction score)*0.2 + (walk score)*0.4 + (body temperature score)*0.5 + (heart rate score)*0.5 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.4 + (respiratory frequency score)*0.5 + (inspiratory time score)*0.5 + (expiratory time score)*0.5 + (respiration asynchrony score)*0.5 + (resp. freq. / tidal vol. score)*0.5 + (minute ventilation score)*0.5 + (patient activity score)*0.5 + (coughs counter score)*0.5 + (home pollution score)*0.5 + (patient position score)*0.5 + (sleep quality score)*0.5+ (asthenia score)*0.5 + (social context , environment score)*0.4 + (age score)*0.3 + (depressive phenotype score)*0.5
- Phenotype 23 = (dyspnoea score)*0.6 + (cough score)*0.6 + (sputum score)*0.6 + (sputum color score)*0.6 + (wheeze score)*0.6 + (weight score)*0.6 + (neurological status score)*0.6 + (ventilator interaction score)*0.2 + (walk score)*0.3 + (body temperature score)*0.6 + (heart rate score)*0.6 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.5 + (respiratory frequency score)*0.6 + (inspiratory time score)*0.6 + (expiratory time score)*0.6 + (respiration asynchrony score)*0.6 + (resp. freq. / tidal vol. score)*0.6 + (minute ventilation score)*0.6 + (patient activity score)*0.6 + (coughs counter score)*0.6 + (home pollution score)*0.6 + (patient position score)*0.6 + (sleep quality score)*0.6+ (asthenia score)*0.6 +

(social context , environment score)*0.5 + (age score)*0.4 + (depressive phenotype score)*0.6

- Phenotype 24 = (dyspnoea score)*0.6 + (cough score)*0.6 + (sputum score)*0.6 + (sputum color score)*0.6 + (wheeze score)*0.6 + (weight score)*0.6 + (neurological status score)*0.6 + (ventilator interaction score)*0.2 + (walk score)*0.4 + (body temperature score)*0.6 + (heart rate score)*0.6 + (ECG score)*0.4 + (arterial pressure score)*0.4 + (SpO₂ score)*0.6 + (respiratory frequency score)*0.6 + (inspiratory time score)*0.6 + (expiratory time score)*0.6 + (respiration asynchrony score)*0.6 + (resp. freq. / tidal vol. score)*0.6 + (minute ventilation score)*0.6 + (patient activity score)*0.6 + (coughs counter score)*0.6 + (home pollution score)*0.6 + (patient position score)*0.6 + (sleep quality score)*0.6+ (asthenia score)*0.6 + (social context , environment score)*0.5 + (age score)*0.4 + (depressive phenotype score)*0.6
- Phenotype 25 = (dyspnoea score)*0.6 + (cough score)*0.6 + (sputum score)*0.6 + (sputum color score)*0.6 + (wheeze score)*0.6 + (weight score)*0.6 + (neurological status score)*0.6 + (ventilator interaction score)*0.5 + (walk score)*0.4 + (body temperature score)*0.6 + (heart rate score)*0.6 + (ECG score)*0.5 + (arterial pressure score)*0.5 + (SpO₂ score)*0.5 + (respiratory frequency score)*0.6 + (inspiratory time score)*0.6 + (expiratory time score)*0.6 + (respiration asynchrony score)*0.6 + (resp. freq. / tidal vol. score)*0.6 + (minute ventilation score)*0.7 + (patient activity score)*0.6 + (coughs counter score)*0.6 + (home pollution score)*0.6 + (patient position score)*0.6 + (sleep quality score)*0.6+ (asthenia score)*0.6 + (social context , environment score)*0.5 + (age score)*0.4 + (depressive phenotype score)*0.6
- Phenotype 26 = (dyspnoea score)*0.6 + (cough score)*0.6 + (sputum score)*0.6 + (sputum color score)*0.6 + (wheeze score)*0.6 + (weight score)*0.6 + (neurological status score)*0.6 + (ventilator interaction score)*0.5 + (walk score)*0.5 + (body temperature score)*0.6 + (heart rate score)*0.6 + (ECG score)*0.5 + (arterial pressure score)*0.5 + (SpO₂ score)*0.6 + (respiratory frequency score)*0.6 + (inspiratory time score)*0.6 + (expiratory time score)*0.6 + (respiration asynchrony score)*0.6 + (resp. freq. / tidal vol. score)*0.6 + (minute ventilation score)*0.7 + (patient activity score)*0.6 + (coughs counter score)*0.6 + (home pollution score)*0.6 + (patient position score)*0.6 + (sleep quality score)*0.6+ (asthenia score)*0.6 + (social context , environment score)*0.5 + (age score)*0.4 + (depressive phenotype score)*0.6
- Phenotype 27 = (dyspnoea score)*0.8 + (cough score)*0.8 + (sputum score)*0.8 + (sputum color score)*0.8 + (wheeze score)*0.8 + (weight score)*0.8 + (neurological status score)*0.8 + (ventilator interaction score)*0.5 + (walk score)*0.4 + (body temperature score)*0.8 + (heart rate score)*0.8 + (ECG score)*0.5 + (arterial pressure score)*0.5 + (SpO₂ score)*0.8 + (respiratory frequency score)*0.8 + (inspiratory time score)*0.8 + (expiratory time score)*0.8 + (respiration asynchrony score)*0.8 + (resp. freq. / tidal vol. score)*0.8 + (minute ventilation score)*0.8 + (patient activity score)*0.8 + (coughs counter score)*0.8 + (home pollution score)*0.8 + (patient position score)*0.8 + (sleep quality score)*0.8+ (asthenia score)*0.8 + (social context , environment score)*0.6 + (age score)*0.5 + (depressive phenotype score)*0.8
- Phenotype 28 = (dyspnoea score)*0.8 + (cough score)*0.8 + (sputum score)*0.8 + (sputum color score)*0.8 + (wheeze score)*0.8 + (weight score)*0.8 + (neurological status score)*0.8 + (ventilator interaction score)*0.5 + (walk score)*0.5 + (body temperature score)*0.8 + (heart

rate score)*0.8 + (ECG score)*0.5 + (arterial pressure score)*0.5 + (SpO₂ score)*0.8 + (respiratory frequency score)*0.8 + (inspiratory time score)*0.8 + (expiratory time score)*0.8 + (respiration asynchrony score)*0.8 + (resp. freq. / tidal vol. score)*0.8 + (minute ventilation score)*0.8 + (patient activity score)*0.8 + (coughs counter score)*0.8 + (home pollution score)*0.8 + (patient position score)*0.8 + (sleep quality score)*0.8+ (asthenia score)*0.8 + (social context , environment score)*0.6 + (age score)*0.5 + (depressive phenotype score)*0.8

- Phenotype 29 = (dyspnoea score)*0.8 + (cough score)*0.8 + (sputum score)*0.8 + (sputum color score)*0.8 + (wheeze score)*0.8 + (weight score)*0.8 + (neurological status score)*0.8 + (ventilator interaction score)*1 + (walk score)*0.6 + (body temperature score)*0.8 + (heart rate score)*0.8 + (ECG score)*0.8 + (arterial pressure score)*0.8 + (SpO₂ score)*0.8 + (respiratory frequency score)*0.8 + (inspiratory time score)*0.8 + (expiratory time score)*0.8 + (respiration asynchrony score)*0.8 + (resp. freq. / tidal vol. score)*0.8 + (minute ventilation score)*0.9 + (patient activity score)*0.8 + (coughs counter score)*0.8 + (home pollution score)*0.8 + (patient position score)*0.8 + (sleep quality score)*0.8+ (asthenia score)*0.8 + (social context , environment score)*0.6 + (age score)*0.5 + (depressive phenotype score)*0.8
- Phenotype 30 = (dyspnoea score)*0.8 + (cough score)*0.8 + (sputum score)*0.8 + (sputum color score)*0.8 + (wheeze score)*0.8 + (weight score)*0.8 + (neurological status score)*0.8 + (ventilator interaction score)*1 + (walk score)*0.7 + (body temperature score)*0.8 + (heart rate score)*0.8 + (ECG score)*0.8 + (arterial pressure score)*0.8 + (SpO₂ score)*0.8 + (respiratory frequency score)*0.8 + (inspiratory time score)*0.8 + (expiratory time score)*0.8 + (respiration asynchrony score)*0.8 + (resp. freq. / tidal vol. score)*0.8 + (minute ventilation score)*0.9 + (patient activity score)*0.8 + (coughs counter score)*0.8 + (home pollution score)*0.8 + (patient position score)*0.8 + (sleep quality score)*0.8+ (asthenia score)*0.8 + (social context , environment score)*0.6 + (age score)*0.5 + (depressive phenotype score)*0.8
- Phenotype 31 = (dyspnoea score)*1 + (cough score)*1 + (sputum score)*1 + (sputum color score)*1 + (wheeze score)*1 + (weight score)*1 + (neurological status score)*1 + (ventilator interaction score)*1 + (walk score)*0.6 + (body temperature score)*1 + (heart rate score)*1 + (ECG score)*0.8 + (arterial pressure score)*0.8 + (SpO₂ score)*1 + (respiratory frequency score)*1 + (inspiratory time score)*1 + (expiratory time score)*1 + (respiration asynchrony score)*1 + (resp. freq. / tidal vol. score)*1 + (minute ventilation score)*1 + (patient activity score)*1 + (coughs counter score)*1 + (home pollution score)*1 + (patient position score)*1 + (sleep quality score)*1+ (asthenia score)*1 + (social context , environment score)*0.8 + (age score)*0.8 + (depressive phenotype score)*1
- Phenotype 32 = (dyspnoea score)*1 + (cough score)*1 + (sputum score)*1 + (sputum color score)*1 + (wheeze score)*1 + (weight score)*1 + (neurological status score)*1 + (ventilator interaction score)*1 + (walk score)*0.7 + (body temperature score)*1 + (heart rate score)*1 + (ECG score)*0.8 + (arterial pressure score)*0.8 + (SpO₂ score)*1 + (respiratory frequency score)*1 + (inspiratory time score)*1 + (expiratory time score)*1 + (respiration asynchrony score)*1 + (resp. freq. / tidal vol. score)*1 + (minute ventilation score)*1 + (patient activity score)*1 + (coughs counter score)*1 + (home pollution score)*1 + (patient position score)*1 +

(sleep quality score)*1+ (asthenia score)*1 + (social context , environment score)*0.8 + (age score)*0.8 + (depressive phenotype score)*1

3 CHRONIOUS CORE DEVELOPMENT: THE CENTRAL CLINICAL DECISION SUPPORT SYSTEM

The core component of CHRONIOUS Guidelines Framework is represented by the *Central Clinical Decision Support System* (CDSS) which supplies all the advanced decision functionalities of the platform. This is the *brain* of the CHRONIOUS platform and its *intelligence* is devoted to aid clinical professionals in managing chronic patients on a daily basis, by assessing their current status, facing worsening conditions and preventing exacerbation events.

As outlined in the previous sections, CHRONIOUS core functionalities rely on a sensing infrastructure which is fundamental for evaluating disease signs, patients' behaviour and activity, and their contextual situations. Such information combined with patients' clinical data is exploited for monitoring disease course and adapting therapeutic plans according to any changed condition.

However, although clinical guidelines pertinent to clinical practice are well established and provide clinicians with general instructions for disease diagnosis and treatment, the interpretation of continuously acquired patients' data and the correlation of specific signs and conditions to acute disease events are still at an early stage of investigation, with only few medical studies carried out in home settings that have obtained assessed results [VITACCA09].

Moreover, the presentation of all the collected data, without any type of pre-processing, might overwhelm clinicians and have a counter effect on their activity, by making their decisions even more difficult.

In this context, a system able to interpret acquired data, combine them with patients' clinical information, issue possible alarms and supply motivated suggestions can ease clinicians' activity in a really effective way. To this end, the CHRONIOUS platform includes intelligent services devoted to the analysis and understanding of patients' monitoring data, which are able to provide clinicians with filtered information and advices for their decision making.

The Central CDSS represents the core of CHRONIOUS intelligence services and is aimed at supporting the medical personnel in their newly defined activity of *telemonitoring* chronic patients', by exploiting patients' data and formalized medical knowledge.

The design and implementation of the system were carried out by deeply analyzing the domain of application, moving from the study of the methodologies introduced in the previous chapter to real practical issues.

In particular, as described and motivated in the next section, different types of knowledge representation and processing techniques were adopted, since different types of knowledge appeared relevant for the CHRONIOUS needs. The criteria followed for the choice were based on main concepts such as simplicity, expressiveness, ease in understanding and cooperating with clinicians, and generality. Plus, the need of having a shared dictionary of terms was taken into account as suggested by the review of the previous chapter. Plus, knowledge upgradability was considered a fundamental requirement for the CHRONIOUS CDSS usage.

According to what stated above and well discussed in the following section, clinical guidelines are relevant to the base of knowledge of CHRONIOUS Central CDSS, but are not the only source of knowledge. This consideration together with the assessment that many of the instruments developed for clinical guidelines formalization are still lacking of an effective execution engine motivated the decision of developing an ad-hoc CDSS system.

Moreover, previous experiences of the developers in the field of clinical decision support were taken into account and exploited in the interactions with clinicians as well as in the design activities.

Finally, a scenario-based approach was selected for better devising the decision system, since discussing real situations allows clinicians to perceive the practical involvement of the system in their activities.

In the next sections, the Central CDSS functionalities and how these are embedded into the CHRONIOUS platform are described by defining how it works, the functional scenarios that correspond to the system interventions into the patients' management, the data processed by the system as well as the results of the same. A description of the system internal structure and functioning is provided by recalling its architecture and software design, and going into detail in the formalization of the corpus of clinical knowledge.

A brief overview of the development tools is also provided.

3.1 FUNCTIONALITIES

Since a chronic disease cannot be relieved but just controlled, a good management of people affected by a chronic pathology should be aimed at helping to prevent crises and deterioration, and enabling people living with chronic conditions to attain the best possible quality of life. This can be achieved by involving the patients themselves in a programme devoted to the collection of information about users' status and actions, their compliance to the therapy, the situation around them, and their interactions with the environment in a long-stay setting.

Common ICT applications to chronic patients' management include home monitoring of vital signs for patients with a chronic disease, as well as replacing home visits by nurses in person with telemedicine videophone consultations.

In this framework, CHRONIOUS provides a sensing infrastructure, consisting of a *Wearable Sensing Infrastructure* and a *Patient Monitor* (see [CHRONIOUS_D3.1]), able to acquire a number of relevant information and data about patients' situation in their normal life settings. These data are suitably stored in the central repository of the platform which collects data coming also from the clinical environment about patients' clinical visits and examinations. All these data represent a precious resource for assessing patients' status, detecting early changes in their conditions and preventing unnecessary hospital admissions. To this end, a careful, adequate and intelligent analysis of the data should be performed and this task is fulfilled by the *CHRONIOUS Intelligence*, whose role can be compared to that of the nurse in tele-assistance programmes when patients are interviewed for understanding their current situation.

CHRONIOUS Intelligence, together with the sensing infrastructure, constitutes the main soul of the platform, as sketched in Fig. 3.1.

The aims of such intelligence are to:

- analyze collected patients' sensor data for identifying worrying conditions
- alert caregivers when an acute event is happening
- combine patients' information for providing suggestions on possible changes of the therapeutic plans.

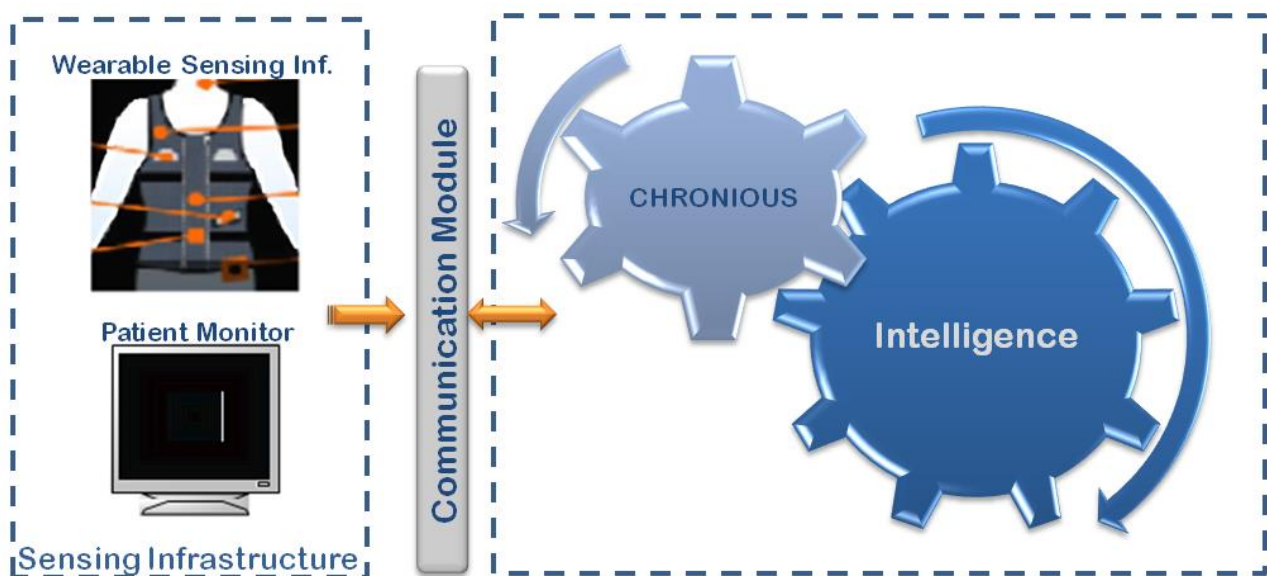


Fig. 3.1. The main soul of the CHRONIOUS platform: the Sensing Infrastructure and CHRONIOUS Intelligence that are connected via a suitable Communication Module

These require processing the relevant clinical knowledge, which comes not only from the clinical practice that relies on assessed protocols specified in the clinical guidelines, but also precise expertise related to the analysis of frequently acquired patients' data.

Actually, programmes of chronic patients' home-monitoring are just in their early stage of development and application, and no assessed knowledge about what to do when monitoring patients is available in official and certified documents such as clinical guidelines. This means that developing effective and reliable intelligent services, able to provide real aid in chronic patients' management, requires the formalization of a dedicated corpus of knowledge by a strict interaction with clinicians specifically expert in patients' monitoring. By this interaction, there is the need to define:

- all the possible acute events that may occur during a chronic disease evolution
- all the conditions that can be considered worrying and should be taken into account
- the relevance of data and parameters about patients' vital signs that are acquired during monitoring and their correspondence to acute events
- the possible actions to be performed for facing acute events.

All this information is not included in clinical guidelines, which provide clinicians instructions about how to treat patients in clinical settings. Hence, the principal source of knowledge for the development of CHRONIOUS intelligence was clinicians' know-how. Moreover, a data driven approach appeared useful in order to mine directly from the collected data the knowledge about which are the relevant information and its evolution in time that should be analysed for predicting or detecting acute events. The box in Fig. 3.2 sketches the main sources of knowledge involved and the focus point of CHRONIOUS intelligence.

Clinicians' know-how can be modelled according to a *symbolic* approach, while the knowledge coming from data results from the development of computational models (so-called *sub-symbolic* or *computational reasoning models*), which, as a shorthand, embed the mined knowledge in the models themselves making it difficult to express such knowledge in a human-understandable form.

According to these observations, CHRONIOUS intelligence is organized in two layers:

- a first level of intelligence, located on the *smart Personal Digital Assistance* device (PDA), is devoted to data analysis and worsening conditions identification by means of *computational reasoning* methods (e.g., *Artificial Neural Networks*, *Bayesian Networks*, and so on);
- a second level correspond to the Central CDSS which is able to supply clinical suggestions by integrating the interpretation of the collected patients' data and the clinical knowledge suitably formalized.

This system solves the requests of supporting chronic disease management by using patients' heterogeneous information (i.e. actual status, anamnesis, clinical history, diagnostic parameters, and clinicians' evaluation) and applying inferential reasoning.

Inferential reasoning consists in inductive and deductive reasoning on the available domain knowledge, and it is strictly correlated to the knowledge representation formalism. Several approaches appeared appropriate for formalizing chronic domain knowledge. The fundamental aim was to develop a formal description of the domain (i.e. relevant concepts, their properties and interrelations) and carefully formalizing the declarative and procedural knowledge, derived from the guidelines and the experts' know-how. Actually, a *symbolic* approach appeared the more appropriate, since easily understandable by a non-specialized audience, e.g. clinicians. In this way, they can be more tempted in contributing to the knowledge elicitation and representation processes. This resulted in the need of inserting a symbolic *Knowledge Base* into the Central CDSS.

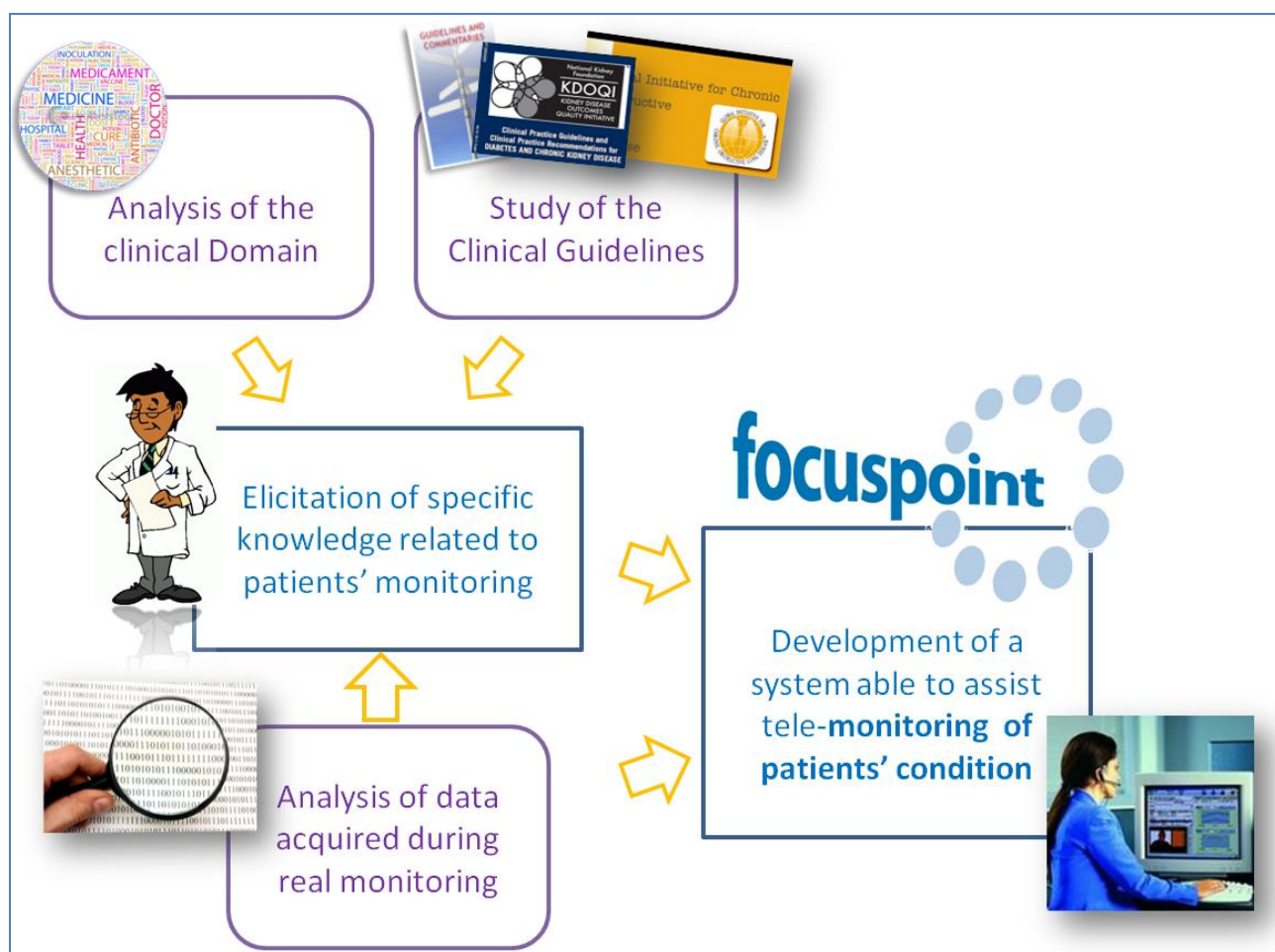


Fig. 3.2. The focus point of CHRONIOUS Intelligence and the main sources of knowledge involved in its development

In particular, according to what stressed above about the absence of officially recognized documents that describe protocols to follow when monitoring chronic patients, new knowledge can come from and during the CHRONIOUS experience, e.g., new possible correlations about sensed parameters and patients' conditions. For this reason, one of the requirements of the Central CDSS was conceived as the possibility to modify the Knowledge Base by letting clinicians add new knowledge. This is carried out through the so-called *Knowledge Base Editor* (KBE) that is described in more details in the next sections.

The functioning of CHRONIOUS intelligent services can be sketched as follows (Fig. 3.3): data gathered by the Sensing Infrastructure are firstly analysed for identifying an abnormal event regarding patient's health status. In particular, in order to decide on patient's current health status, the intelligent services of the first level on PDA combine data acquired from wearable sensors, environmental sensors and data inserted directly by the patients through the *Patients' Monitor* about food and drug intake, lifestyle and questionnaires data. When an abnormal health condition is identified, an alarm is issued and caregivers are alerted. Anytime new data are acquired or an alarm is issued, the second level CDSS is called for understanding the novel situation. This choice is motivated by the capability of the CDSS to access the more complete patients' historical data and employ more complex knowledge suitably formalized by encoding guidelines and clinicians' expertise. A more detailed advice is hence displayed to clinicians, combined with possible suggestions on next actions. This behaviour is principally related to patients' long stay settings and based on the analysis of sensed data.

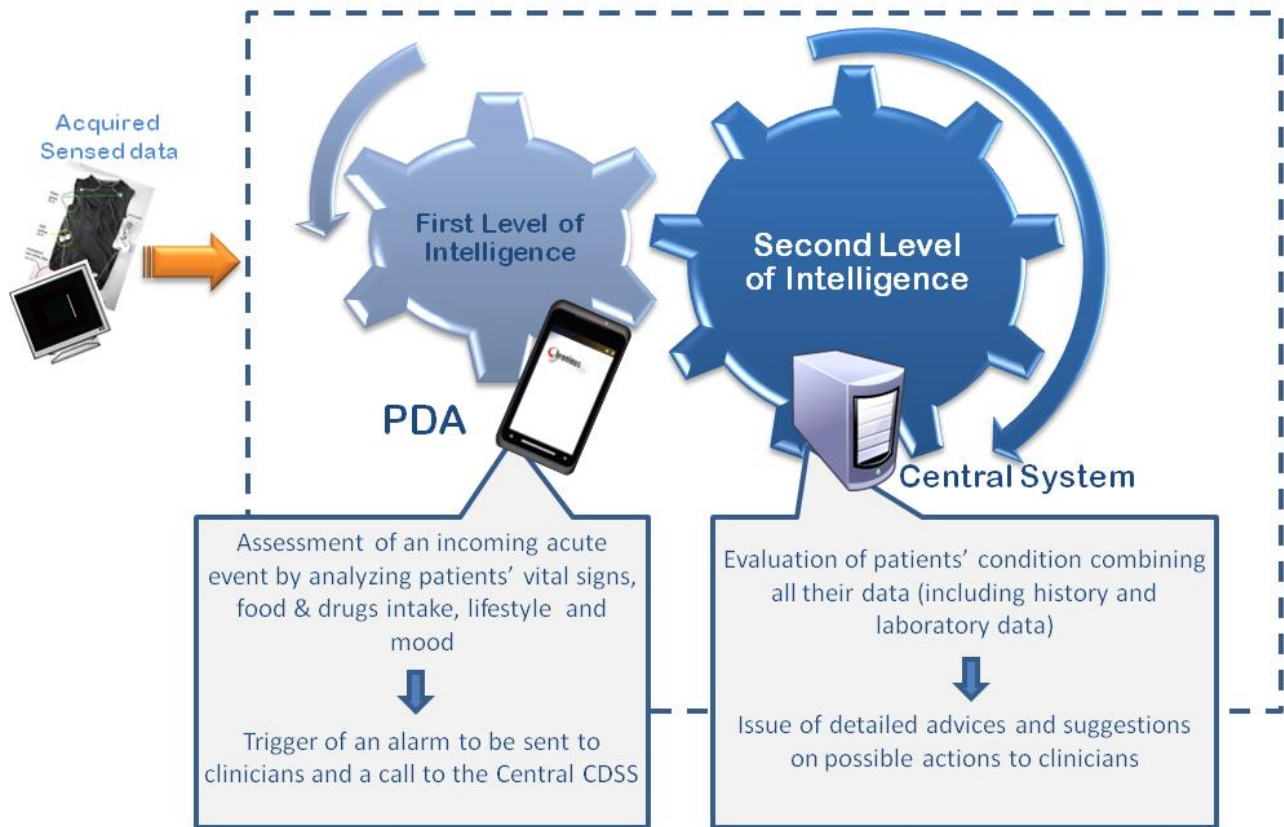


Fig. 3.3. The two levels of the CHRONIOUS Intelligence: analysis of data acquired by the Sensing Infrastructure

Other patients' situations are relevant for the specifications of the system intelligence. Actually, chronic patients usually undergo clinical visits that are aimed at assessing patients' conditions through a number of laboratory and clinical examinations. Data coming from these visits are fundamental also within a chronic patients' management infrastructure, since, as it can be easily understood, they integrate with precious information the data collected in the long stay settings. This is the reason why CHRONIOUS provides integration with clinical sites for the acquisition of patients' data recorded in the clinical environment. Such data are stored in the central repository and are used by the Central CDSS for evaluating patients' conditions both after a clinical visit and during the long stay settings by the integration of the sensed data with the clinical data (Fig. 3.4).

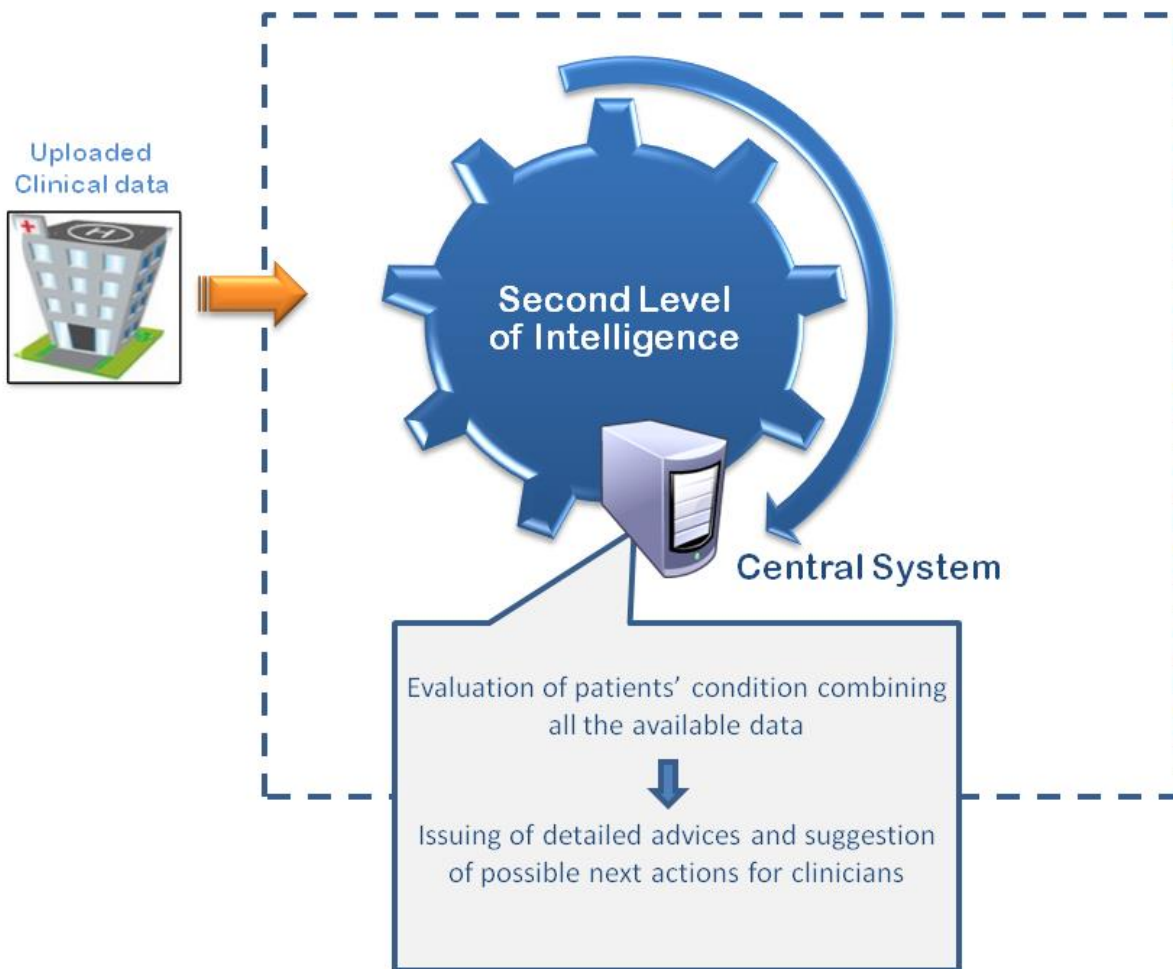


Fig. 3.4. The CHRONIOUS Intelligence involved in the analysis of data acquired from the clinical environment

3.1.1 Functional Scenarios of the Central CDSS

This general functioning was mapped on a careful design of the Central CDSS functionalities. In particular, in accordance to clinicians' suggestions and to the global arrangement of the CHRONIOUS platform, the Central CDSS was conceived as a *resource* of the system that is called on demand when data interpretation and suggestions to clinicians are needed.

A scenario-based approach was followed for defining the interventions of the CDSS. In particular, three different scenarios were agreed with clinicians and correspond to the requests of calling the Central CDSS:

- the *Alarm Checking* scenario, which corresponds to an assessment of patients' status after an alarm has been issued by the first level of intelligence, i.e. the PDA, for alerting about a possible exacerbation;
- the *Home Monitoring* scenario, which corresponds to a periodic assessment of patients' status, more precisely once a day, even without any alerting exacerbation;
- the *Clinical Assessment* scenario, which corresponds to the evaluation of patients' status after a clinical visits, i.e., when new data comes from the clinical environment.

A more detailed description of how the entire platform works within these scenarios can be helpful for better figuring out the functionalities of the Central CDSS, which can be summarized as follows:

- to provide suggestions about a possible diagnosis and treatments
- to determine the steps to be followed for each patient case
- to suggest the next actions: e.g. a requirement for medical examinations and/or additional data retrieval required for reliable diagnosis and treatment proposals
- to recognise trends in the development of a specific acute situation, and hence suggest new approach to the management and treatment processes → insertion of new codified knowledge into the Knowledge Base.

Each of these scenarios is characterized by a flow that starts from data, acquired in different modalities, passes through the Central CDSS and ends with advices and/or suggestions to the caregivers/clinicians or the patients. We can, then, identify a *patients' management loop* that involves different components and functionalities of the CHRONIOUS platform. Fig. 3.5 shows the main components of such a loop for the first two scenarios.

In particular, these scenarios were defined on the basis of the data movement within the platform and are in accordance to the functioning of the Sensing Infrastructure that stores the acquired data in the CHRONIOUS *Central DataBase* (DB) in two cases:

- when an abnormal event is identified
- periodically, after a specified time interval, usually at the end of each day.

These two cases correspond to a call to the Central CDSS in order to assess patients' status.

Similarly, when a patient undergoes a clinical visit, new clinical data are uploaded into the Central DB and a call to the Central CDSS is issued in correspondence.

Alarm Checking scenario

Data gathered by the Patient's Sensing Framework via Wearable Sensors are collected by the *Data Handler* (DH), which checks the validity of the acquired signals. If some abnormal event is identified by applying some simple threshold checking to the acquired signals, DH triggers the PDA, which is not constantly operative, in order to transmit recent data.

The PDA receives also data from the *Home Patient Monitor* (HPM), which are acquired through the external devices, the environmental sensors and the input interfaces used for communicating directly with patients and gathering food, drug and questionnaires data.

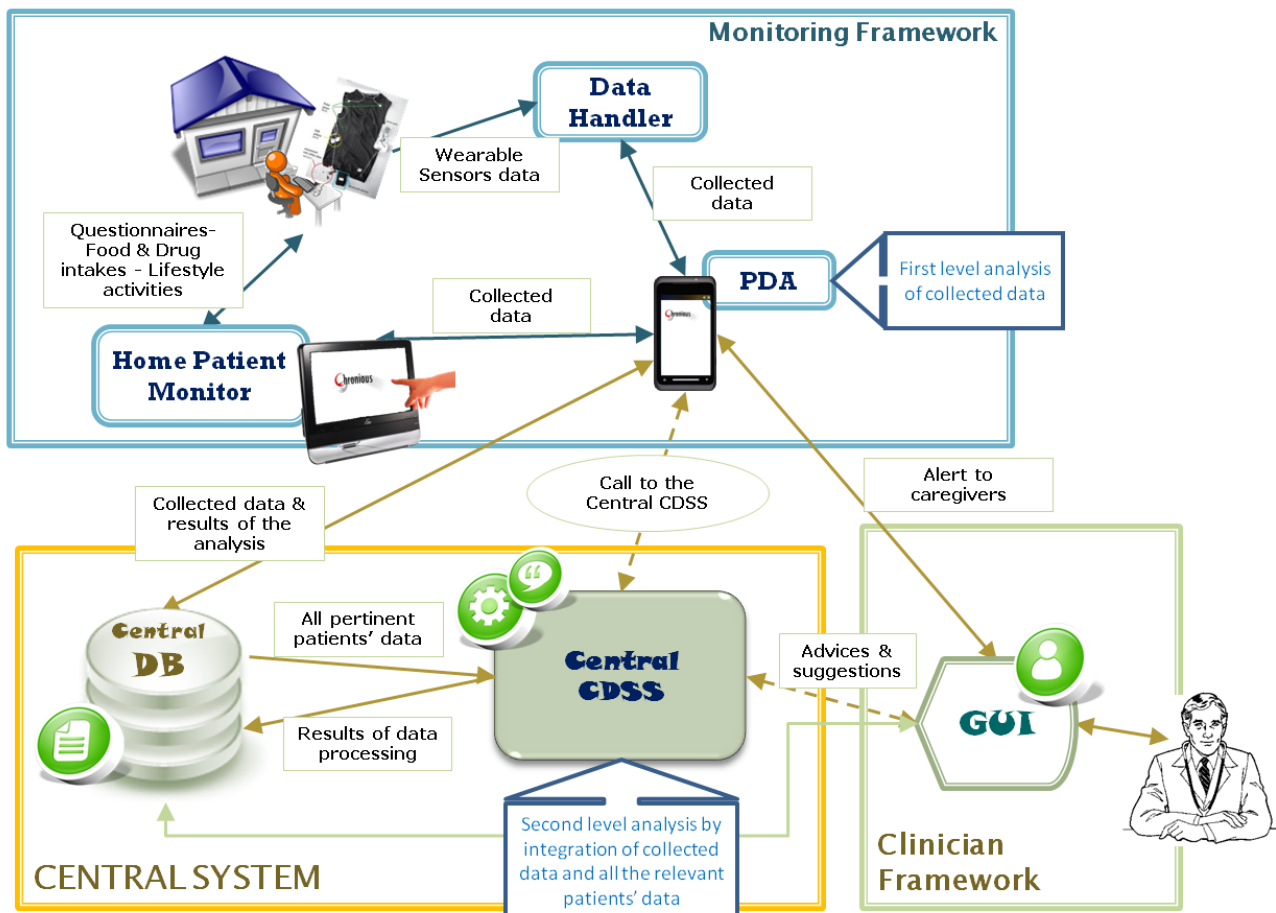


Fig. 3.5. The components and data-flow in the *Patients' Management Loop* for the *Alarm Checking* and *Home Monitoring* scenarios

The first level intelligence on PDA applies computational reasoning models to decide on patient's current health status. If a worsening is detected, an alarm is sent, via sms, to caregivers that are in charge of chronic patients' assistance. An advice is also shown through the clinical Graphical User Interface (GUI). At the same time, acquired data are stored in the Central DB and the Central CDSS is triggered for their analysis: the knowledge elicited from clinicians that are expert in patients' monitoring is applied to the data newly acquired combined with the other relevant patient's data stored in the Central DB. A more in depth evaluation of patient's status is obtained, stored in the Central DB and an advice issued for caregivers, which is shown through the Clinician GUI and provides information about patients' diagnosis, e.g., "*suspected respiratory failure*" or "*hypertension condition*" and possible actions to be undertaken. In Fig. 3.5 this flow is depicted, dashed arrows specify only logical connections: as it will be described in the next chapter, the call to the Central CDSS is done not by the PDA directly, but follows the storage of data into the Central DB; similarly, the advice shown in the Clinician GUI is not sent directly by the Central CDSS but is stored in the Central DB and read from there by the GUI itself.

Home Monitoring scenario

This scenario is similar to the previous: in this situation, data are stored in Central DB by the PDA not after the detection of an abnormal situation, but according to an established deadline. In other words, periodically, at the end of each day, the PDA stores the acquired data into the DB. When this happens, the Central CDSS is triggered and all the data pertinent to the patient are analyzed in order to diagnose patient's status. If necessary, an advice is provided to caregivers through the Clinician GUI.

Clinical Assessment scenario

Chronic patients can go through a clinical visit for different reasons, e.g., for periodically checking the evolution of the chronic pathology with specific examinations, such as spirometry for COPD patients, or for undergoing laboratory analysis for concurrent situations.

In any case, data collected during these visits are fundamental to complete the view of patients' status and are, then, specifically included into the CHRONIOUS platform. When new clinical data are uploaded into the Central DB via specific interoperable services connected to clinical validation sites, a call to the Central CDSS is issued and the system analyzes such data plus other patients' data according to the knowledge elicited from the clinical guidelines and clinicians' know-how. See Fig. 3.6 for the data flow and the components involved.

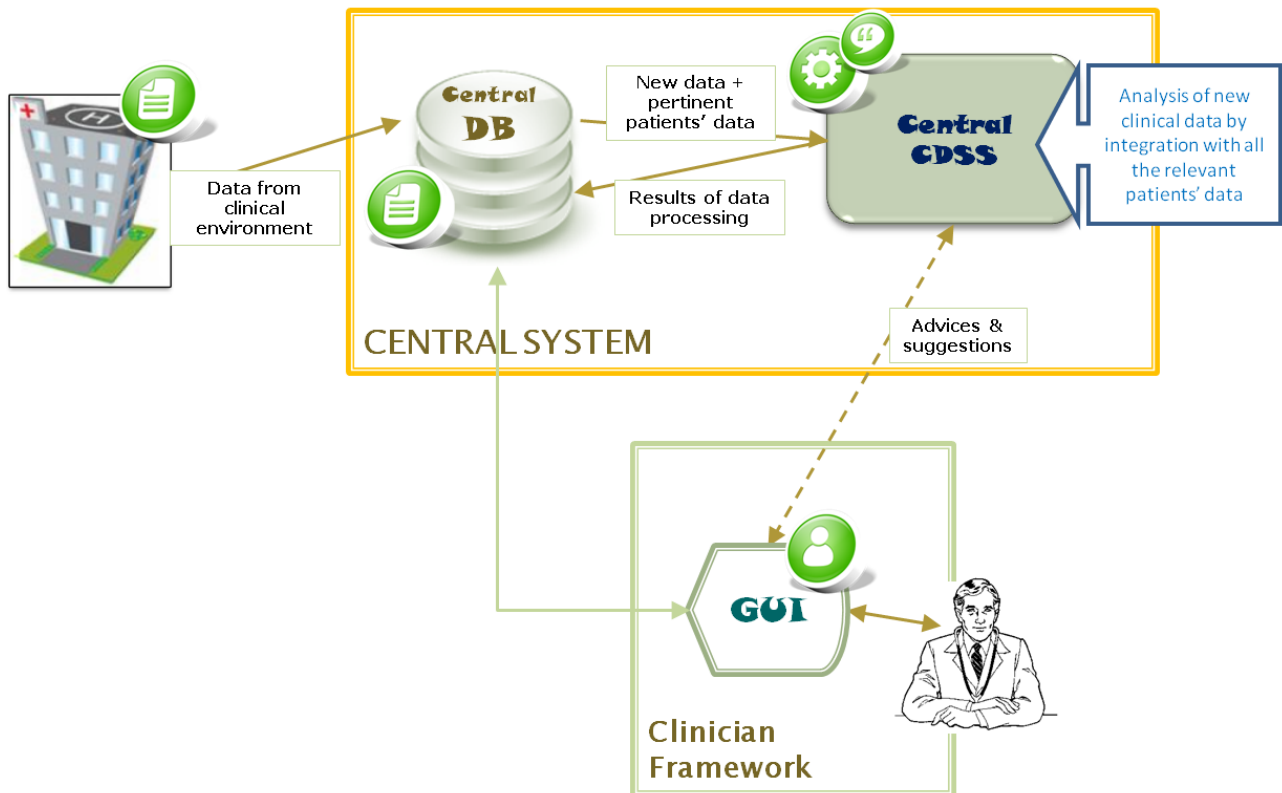


Fig. 3.6. The components and data-flow in the *Patients' Management Loop* for the *Clinical Assessment* scenario

3.1.2 Data Processed by the Central CDSS

According to the specification given in the previous sections, the data processed by the Central CDSS include all the information relevant to an in depth understanding of chronic patients' conditions. The rich umbrella of data acquisition functionalities of the CHRONIOUS platform allows the collection and analysis of the following list of data:

- vital signs data acquired by the wearable sensors of the Sensing Infrastructure
- vital signs and environmental information acquired by the external devices and collected by the Home Patient Monitor
- periodical questionnaire data plus drug and food intake and lifestyle activity collected via the Home Patient Monitor.

All these data are stored into the Central DB and passed to the Central CDSS when their analysis is required.

Data are suitably organized temporally so as to allow the Central CDSS analyzing the trends of parameters that express patients' vital signs. This means that the Central CDSS is able to access different measurements performed in different times, compare them and evaluate the evolution.

3.1.3 Results provided by the Central CDSS

The Central CDSS analyses data by applying the suitably encoded clinical knowledge. The aim of such an analysis is the provision of a number of information to caregivers responsible of managing chronic patients. In particular, the results of the analysis consist in an advice about the status of the patient and a suggestion about the action to be undertaken for managing the situation.

In agreement with clinicians' requirements, the results are shown as a kind of alert/alarm through the Clinician GUI, listing up a number of information. More in detail, the results can be formalized as follows:

- An advice about patient's status diagnosis, e.g., "*suspected bronchospasm*", "*suspected respiratory failure*", "*worsening of patient's condition*"
- A suggestion about what to do, e.g., the necessity to contact the patient to understand better the situation, an anticipation of a scheduled clinical visit, the need of repeating an home setting measurement.

Some additional information is considered for better presenting such results:

- For simplifying the reading of the results, a colour that indicates the severity of the advice or alarm
- The explanation of the advice and suggestion produced, which can come from the guideline or from the motivation given by the clinicians during the elicitation process.

3.2 SOFTWARE ARCHITECTURE AND DESIGN

The Central CDSS was modelled according to the system functionalities described in the previous sections. The main issues that drove the design of the system were:

- the need of modelling not only well-assessed knowledge contained in the clinical guidelines, but also specific knowledge that a group of clinicians had gathered during their experience in monitoring chronic patients
- the need of developing a system able to dynamically change its corpus of knowledge
- the consequent need of selecting a rule representation formalism able to foster the knowledge elicitation process and the clinicians' willingness to contribute
- the analysis of the State of the Art methods for modelling clinical guidelines
- the aim of developing a really functioning system able to provide an effective aid within chronic patients' management
- the complexity and diversity of data processed and tasks to be fulfilled by the system
- the experience matured in previous projects aimed at supporting the management of chronic patients.

All these together resulted in avoiding the reuse of existing methods for modelling clinical guidelines, since they are, so far, only modelling methodologies and none of them has a really working engine for running the encoded guidelines. Moreover, the knowledge relevant for CHRONIOUS purposes cannot be resembled to standard clinical procedures, but is more similar to a cross-analysis of patients' vital signs parameters aimed at assessing or predicting the occurrence of an acute event.

In this context, the Central CDSS was modelled by designing an ad-hoc architecture that was carefully defined by identifying the tasks that the system should address, and its logical-functional structure, i.e. its modular organization in independent components, their relations and functionalities.

In particular, in the first stage of the system modelling activity, a general purpose perspective was adopted, by considering both a symbolic based and a data driven approach for modelling the clinical knowledge. This means that, besides the encoding of explicit knowledge contained in the clinical guidelines, it was considered to face the problem of patients' monitoring by developing knowledge based models as well as computational reasoning models.

A recall to the architecture, which was initially defined and was already presented and discussed in the Deliverable D3.1, can be useful in this section to better remind its main features.

The complexity and diversity of data, processes and tasks involved required a careful conceptualization of the Central CDSS in order to assure its reliability. Three fundamental levels have been identified within the system structure:

- the *knowledge level*, corresponding to all the information needed by the system for performing tasks, e.g. data, domain knowledge, computational decision models;
- the *processing level*, consisting of the system components that are responsible of tasks accomplishment by using the knowledge level;
- the *end-user application level*, including the system components whose functionalities are specifically defined for interacting with the user.

Besides, the knowledge level has been further specialized in three sub-levels, i.e.:

- *Strategy level*, concerning the knowledge about the tasks performed by the system, e.g. their decomposition in sub-tasks or actions, as well as their application order, and when and under what conditions they have to be performed.
- *Reasoning level*, composed by the procedural and computational knowledge used by the system for performing its task.
- *Domain level*, containing the formalization of the domain structure, which has to be known to make inferences and execute tasks.

In particular, this conceptualization induces a similar division also onto the processing level, which is, then, composed by:

- a *meta level*, devoted to task accomplishment and sub-tasks organisation;
- an *object level*, responsible of performing sub-tasks, by processing the reasoning and domain knowledge.

This approach is particularly suitable when modelling care plans and clinical workflows, just like any other guidelines modelling solution. Actually, the *meta level* can be assimilated to a workflow engine that, according to its own encoded knowledge, orchestrates the pieces of knowledge of the object level, which consists of two bases of decisional models: a *symbolic Knowledge Base* and a *base of computational reasoning models*.

Central CDSS Architecture

More in detail, the CDSS architecture consists of the following components (Fig. 3.7):

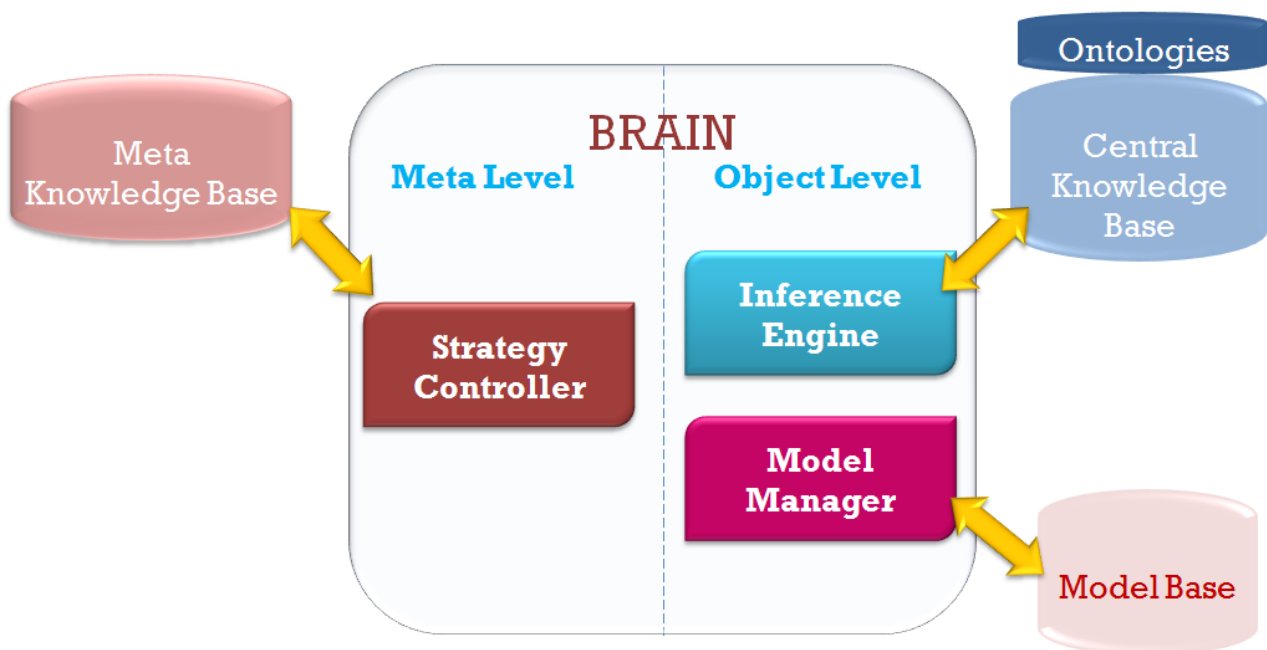


Fig. 3.7. The general view of the Central CDSS architecture

- **Central Knowledge Base**, consisting of reasoning knowledge, formalized from the guidelines and of the clinicians' know-how, and is based on the formalization of the domain knowledge in a suite of *ontologies*;
- **Model Base**, containing the computational decision models;

- **Meta Knowledge Base**, composed by the strategy knowledge, i.e. about the organization of the system tasks.
- **Brain**, the system component endowed with the reasoning capability, which is divided into the meta and object levels.

In particular, the *Central KB* and the *Model Base*, which represent the reasoning knowledge of the system, are used by the object level, namely by the *Inference Engine* and the *Model Manager*, respectively, for inferential and computational reasoning. The *domain level*, introduced in the previous section, is completely represented by the ontologies, which are considered part of the *Central KB*. The *Meta KB* constitutes the knowledge strategy level and is controlled by the *Strategy Controller*, which is responsible for task accomplishment.

Before detailing each component, a brief description of how the system works can be useful. As specified in the previous sections, the Central CDSS is conceived as a resource of the platform that answers requests coming from outside: each request correspond to a decisional service of the system. When a request is committed, the *meta* level component, i.e. the *Strategy Controller*, catches it and organises the task for supplying its response, according to the content of the *Meta KB*. This entails searching or more exactly querying the *Meta KB* for the strategy that best fits the actual task. Once found the strategy, being it a simple action or a sequence of subtasks, the *Strategy Controller* is responsible of its accomplishment, by controlling and supporting the activities of the object level components.

Considering the case of a request that entail both inferential and computational reasoning, e.g., a prognostic evaluation, the procedure followed by the *Strategy Controller* consists in activating both the object components, by forwarding them the necessary data; then waiting for their results, combining them (according to a suitable combination mechanism) and supplying the final response. Once activated, the *Inference Engine* performs its sub-task by reasoning on the actual data and the specific *sub-domain* knowledge of the *Central KB*, i.e. related to prognosis, inferring new facts about the patients. If during the inference process, additional patient's data are necessary, the *Inference Engine* should request their provision to the *Strategy Controller*, which has the responsibility to solve such kind of *crisis*, since the only component interacting with the external environment.

The *Model Manager* applies the computational decision model corresponding to prognosis, decides this way the prognostic class the patient belongs to (e.g. *stable*, *improving*, *rapidly worsening*, or *slowly worsening*) and provides the result to the *Strategy Controller*.

If coded in the strategy, after supplied the prognostic result, the *Strategy Controller* can start a new inferential process of the *Inference Engine* for finding out suggestion on the successive clinicians' actions.

The proposed architecture assured several advantages, which fulfil the system requirements, i.e.:

- Effective scalability
- High modularity
- High degree of portability.

First of all, the careful separation of processing and knowledge level, both for the strategy and reasoning levels, assures the effective scalability, and adaptability to changes and growth of the system. Actually, any addition, deletion or adjustment of the knowledge and model bases does not affect the processing level of the system. High modularity, careful task decomposition and flexibility are also assured by the separation of the different types of processing, i.e. inference, computational and strategic. On the other hand, the combination of all these different processing capabilities represents an innovative feature that improves the value of the entire platform.

Finally, the virtualization of the CDSS functionalities assures a high degree of portability, fostered also by the system multilevel structure, i.e. only the strategic level and the ontologies are in contact with the external environment.

Going further in the development of the Central CDSS, it was argued that splitting the modalities of data processing could have different advantages in terms of CHRONIOUS intelligence reliability. Hence, the computational reasoning models were moved to the first level of the intelligence, i.e., on the PDA, while the Central KB was kept in the Central CDSS.

The new resulting architecture is shown in Fig. 3.8.

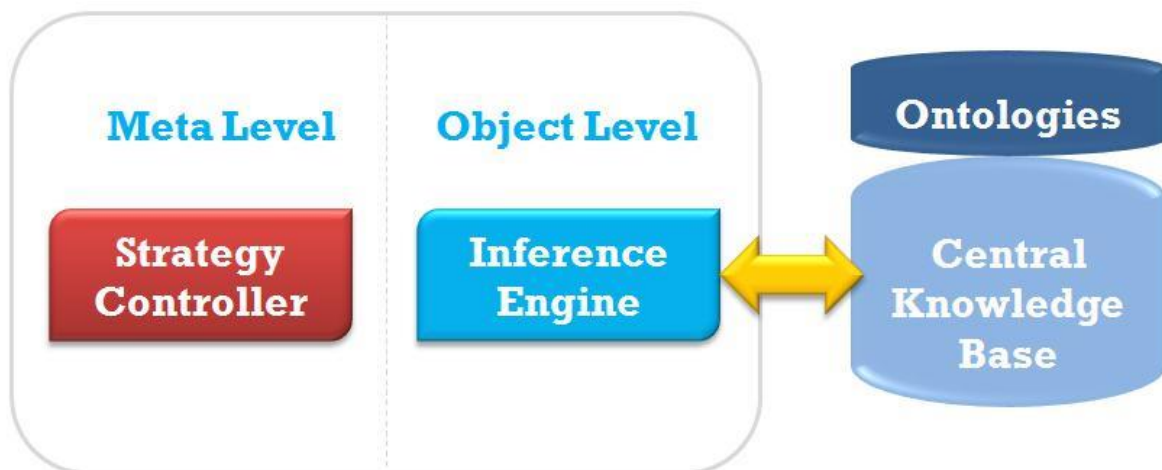


Fig. 3.8. The updated Central CDSS architecture

As will be described in more detail in the next section, the Central KB was modelled by using ontologies for modelling the structure of the clinical domain, i.e. of chronic pathologies, by particularly focusing on COPD. The corpus of knowledge elicited from clinicians and clinical guidelines was then encoded by using the terms of the ontologies in production rules.

The adoption of terminologies in general for modelling the domain is quite common among clinical guidelines modelling tools, since the terms listed are useful in the guideline formalization process. Within CHRONIOUS Central CDSS, a more powerful representation was selected based on the ontology formalism, so as to have a more formal representation of the domain, with terms, relations and properties, and also the terminology for letting the non-expert users modifying the KB through the Knowledge Base Editor.

Production rules were preferred to other symbolic representation formalisms since they resemble and are closer to clinicians' reasoning habit, i.e., the *cause-effect* strategy which is also the foundation of the evidence-based medicine.

The encoded rules were elicited according to the different scenarios described in the previous section. This way, a focus on the purpose of the different pieces of knowledge was maintained. This, coupled with the fact that the Central CDSS is modelled as resource called on demand, resulted in the design of the system as a set of processing units, the *decisional services*, which are launched in correspondence to different requests and correspond to each of the identified scenarios.

In the next sections, the methodology applied for modelling the Central KB as well as a high level description of its content is reported, together with a description of the decisional services developed.

The chapter ends with an introduction to the development tools used for developing the different components of the architecture.

3.3 THE CENTRAL KNOWLEDGE BASE

3.3.1 The methodology

The clinical knowledge to be modelled and inserted into the Central Knowledge Base implicitly includes

- i) the structure of the domain knowledge, named *declarative knowledge*, and
- ii) the processing which takes place throughout the whole course of the decision making activity, named *procedural knowledge*.

In particular, the declarative knowledge concerns the domain compositional elements, such as raw and abstract concepts, their properties and inter-relations. On the other hand, procedural knowledge captures the behavioural logic and provides more explicit information about which actions can be taken or which conclusions can be drawn from declarative knowledge.

The process of knowledge representation is fundamentally aimed at developing a formal description of both the declarative and procedural knowledge, derived from the guidelines and the experts' know-how, respectively in terms of one ontology and a set of production rules (i.e. a set of conditional statements expressed in form of "if *antecedents* then *consequent*") built on the top of it (Fig. 3.9).

In more detail, the approach used in the project merges both theoretical and practical issues and was divided into the following phases:

- *Specification*, when requirements were captured and sources of declarative and procedural knowledge were identified.
- *Conceptualisation*, when declarative and procedural knowledge was extracted and initial versions of the ontology and the rules were formed.
- *Elaboration & Evaluation*, when both the ontology and rules were elaborated and evaluated
- *Implementation*, when the ontology and rules were formalized.

It is worth noting that the elaboration and evaluation phases came in cycles, as it usually happens – if the evaluation of the ontology and rules proved an existence of some inconsistencies, the elaboration phase was repeated. In the following section we describe our approach in more detail.

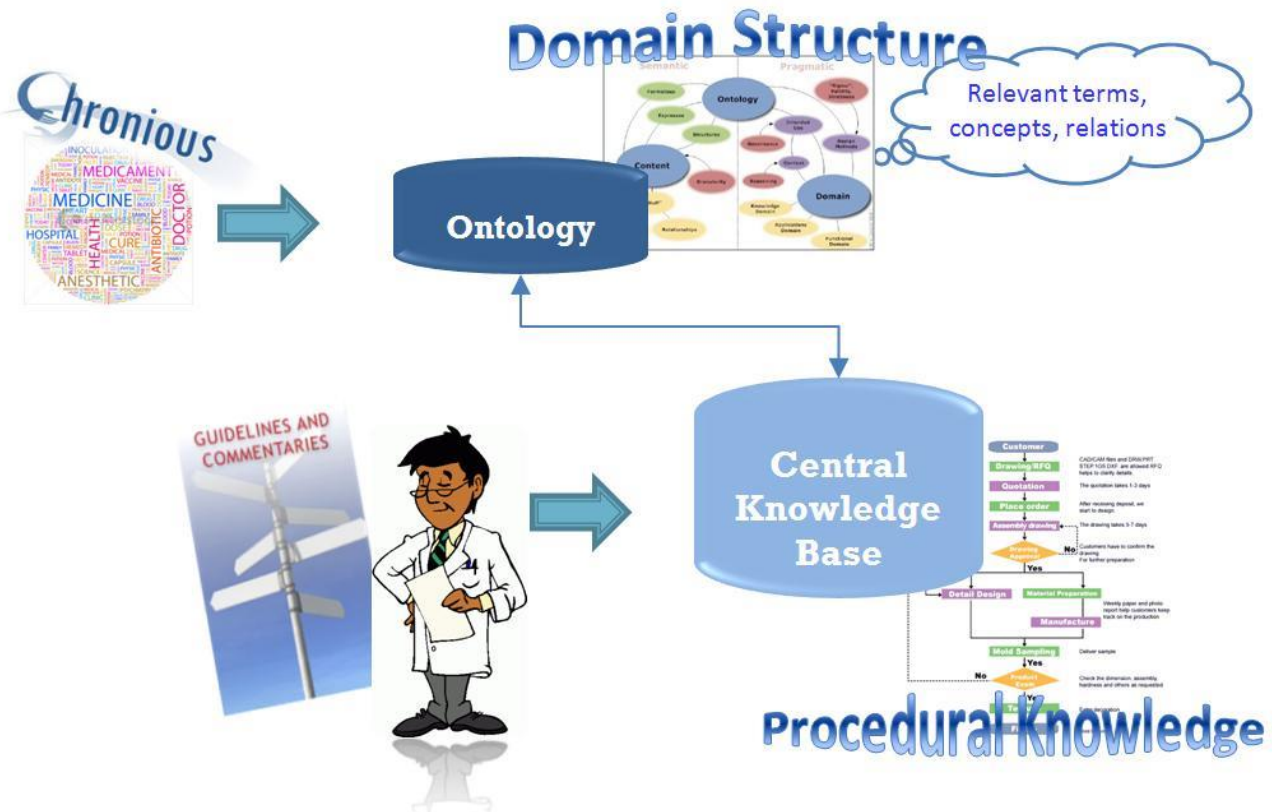


Fig. 3.9. The content and components of the Central Knowledge Base

Specification

The role of ontology and rule specification is to define the area for their application and to guide the developers around the structure of the ontology and the form of rules.

We defined the following information to be a part of the ontology and rule specification:

- *Goal*, a clearly defined reason for creating the ontology and rules – in short: for what the ontology and rules had to be used and how.
- *Domain and Scope*, the domain defined the knowledge domain the ontology and rules describe. The scope narrowed the domain, adding additional boundaries within the domain.
- *Formality Level*, this addressed the language chosen for the implementation of the ontology and rules. Humans prefer informal, natural language descriptions while machines need them to be put into a formal and structured way.
- *Knowledge Sources*, the nature of the knowledge source (interviews, text-analyses, ontology re-use, etc.) may influence the creation of the ontology and rules, thus it was essential to define all the most important sources here. The list of possible knowledge sources consisted of:
 - Interviews with domain experts
 - Internal documents (dictionaries, technology white papers, product descriptions, web pages, etc.)
 - Brainstorming
- *Usage scenarios*, the aim of the usage scenarios was to provide an idea of the planned semantics identified for the ontology and rules. Putting them in the form of use cases made identification of the most important concepts and rules quite easy. This helped making a ‘fast start’ on the conceptualization phase.

The specification stage was crucial to the development process of the ontology and rules. It was used in two ways:

- It facilitated the conceptualization phase. It identified the core concepts and the first set of rules thus giving the conceptualization phase a ‘kick-start’. In addition, by clearly defining the scope of the ontology, it helped to make decisions about concept and rule inclusion or removal.
- It was used in the evaluation phase. In this phase the ontology and rules was validated against the general requirements specified in this initial phase, specific usage scenarios (it was possible to perform the scenario with the ontology and rules created) and the requirements defined in the form of competence questions.

Conceptualisation

The goal of this phase was to structure the declarative knowledge in a conceptual model so as to make the intended usage possible. In other words –a information model was built from the domain defined in the specification. The model consisted of concepts and relations between them. The starting point was the list of the most important concepts along with their definitions. In particular, the usage scenarios and competency questions of the specification phase were used to identify not the list of all the ontology concepts, but only the most important ones ‘covering’ the domain identified in the specification. After that, the concepts were put into a taxonomy. If it was not be possible to create a single taxonomy and some concepts were not part of any taxonomy tree, these latter were connected using some kind of relation other than subsumption. After the taxonomy was created, relations were added. Also a need for concept addition, removal or redefinition arose at some points. Taxonomy was then altered in this way and became an ontology prototype which contained only the most important concepts and might be treated as a skeleton upon which the final version was built.

Elaboration & Evaluation

In this phase, the ontology prototype developed in the previous phase was elaborated on, that means concepts were added, removed or redefined, relations were introduced, etc., and, then, the procedural knowledge was formalized in accordance with the elaborated prototype in form of rules. Afterwards, both the ontology and rules were evaluated and then released.

The process of enriching the ontology, formalizing the rules and evaluating both the ontology and rules was, as usual, cyclical. The ontology prototype was enriched by adding new concepts, concept properties, axioms and restrictions. The rule formalization was realized taking into account the enriched prototype and required the addition of new concepts or concept properties. Both these phases were repeated a few times, each time the evaluation phase proved there was a need for improving the ontology or for adding new rules.

The goal of evaluation was to ensure that the ontology and rules correctly implemented the requirements (specification), were compliant to the modelled domain (within constraints defined in the specification), and completely covered the usage scenarios. From a general point of view, the evaluation might result in some changes that need to be introduced, which in turn might trigger some ontology rebuilding or rule adding which in turn would require the re-evaluation of both the ontology and rules.

Two types of evaluation were defined:

- *User-focused*, which consisted in checking whether the ontology and rules that were developed matched the prerequisites placed in the specification.
- *Consistency-focused*, which aimed at checking whether there were any inconsistencies in the ontology and rules.

In each loop, the evaluations were performed, the ontology and rules were validated against its specifications and inconsistencies were detected and removed.

Implementation

The implementation phase dealt with translating the ontology and rules from human-understandable into machine-understandable form.

3.3.2 The ontology and rules

Goal of the ontology and rules

The ontologies combined with production rules were devised as formal, explicit models to provide the Central CDSS with information about the specific medical domain that can be processed efficiently.

The main purpose of the ontology and rules devised for the CDSS was to be able to represent domain-specific knowledge necessary to remotely support clinical operators in the daily home-monitoring of chronic patients. The approach aimed at chronic disease management, but specific focus was given to one of the pathologies chosen as system demonstration, namely COPD.

As a matter of fact, the way the knowledge is represented for clinical decision support is one of the most key facets for having a successful CDSS, starting from the analysis and design of the CDSS at the very beginning and ending to the implementation of the CDSS at the final stage. Ontologies combined with production rules seemed the more suitable and up-to-date methodology for solving this task since easily understandable by a non-specialised audience, e.g. clinicians. In this way, they could be involved not only in the knowledge elicitation and representation, but also in both the process of modification/updating of existing knowledge.

Formality level

The ontology and rules had to be automatically processed by the CDSS. In addition, at the same time, the expressiveness of the ontological terminology and the simplicity of the rule structure had to be guaranteed to facilitate the writing/editing of medical knowledge. This put some requirements on both the ontology and rule languages chosen to represent respectively the ontology and the rules.

The choice of OWL (*Web Ontology Language*), which will be described in more detail in the next section, as ontology language was carried out with the final aim of granting both formality and expressive power. OWL is the recommended formalism for providing 'semantics' to the Semantic Web and is a de facto standard for expressing ontologies. In particular, the OWL specification includes an abstract syntax which provides a higher level and less cumbersome way of writing ontologies. The practical advantages of this choice are its broad scope and visibility, expressivity, active community behind and permanent improvement of related ontology management and editing tools.

Different versions of OWL are currently available. Version 1 provides three increasingly expressive sublanguages, named respectively OWL Full, OWL DL, and OWL Lite. The version of OWL chosen to formalize the ontology for supporting the daily management of COPD patients by means of the CDSS was OWL Full. OWL Full is not actually a sublanguage, as it contains all the OWL language constructs. It provides a complete vocabulary enabling maximum expressive power and syntactic freedom, even if decidable reasoning procedures cannot exist for an OWL Full ontology.

This choice may be surprising at first sight, since most ontology applications that use some kind of reasoning presuppose OWL DL compliant ontology for the sake of decidability and availability of reasoning tools. Differently, the ontology for the Central CDSS was conceived to provide only a definitional description of terms to be used in the rules for assembling the antecedent and consequent parts. As a result, since the ontology must not serve directly the reasoning and no new implicit knowledge was to be inferred, there was no reason to limit the expressiveness of the representation by using OWL DL.

As regards to the rule representation, *Jena rule language*, described in the next section, was identified as the most appropriate language for writing rules that can be combined with OWL ontologies. In particular, such a language enables to build rules starting from the terminological elements defined in the OWL ontology. It uses a very simple syntax for the rules, essentially based on triples expressed in the form of *<subject, predicate, object>*, and, in addition, applies built-ins to represent user defined operations (actions). Moreover, it offers support for a form of *Negation-as-Failure*, expressed by using the *'noValue'* built-in.

The structure of each rule was composed of one or more premises expressed in terms of concepts and relations concatenated by logical conjunctive operators, which could be evaluated to be either true or false. Disjunction was not supported. In contrast, each rule had exactly one conclusion. As a result, thanks to its succinct but at the same time very expressive syntax, Jena rule language was not only easy to use for writing rules but also extremely simple to read and understand also for a non-specialised audience, and, for these reasons, it was very adequate to provide reasoning support that met the Central CDSS requirements.

Domain and Scope

The ontology and rules for CDSS were focused on domain of the clinical knowledge necessary to remotely support clinical operators in the daily home-monitoring of COPD patients.

In more detail, the ontology was used to represent declarative knowledge containing the concepts, relations and concept attributes that exist in the given domain. The scope of the ontology was the definition of the terminology to be used in the rules for the home-monitoring of COPD patients, with a focus on the simplicity of representation. On the other hand, production rules were employed to represent procedural knowledge.

Moreover, another feature of the ontology and rules was their reusability. The first activity in the task of ontology development for COPD was the identification of the state-of-the-art ontologies or rules to be opportunely adapted.

After a literature search, the conclusion was made that neither existing ontology fits the intended scope (i.e. a very simple representation of the vocabulary necessary to describe rules for remotely supporting the home-monitoring of COPD patients), nor rule have been developed for the same scope. As a consequence, a decision was made to first build from scratch a new ontology for the Central CDSS purposes, by starting from the domain-specific declarative knowledge and to, successively, develop on the top of it the production rules that aimed at modelling the domain-specific procedural knowledge. Ontologies from WP5 could not be adopted due to their different purposes, but they were monitored to employ compatible terminology when meaningful.

Usage scenarios

The usage of the ontology and rules was defined for the scenarios reported in section 7.1. Summarizing, the ontology combined with the rules was used for the patient's condition assessment, for the patient's severity class assessment and for the alarm issuing in the following scenarios:

- the *Alarm Checking* scenario, when PDA sends an alarm;
- the *Home Monitoring* scenario, every 24 hours, when monitoring data are upgraded in the central DB.
- the *Clinical Assessment* scenario, when new assays data come from clinical sites.

A decisional service was developed for each of these scenarios.

Knowledge Sources

Multiple knowledge sources for eliciting respectively the declarative knowledge to be captured by the ontology and the procedural knowledge to be formulated in rules were identified. They were split into two main groups: existing clinical guidelines and CHRONIOUS clinical guidelines.

In more detail, the first group included the knowledge that could be elicited from existing clinical guidelines. This knowledge provided only generic indications on the patient clinical management and does not provide any information about the procedures to be followed in cases of home-monitored COPD patients since it did not consider the parameters measured by wearable devices as the ones supported by the CHRONIOUS Patient Sensing Framework.

The existing clinical guidelines for COPD belonging to this first group were the following:

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD), Global Strategy for Diagnosis, Management, and Prevention of COPD, 2009 [GOLD07];
- National Institute for Clinical Excellence (NICE), Chronic obstructive pulmonary disease: Full Guideline, published in February 2004 and updated in 2010
- American Respiratory Society, COPD Guidelines, 2004
- European Respiratory Society, Standards for the diagnosis and treatment of patients with COPD, 2004
- British Thoracic Society, Guidelines on the Management of COPD, 1997

The second group included the CHRONIOUS **clinical guidelines reported in section 5.2** for COPD diseases and was specifically devised with the final aim of formulating ad-hoc indications and actions to remotely support clinical operators in the daily home-monitoring of COPD patients.

Description of rules

By applying the methodology reported and in accordance with the design specifications described, production rules were devised for the three scenarios reported in section 3.1.1 with the final aim of representing procedural knowledge of the Clinical Knowledge Base.

Rules are simple conditional declarations that link a logical combination of antecedent conditions to a consequent, according to the following “if-then” structure:

If (antecedents) then consequent

They formalize, in accordance with the terminological elements defined in the OWL ontology, the procedural knowledge described in form of guidelines in section 2.2.

Formally,

- The **antecedents** part is a conjunction of pairs composed of two parameters (p_{k1}, p_{k2}), connected by a logical operator op_k , i.e. :

$$\text{antecedents} = (p_{11} \text{ op}_1 p_{12}) \text{ AND } (p_{21} \text{ op}_2 p_{22}) \text{ AND } \dots \text{ AND } (p_{k1} \text{ op}_k p_{k2}),$$

where

op_k is a logical operator $\{=, \neq, <, >, \leq, \geq\}$,

each *parameter* can be:

- a simple ontology term,
 - a numeric/string value,
 - a more complex arithmetical expression composed of one (or more) ontology term, arithmetical operators $\{+, -, *, /\}$, and numeric/string values.
- The **consequent** part is a parameter-value pair (p,v) , connected by an assignment operator, representing the result of the rule, i.e.:

$$\text{consequent} = (p \text{ op } v)$$

where

op is an assignment operator,

parameter is a simple ontology term,

value can be a number or a string.

As a result, the structure of each rule is composed of one or more antecedents expressed in terms of ontology properties concatenated by logical conjunctive operators, which can be evaluated to be either true or false. Disjunction is not supported. Moreover, each rule has exactly one conclusion.

In the next sub-sections, a tabular representation of the guidelines described in section 2.2 is reported in accordance with this structure.

COPD: Home Monitoring

COPD guidelines formalized for the usage scenario of *Home Monitoring* reported in section 2.2.1 can be synthesized in the CHRONIOUS Card. The CHRONIOUS Card has been studied by CNR also on the base of the study Vitacca *et al.* [VITACCA09] and approved by the CHRONIOUS Medical Board.

Synthetically, a score is assigned to monitoring parameters and answers given to the CHRONIOUS questionnaires.

The questionnaires used for the CHRONIOUS Card, namely *Symptom Questionnaire* and *Mental Questionnaire*, have been approved by the CHRONIOUS Medical Board.

The *Symptom Questionnaire* is reported in the following Fig. 3.10:

| Question | Answer Type | Possible Answers/Sample Answers |
|--|-------------------------------------|---|
| (COPD1) How do you feel? | Multiple Choice (single answer) | <input checked="" type="checkbox"/> the same <input type="checkbox"/> better <input type="checkbox"/> worse |
| (COPD2) How much difficulty did you have breathing today? [ref. BCSS questionnaire] | Multiple Choice (single answers) | <input type="checkbox"/> =none, unaware of any difficulty <input type="checkbox"/> =mild: noticeable during strenuous activity <input type="checkbox"/> =moderate: noticeable when washing and dressing <input type="checkbox"/> =severe: almost constant, present even when resting |
| (COPD3) How was your cough today? [ref. BCSS questionnaire] | Multiple Choice (single answer) | <input type="checkbox"/> =none <input type="checkbox"/> =rare <input type="checkbox"/> =occasional <input type="checkbox"/> =frequent <input type="checkbox"/> =constant |
| (COPD4) How much trouble was your sputum today? [ref. BCSS questionnaire] | Multiple Choice (single answer) | <input type="checkbox"/> =none, unaware of any difficulty <input type="checkbox"/> =mild: rarely caused problem <input type="checkbox"/> =moderate: noticeable as a problem <input type="checkbox"/> =marked: caused a great deal of inconvenience <input type="checkbox"/> =severe: an almost constant problem |
| (COPD5) How was the color of your sputum today? [ref. RespiCard questionnaire] | Multiple Choice (single answer) | <input type="checkbox"/> = no sputum <input type="checkbox"/> = white <input type="checkbox"/> =yellow <input type="checkbox"/> =yellow/green <input type="checkbox"/> =green/brown <input type="checkbox"/> =with blood |
| (COPD6) Did you have difficulty in breathing with wheeze and whistle? [ref. RespiCard questionnaire] | Multiple Choice (single answer) | <input type="checkbox"/> =never <input type="checkbox"/> =occasionally <input type="checkbox"/> =under strong efforts <input type="checkbox"/> =under moderate efforts <input type="checkbox"/> =at rest |
| (COPD7) Did you feel your ankle swollen today? | Multiple Choice (single answer) | <input type="checkbox"/> yes <input type="checkbox"/> no |

Fig. 3.10 COPD Symptom Questionnaire for CHRONIOUS Card

The *Mental Questionnaire* is reported in the following Fig. 3.11:

| Question | Answer Type | Possible Answers/ Sample Answers |
|---|--|--|
| <i>Mental state 1 How do you feel?</i> | <i>Multiple Choice (single answer)</i> | <input checked="" type="checkbox"/> Very good <input type="checkbox"/> Good <input type="checkbox"/> Not so good <input type="checkbox"/> Bad |
| <i>Mental state 2 How is your mood today?</i> | <i>Multiple Choice (single answer)</i> | <input checked="" type="checkbox"/> Very happy <input type="checkbox"/> Happy <input type="checkbox"/> Upset <input type="checkbox"/> Angry <input type="checkbox"/> Bored <input type="checkbox"/> Tired |
| <i>Mental state 3 How is your energy level?</i> | <i>Multiple Choice (single answer)</i> | <input checked="" type="checkbox"/> Very high <input type="checkbox"/> High <input type="checkbox"/> Normal <input type="checkbox"/> Low <input type="checkbox"/> Very Low |
| <i>Mental state 4 Any sleep disturbances?</i> | <i>Multiple Choice (single answer)</i> | Yes or No |

Fig. 3.11 COPD Mental Questionnaire for CHRONIOUS Card

We have logically divided into three phases the evaluation of the CHRONIOUS Card. In the next paragraphs, the tables introduced in Chapter 4 are reported for making the reading easier.

The first logical step corresponds to the deduction of the BODE index score, which is evaluated according to the following Table 3-I, where: FEV1% pred = predicted amount as a percentage of the forced expiratory lung volume in one second; 6MWD = six minute walking distance; MMRC = modified medical research council dyspnea scale; BMI = body mass index

| | BODE Index Scores | | | |
|--------------|--------------------------|----------|----------|----------|
| | 0 | 1 | 2 | 3 |
| FEV1% pred | ≥65 | 50-64 | 36-49 | ≤35 |
| 6MWD (m) | ≥350 | 250-349 | 150-249 | ≤149 |
| MMRC | 0-1 | 2 | 3 | 4 |
| BMI (kg.m-2) | >21 | ≤21 | | |

Table 3-I. Total BODE Index score = 0 to 10 units.

The second logical step consists in the assessment of the patients' phenotype, which is evaluated by considering the values of following parameters according to Table 3-II and Table 3-III:

- BODE Index
- smoking addiction
- number of exacerbations per year
- number of steps per die.

| | | Criteria | | | | |
|---|-------------------------|----------|------|-----|------|--|
| | | 1 | 2 | 3 | 4 | |
| 1 | BODE Index | 0-2 | 3-4 | 5-6 | 7-10 | Bode 0-2 / 3-4 / 5-6 / 7-10 |
| 2 | smoking addiction | yes | no | | | smoker / not a smoker |
| 3 | exhacerbation per year | ≥ 2 | <2 | | | <2 exhacerbations per year / ≥ 2 exhacerbations per year |
| 4 | number of steps per day | >500 | <500 | | | active / sedentary |

Table 3-II. Criteria for the definition of the Patients' Phenotypes

| Phenotypes: | BODE | Smoker | exhacerb. | steps | = | Category name |
|-------------|------|--------|-----------|----------|---|---|
| 1 | 0-2 | no | <2 | >50 0 | = | Bode 0-2, not a smoker, <2 exhacerbations per year, active |
| 2 | 0-2 | no | <2 | <50 0 | = | Bode 0-2, not a smoker, <2 exhacerbations per year, sedentary |
| 3 | 0-2 | no | ≥ 2 | >50 0 | = | Bode 0-2, not a smoker, ≥2 exhacerbations per year, active |
| 4 | 0-2 | no | ≥ 2 | <50 0 | = | Bode 0-2, not a smoker, ≥2 exhacerbations per year, sedentary |
| 5 | 0-2 | yes | <2 | >50 0 | = | Bode 0-2, smoker, <2 exhacerbations per year, active |
| 6 | 0-2 | yes | <2 | <50 0 | = | Bode 0-2, smoker, <2 exhacerbations per year, sedentary |
| 7 | 0-2 | yes | ≥ 2 | >50 0 | = | Bode 0-2, smoker, ≥2 exhacerbations per year, active |
| 8 | 0-2 | yes | ≥ 2 | <50 0 | = | Bode 0-2, smoker, ≥2 exhacerbations per year, sedentary |

| | | | | | | |
|-----------|------|-----|-----|----------|---|--|
| 9 | 3-4 | no | <2 | >50 0 | = | Bode 3-4, not a smoker, <2 exacerbatons per year, active |
| 10 | 3-4 | no | <2 | <50 0 | = | Bode 3-4, not a smoker, <2 exacerbatons per year, sedentary |
| 11 | 3-4 | no | ≥ 2 | >50 0 | = | Bode 3-4, not a smoker, ≥2 exacerbatons per year, active |
| 12 | 3-4 | no | ≥ 2 | <50 0 | = | Bode 3-4, not a smoker, ≥2 exacerbatons per year, sedentary |
| 13 | 3-4 | yes | <2 | >50 0 | = | Bode 3-4, smoker, <2 exacerbatons per year, active |
| 14 | 3-4 | yes | <2 | <50 0 | = | Bode 3-4, smoker, <2 exacerbatons per year, sedentary |
| 15 | 3-4 | yes | ≥ 2 | >50 0 | = | Bode 3-4, smoker, ≥2 exacerbatons per year, active |
| 16 | 3-4 | yes | ≥ 2 | <50 0 | = | Bode 3-4, smoker, ≥2 exacerbatons per year, sedentary |
| 17 | 5-6 | no | <2 | >50 0 | = | Bode 5-6, not a smoker, <2 exacerbatons per year, active |
| 18 | 5-6 | no | <2 | <50 0 | = | Bode 5-6, not a smoker, <2 exacerbatons per year, sedentary |
| 19 | 5-6 | no | ≥ 2 | >50 0 | = | Bode 5-6, not a smoker, ≥2 exacerbatons per year, active |
| 20 | 5-6 | no | ≥ 2 | <50 0 | = | Bode 5-6, not a smoker, ≥2 exacerbatons per year, sedentary |
| 21 | 5-6 | yes | <2 | >50 0 | = | Bode 5-6, smoker, <2 exacerbatons per year, active |
| 22 | 5-6 | yes | <2 | <50 0 | = | Bode 5-6, smoker, <2 exacerbatons per year, sedentary |
| 23 | 5-6 | yes | ≥ 2 | >50 0 | = | Bode 5-6, smoker, ≥2 exacerbatons per year, active |
| 24 | 5-6 | yes | ≥ 2 | <50 0 | = | Bode 5-6, smoker, ≥2 exacerbatons per year, sedentary |
| 25 | 7-10 | no | <2 | >50 0 | = | Bode 7-10, not a smoker, <2 exacerbatons per year, active |
| 26 | 7-10 | no | <2 | <50 0 | = | Bode 7-10, not a smoker, <2 exacerbatons per year, sedentary |
| 27 | 7-10 | no | ≥ 2 | >50 0 | = | Bode 7-10, not a smoker, ≥2 exacerbatons per year, active |

| | | | | | | |
|-----------|------|-----|-----|----------|---|---|
| 28 | 7-10 | no | ≥ 2 | <50 0 | = | Bode 7-10, not a smoker, ≥2 exacerbations per year, sedentary |
| 29 | 7-10 | yes | <2 | >50 0 | = | Bode 7-10, smoker, <2 exacerbations per year, active |
| 30 | 7-10 | yes | <2 | <50 0 | = | Bode 7-10, smoker, <2 exacerbations per year, sedentary |
| 31 | 7-10 | yes | ≥ 2 | >50 0 | = | Bode 7-10, smoker, ≥2 exacerbations per year, active |
| 32 | 7-10 | yes | ≥ 2 | <50 0 | = | Bode 7-10, smoker, ≥2 exacerbations per year, sedentary |

Table 3-III. The Patients' Phenotypes

The third logical step corresponds to the deduction of CHRONIOUS Card Score that is evaluated according to data coming from devices and from the questionnaires, as synthesized in the Table 3-IV.

| CHRONIOUS Card Scores | | | | | |
|-------------------------------|------------------------------|---------------------------------|---|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Dyspnoea | Under strong activity | Speed walk or climb | Moderate activity with stops | Light activity, stop after few steps | At rest during daily activities |
| Cough | Spontaneous and strong | Weak, not productive | Strong but extremely productive | Weak, productive, frequent | No spontaneous cough; need for suction |
| Sputum | No need for sputum | Moderate | Copious | Very copious | Unbearable |
| Sputum Colour | No sputum | white | Yellow | Yellow/green | Green/brown or with blood |
| Wheeze | Never | Occasional | Under strong efforts | Under moderate efforts | At rest |
| Ventilator Interaction | No troubles or no ventilator | Occasional alarms on ventilator | Alarms and need for suction, or mask discomfort | Alarms, occasional contrasts and dyspnoea under ventilator | Ventilator break; alarms and fighting against ventilator |
| Walk | Autonomous | Walk with stops, no dyspnoea | Walk with stick and dyspnoea | Assisted walk, few steps, armchair use | No deambulation, bedridden |

| | | | | | |
|---|--------------------------------|---------------------------------------|----------------------------------|---|----------------------------------|
| Body temperature (T) | Normal | >37°C and <37.5°C without antipiretic | >37°C and <38°C with antipiretic | >38°C with antipiretic and antibiotic for 1 day | >38°C with antibiotic for 3 days |
| Weight | Stable weight, no ankle oedema | Increase of <2Kg in 2 days | 2-4Kg in 2 days | 2-4Kg in 1 day | >4Kg in 1 day |
| Heart Rate (HR) | <90 BPM | 90-100 BPM | 100-110 BPM | 110-120 BPM | >120 BPM |
| ECG | regular | extrasystols | atrial fibrillations | atrial flutter | ventricular arrhythmia |
| Arterial Pressure (systolic) | 120 | 120-140 | 140-160 | 140-160 | >190 |
| Arterial Pressure (diastolic) | 70 | 70-90 | 90-100 | 100-110 | >110 |
| SpO2 | >92% with room air and O2 | 91% with air and 90-92% with O2 | <90% with room air | <90% with O2 | <80% with O2 |
| Respiratory Frequency (f) | <14 | 14-16 | 16-20 | 20-25 | >25 |
| Inspiratory Time (Ti) | 1.6-1.8 | < 1.6 > 1.20 | < 1.2 > 1.0 | > 0.80 < 1.0 | <0.80 |
| Expiratory Time (Te) | 3.0-3.4 | < 3 > 2.5 | < 2.5 > 2.0 | < 2.0 > 1.60 | <1.60 |
| Respiration Asynchrony (LBI mean value in the last 30mins) | 1.0 | 1.2 | 1.4 | 1.6 | 1.8 |
| (Resp. Freq.)/(tidal volume) = f/Vt | <80 | 80-95 | 95-110 | 110-120 | > 120 |
| Minute Ventilation (Ve) | <12 > 10 | < 10 | < 8 | < 7 | < 6 |
| Patient Activity (steps num. per day) | >2000 | < 2000 > 1800 | < 1800 > 1000 | < 1000 > 500 | <500 |
| Coughs Counter (n/min) | 0 | <2 | <10 | <15 | >15 |
| Ambient Temperature | 22°C | 24-26°C | 26-28°C | 28-30°C | >30°C |
| Ambient Humidity | 50% | 40% or 60% | 30% or 70% | 20% or 80% | <20% or >80% |

| | | | | | |
|--|---------|--------------|----------------------|----------------------|------------------------------|
| Patient Position (supine) h | < 8 | > 8 < 10 | > 10 <15 | >15 <18 | > 18 |
| Sleep Quality (N° position changes/h) | <10 | > 10 < 15 | > 15 < 25 | 25-30 | > 30 |
| sleep quality (questionnaire) | optimal | good | sufficient | bad | very bad |
| Do you feel tired? (asthenia) | never | occasionally | after light activity | after heavy activity | for the most part of the day |
| Age | <55 | >55 and <60 | >60 and <70 | >70 and <75 | >75 |
| Depressive Phenotype (HAD) | Never | sometimes | frequent | very frequent | pathological |

Table 3-IV. The CHRONIOUS Card Scores

Obviously, the total score is calculated by adding the different partial scores associated to each monitoring parameter and each questionnaire answer, and weighting them according to what suggested by the clinicians for each phenotype.

Since the total score for the CHRONIOUS Card can reach a maximum value of 44 whereas the total score for the RespiCard is 48, we have rearranged the stage ranges proportionally, i.e. 0-15, 16-34, 35-99, 100-120, according to the Medical Board.

In the following, the rules devised to generate suggestions depending on the total score are reported. Their representation is reported in the table shown in the next Fig. 3.12:

| Antecedents | | Consequents | | |
|--------------------|----------------|--------------------|-------------------|----------------|
| Description | Inferred Stage | Suggested Action | Patient Condition | Alert Severity |

| | | | | |
|---------------------------|---|--|----------|-------|
| totalscore <=15 | 1 | CHRONIOUS Card – Questionnaire and monitoring measurement – Normality – CHRONIOUS Card score between 0 and 15 | | |
| 16<=totalscore<=34 | 2 | CHRONIOUS Card – Questionnaire and monitoring measurement – Normality – CHRONIOUS Card score between 16 and 34 | | |
| 35<=totalscore<=99 | 3 | CHRONIOUS Card – Questionnaire and monitoring measurement – Normality – CHRONIOUS Card score between 35 and 99 | | |
| totalscore>=100 | 4 | CHRONIOUS Card – Questionnaire and monitoring measurement – Normality – CHRONIOUS Card score between 100 and 120 | | |
| stage < previous_stage | | No advice | Worse | Red |
| stage = previous_stage | | No advice | Stable | White |
| stage > previous_stage | | No advice | Improved | White |

Fig. 3.12. Rules for generating suggestions depending on the total score of the CHRONIOUS Card

We synthesize here minor incongruence found in the RespiCard for body temperature scores:

- . >37 and <37.5 without antipiretics
- . >37.5 and <38 with antipiretics
- . (>37 with antipiretics? >=37.5!)
- . >38 with antibiotics for 1 day (=38? >=38!)
- . >38 with antibiotics for 3days (=38? >=38!)

Finally, according to the Medical Board, another rule has been added for the usage scenario of *Home Monitoring*, as shown in the following Fig. 3.13.

| Antecedents | | Consequents | | |
|--|----------------|--|-------------------|----------------|
| Description | Inferred Stage | Suggested Action | Patient Condition | Alert Severity |
| <i>exacerbation of symptoms since 2 days</i> | | <i>visiting the patient is suggested since the patient refers exacerbation since at least 2 days</i> | | <i>Red</i> |

Fig. 3.13. An additional rule for the usage scenario of *Home Monitoring*

COPD: Clinical Assessment

COPD guidelines formalized for the usage scenario of Clinical Assessment reported in section 2.2.1 are aimed at evaluating the patient's severity stage depending on spirometry and arterial blood gas analysis. They can be synthesised as follows:

- Stage I: mild COPD: Characterized by mild airflow limitation ($FEV_1/FVC < 0.70$, $FEV_1 \geq 80\%$ predicted). Symptoms of chronic cough and sputum production may be present, but not always. At this stage, the individual is usually unaware that his or her lung function is abnormal.
- Stage II: moderate COPD: Characterized by worsening airflow limitation ($FEV_1/FVC < 0.70$, $50\% \leq FEV_1 < 80\%$ predicted), with shortness of breath typically developing on exertion and cough and sputum production sometimes also present. This is the stage at which patients typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease.
- Stage III: severe COPD: Characterized by further worsening of airflow limitation ($FEV_1/FVC < 0.70$, $30\% \leq FEV_1 < 50\%$ predicted), greater shortness of breath, reduced exercise capacity, fatigue, and repeated exacerbations that almost always have an impact on patients' quality of life.
- Stage IV: very severe COPD: Characterized by severe airflow limitation ($FEV_1/FVC < 0.70$, $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus the presence of chronic respiratory failure). Respiratory failure is defined as an arterial partial pressure of O_2 (Pa_{O_2}) less than 8.0 kPa (60 mm Hg), with or without an arterial partial pressure of CO_2 (Pa_{CO_2}) greater than 6.7 kPa (50 mm Hg) while breathing air at sea level. Respiratory failure may also lead to effects on the heart such as cor pulmonale (right heart failure). Clinical signs of cor pulmonale include elevation of the jugular venous pressure and pitting ankle edema. Patients may have stage IV COPD even if their FEV_1 is greater than 30% predicted, whenever these complications are present. At this stage, quality of life is very appreciably impaired and exacerbations may be life threatening.

Their representation in rules is reported in the following Fig. 3.14:

| Antecedents | | Consequents | | |
|--|----------------|---|-------------------|----------------|
| Description | Inferred Stage | Suggested Action | Patient Condition | Alert Severity |
| <i>FEV1 / FVC is less than 0.7 and FEV1 less than 30% predicted</i> | 4 | | | |
| <i>FEV1 / FVC is less than 0.7 and FEV1 less than 50% predicted plus chronic respiratory failure</i> | 4 | | | |
| <i>FEV1 / FVC is less than 0.7 and FEV1 greater than or equal 30% predicted and FEV1 less than 50% predicted</i> | 3 | | | |
| <i>FEV1 / FVC is less than 0.7 and FEV1 greater than or equal 50% predicted and FEV1 less than 80% predicted</i> | 2 | | | |
| <i>FEV1 / FVC is less than 0.7 and FEV1 greater than or equal 80% predicted</i> | 1 | | | |
| <i>stage < previous stage</i> | | <i>Contact the patient since his/her stage is worse</i> | <i>Worse</i> | <i>Red</i> |
| <i>stage = previous stage</i> | | <i>no advice</i> | <i>Stable</i> | <i>White</i> |
| <i>stage > previous stage</i> | | <i>no advice</i> | <i>Improved</i> | <i>White</i> |

Fig. 3.14. Rule representation of the guidelines regarding the usage scenario of Clinical Assessment

COPD: Alarm Checking

COPD guidelines formalized for the usage scenario of Alarm Checking reported in section 2.2.1 can be synthesized in natural language as follows:

- COPD_Guideline_Alarm_Checking_1 – Respiratory Failure
All individuals with values of $spO_2 < 88\%$, heart rate > 100 beats/min, and respiratory rate > 24 are assumed as being in an abnormal condition due to suspected Acute Respiratory Failure. An alert with red severity code is contextually sent to the medical doctor to report the situation.

Their representation in rules is reported in the following Fig. 3.15:

| Antecedents | | Consequents | |
|---|-----------------------------|----------------------------------|----------------|
| Description | Suggested Action | Patient Condition | Alert Severity |
| <i>spO2_curr < 88 and heartRate_curr >100 and respiratoryRate_curr >24</i> | <i>Alert Medical Doctor</i> | <i>Acute Respiratory Failure</i> | <i>Red</i> |

Fig. 3.15 Rule representation of the guidelines regarding the usage scenario of *Clinical Assessment*

All the other rules for the detection of relevant symptoms of an *Arterial Hypertensive Crisis* an *Abnormal Heart Rhythm*, and *Tachycardia* or *Bradycardia* are encoded.

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5 LIST OF ABBREVIATIONS

| | |
|---|-------|
| COPD: Chronic Obstructive Pulmonary Disease | 3, 38 |
| DB: DataBase..... | 36 |
| DH: Data Handler | 37 |
| DSS: Decision Support System | 3 |
| FEV1: Forced Expiratory Volume in the first second | 62 |
| GOLD: the Global Initiative for Chronic Obstructive Lung Disease..... | 52 |
| GP: General Practitioner | 12 |
| GUI: Graphical User Interface | 38 |
| HPM: Home Patient Monitor | 37 |
| ICT: Information and Communication Technologies | 29 |
| KBE: Knowledge Base Editor | 33 |
| kPa: kiloPascal | 62 |
| NICE: National Institute for Clinical Excellence..... | 52 |
| PaCO ₂ : partial pressure of carbon dioxide | 62 |
| PaO ₂ : partial pressure of oxygen in arterial blood | 62 |
| PDA: Personal Digital Assistance..... | 31 |