Comorbidities Modeling for Supporting Integrated Care in Chronic Cardiorenal Disease

E. Kaldoudi and N. Dovrolis

School of Medicine, Democritus University of Thrace, Alexandroupoli, Greece

Abstract—**This paper presents work towards constructing a generic information model for comorbidities management. This involves the following conceptual steps: (a) develop an information model and ontology of the management of disease and comorbidities based on ground medical knowledge; (b) enrich the generic model to reflect current-state-of-the-art medical evidence, which will determine in detail the connections and conditions for such connections for comorbid progression pathways; (c) instantiate the enriched model for each specific patient, coupling patient personal information of a variety of sources. The model is based on the UMLS semantic network. Our specific aim is to address the medical domain of cardio-renal disease and comorbidities. The ultimate goal is to provide the means for patients with comorbidities to take an active role in care processes, including self-care and shared decision making, and also to support medical professionals in understanding and treating comorbidities via an integrative approach.**

Keywords—**comorbidity management, information modeling, medical ontologies.**

I. INTRODUCTION

Comorbidity refers to the presence of one or more disorders in addition to a primary disease or disorder (either independently, or as a consequence of the primary condition or otherwise related) [1]. As approximately half of all patients with chronic conditions, even in a nonelderly population, have comorbidities [2], comorbidity management is a hot topic in current medical literature [3,4]. When addressing disease in the presence of comorbidities, each different medical condition the patient presents should not be viewed independently, but a "patient as a whole" view approach should be followed [5]. This places an emphasis on and extra burden of dealing successfully with all associations, interactions, co-dependencies, implications, adverse events, etc. that occur between different conditions co-presenting at the same patient at the same time, as well as between the different treatment regimens these conditions involve.

Our work aims at developing the technological infrastructure for understanding and managing disease progression pathways and comorbidities trajectories and their dynamics, enriched with up-to-date medical evidence and personalized for the individual patient. This involves the following conceptual steps: (a) develop an information model and ontology of the management of disease and comorbidities based on ground medical knowledge; (b) enrich the generic model to reflect current-state-of-the-art medical evidence, which will determine in detail the connections and conditions for such connections for comorbid progression pathways; (c) instantiate the enriched model for each specific patient, coupling patient personal information of a variety of sources, including medical patient data demographics, general medical status, physiological and activity related real-time signals, information on personal intention, mood, preferences, lifestyle, travel planning, etc. The ultimate goal is to employ the personalized model of comorbidities for shared decision support services targeting personalized education, complex risk calculation for disease progression and comorbidity trajectories, alerts for adverse events of multiple co-existing treatments and personalized planning for monitoring

In this paper we present initial work towards constructing a generic information model for comorbidities. Our specific aim is to address the medical domain of cardio-renal disease and comorbidities as this is a very common, life threatening and costly condition and because it also presents a number of challenges and opportunities for the demonstration of comorbidities patient empowerment and management.

II. BACKGROUND

Chronic cardiorenal disease is the condition characterized by simultaneous kidney and heart disease while the primarily failing organ may be either the heart or the kidney. Very often the dysfunction occurs when the failing organ precipitates the failure of the other. The cardio-renal patient (or the person at risk of this condition) presents an interesting case example for addressing and demonstrating novel patient empowerment services for personalized disease & comorbidities management and prevention for a number of reasons as chronic cardiorenal disease has an increasing incidence and a number of serious (and of increasing incidence) comorbidities.

One of the most important aspects of cardiorenal disease and comorbidities diagnosis and treatment is early detection and aggressive management of underlying causes. Preventing progression to end stage renal and cardiac deficiency may improve quality of life and help save health care costs.

Prevention of the disease includes: lifestyle modification (controlling obesity, diabetes and hypertension), public-health education for reduction of excessive bodyweight, regular exercise, and dietary approaches, control of hypertension, dietary protein restriction and blood-pressure control, proteinuria management, dyslipidaemia management and smoking cessation. Delaying disease progression is crucial and must include patient education and aggressive treatment and management of chronic cardiorenal disease and its comorbidities [6]. However, effective implementation of such strategies will only come when both the general public and the renal community work together towards public awareness and lifestyle management on a personal basis and following an integrated care approach. The notion of integrated care is a central issue in the domain of healthcare. Integrated care has many meanings [7]; the notion of "re-unite parts of a whole" is an underlying commonality, whether integration refers to integration within different healthcare settings or in terms of integration of healthcare, social care, long-term and self-care or even integration of patient management for different conditions. In any case, a patient-centered bottom-up approach is favored [7].

The etiology of comorbidity in relation to the risk factors associated with individual diseases led clinical researchers to propose 13 clinical models of comorbidity (including risk factors) [8,9]. These models formalize the process of risk factors affecting one or more comorbid diseases, the diseases themselves affecting each other in various degrees and even signifying the presence of another previously unrelated condition that plays a significant role. A simplified approach summarizes comorbidity in 5 etiological models [10]:

1. No etiological association between coexisting diseases (the "luck" factor)
2. Direct causation: one of the diseases may cause the others;
3. Associated risk factors: the risk factors for each disease are correlated;
4. Heterogeneity: the risk factors for each disease are not correlated but each one of them can cause either disease;
5. Independence: the presence of the diagnostic features of each disease is actually due to a different distinct disease.

Although a lot of work has been conducted towards a common understanding and integration within the healthcare enterprise, as presented by a recent thorough healthcare standards review [11] a "semantic gap" is revealed. This gap mainly refers to (a) the still missing semantic integration of the personal environment of the patient; (a) the lack of integration amongst clinical guidelines addressing individual medical conditions; and (c) the lack of modeling medical context in an integrative approach.

Many approaches have been proposed for the modeling and management of information in healthcare. One of the common approaches relies on traditional database modeling principles, explicitly representing information that is required to be in the relevant biomedical domain [12]. The other approach [13] is based on ontology modeling, which provides semantic descriptions of the concepts used in the healthcare field under study. The semantic descriptions facilitate the integration and interoperation of independent datasets and applications. Data sources are represented using additional (mediator) layers that can expose the sources in terms of domain ontology, following a local-as-view approach to data integration [14]. The scalability of this viewpoint largely depends on the effort required to create the domain ontology. Some initiatives build it anew [13], while others try to reuse as much as possible [14].

The aim of the work presented here is to use the clinical models of comorbidity in order to create an information model that connects comorbid diseases with their respective risk factors and symptoms, weighing their influence on each other and on the patient's health.

III. TOWARDS A MODEL FOR ADDRESSING COMORBIDITIES

The health environment for the patient and/or the healthy citizen comprises of various coexisting and strongly inter-linked entities: (a) individuals, including patients, healthy citizens and healthcare professionals; (b) organizations, including any institutional or organizational entity involved in any way in the healthcare process, e.g. healthcare providers, social services, health insurances, medical research institutions, research projects, pharmaceutical companies, well-being and fitness clubs, etc.; (c) health conditions, i.e. any health or medical condition; and (d) health interventions, including interventions on diet, life-style, therapy and drugs, supporting devices, etc.

The UMLS (The Unified Medical Language System, http://www.nlm.nih.gov/research/umls/) semantic network [15] concepts and relationships have been used a basis for developing the proposed model. This network has 135 semantic types and 54 relationships, and covers with these effectively all concepts and connections in the healthcare domain. The Unified Modeling Language (UML) version 2.4.1 has been used for this work (http://www.uml.org).

The proposed model presented here focuses on health conditions and their inter-relations in the case of comorbidities. In terms of modeling, risk factors and diseases in the case of comorbidity can be viewed as subclasses of the same superclass named 'condition'.

Table 1 Building blocks of the proposed model

Model Entity	UMLS SN Term
Disease	Disease or Syndrome
Risk Factor	Qualitative Concept
Symptom	Sign or Symptom

A condition is a UMLS semantic type 'event'. It is mainly characterized by a start and end times (or groups of such when more than one episode occur). A condition may can be managed (i.e. diagnosed and/or treated) via clinical protocols, that contain a series of diagnostic and therapeutic procedures.

Finally, a condition may be caused by and may cause other conditions. This casual association is subject to one or more factors (referred to as Evidence Reference Values) as described by dynamically changing medical evidence. Such an evidence reference value may have one more value ranges and the likelihood attached to them of causing one or more conditions. The class diagram picturing the above is given in Fig 1.

Table 2 Relationships between model entities

Entities Involved	UMLS SN Relationship
Disease - Diseases	Precedes, co-occurs with, result of, affects, associated with, temporally related to, causes, degree of
Risk Factor – Risk Factor	Co-occurs with, complicates, Evaluation of, issue in, result of, affects, causes, degree of
Risk Factor - Disease	

The generic entity "condition" refers both to a disease as well as a risk factor and is modeled as a parent class. The main entities 'disease' and 'risk factor' and their respective UMLS semantic network types are shown in Table 1. The main relationships between these entities and their corresponding UMLS semantic network associations are listed in Table 2.

Risk factors can be of a general nature and can be traced for every possible disease/disorder. Genetics, demography, life style, social and physical environment all affect a person's health in specific ways. Even more specific ones like biological or medical factors contribute to the onset and course of diseases. Thus, in terms of modeling risk factors correspond to a variety of UMLS semantic network entities as shown in Table 3.

Table 3 Risk factors and their respective UMLS SN Terms

Risk Factor	UMLS SN Term
Genetics	Genetic Function, Family Group
Demography	Age Group, Geographic Area
Lifestyle (e.g. smoking, drinking, nutrition, activity)	Social Behavior, Daily or Recreational Activity, Occupational Activity
Environmental (e.g. air pollution)	Environmental Effect of Humans, Hazardous or Poisonous Substance
Biological risk factor (e.g. gender, cholesterol, obesity)	Organism Attribute, Immunologic Factor,
Health care	Health Care Activity

Based on the above, the five different clinical models of comorbidity can be described in the activity diagram shown in Fig 2.
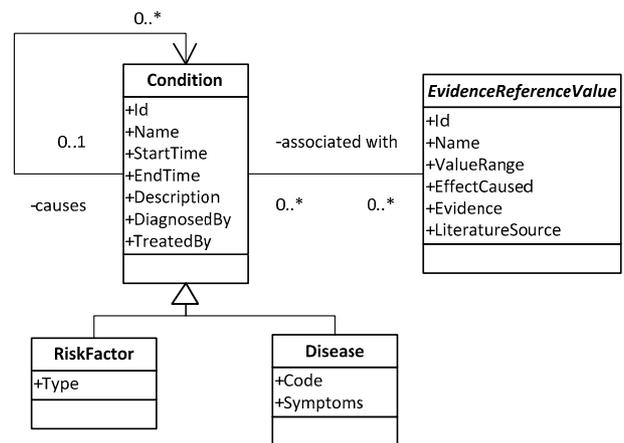

Fig. 1 A simplified class diagram of condition and sub-classes.

IV. CONCLUSIONS

The work presented here addresses comorbidity management via an information model based on standardized technologies in healthcare. The model is expected to allow for semantic interlinking of three types of data (a) medical ground knowledge (b) up-to-date medical evidence and (c) personal patient data in order to create a personalized model of the disease and comorbidities progression pathways and trajectories. Finally, the personalized model of comorbidities will be used for shared decision support services targeting personalized education, complex risk calculation for disease progression and comorbidity trajectories, alerts for adverse events of multiple co-existing treatments and personalized planning for monitoring.

The ultimate goal is to use this personalized model of comorbidities in order to provide the means for patients with comorbidities to take an active role in care processes, including self-care and shared decision making, and also to support medical professionals in understanding and treating comorbidities via an integrative approach.
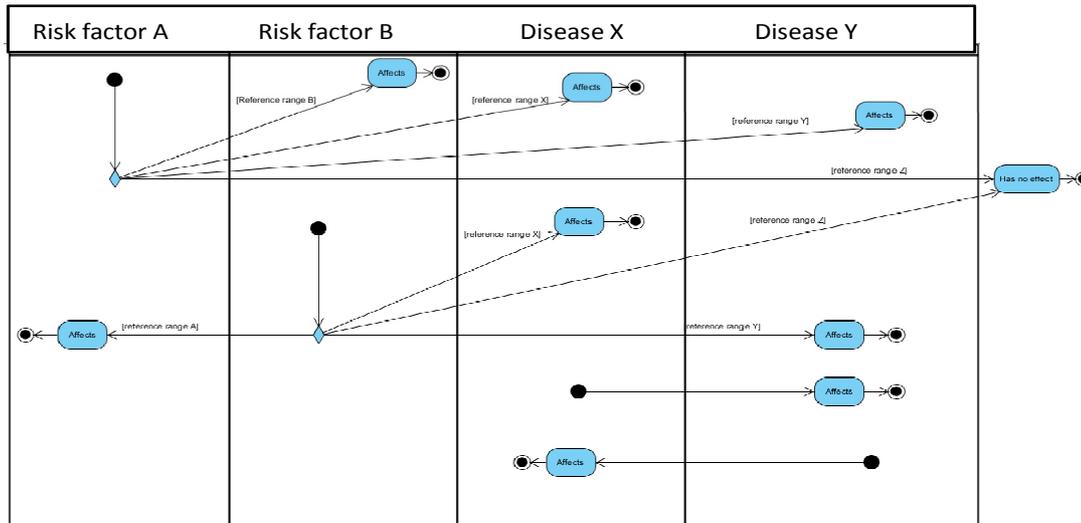

Fig. 2 An activity diagram of the 5 clinical models of comorbidity.

REFERENCES

1. Akker M van den, Buntix F, Knottnerus JA (1996) Comorbidity or multimorbidity: what's in a name? Eur J Gen Pract, 2:65-70
2. Starfield B, Lemke KW, Bernhardt T et al. (2003) Comorbidity: implications for the importance of primary care in 'case' management. Ann Fam Med. 1:8-14
3. Barnett K, Mercer SW, Norbury M et al. (2012) Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 380:37-43
4. Tinetti ME, Fried TR, Boyd CM (2012) Designing healthcare for the most common chronic condition: multimorbidity. JAMA 307:2493
5. Nagarajan V, Tang WH (2012) Management of comorbid conditions in heart failure: a review. Med Clin North Am 96: 975-85
6. Khwaja A, Kossi M El, Floege J et al (2007) The management of CKD: a look into the future. Kidney Int 72:1316-23
7. Kodner DL, Spreeuwenberg C (2002): Integrated care: meaning, logic, applications, and implications – a discussion paper. Int J Integrated Care 2:e12
8. Neale, M.C., Kendler, K.S. (1995) Models of comorbidity for multifactorial disorders. American journal of human genetics 57, 935.
9. Klein, D. N., & Riso, L. P. (1993). Psychiatric disorders: problems of boundaries and comorbidity.
10. Valderas, J.M., Starfield, B., Sibbald, B., Salisbury, C., Roland, M.(2009) Defining Comorbidity: Implications for Understanding Health and Health Services. Ann Fam Med 7, 357–363.
11. Lenz R, Beyer M, Kuhn KA (2007) Semantic integration in healthcare networks, Int J Med Inform 76:201-207
12. Elger BS, Ianvindrasana J, Iacono LL et al (2010) Strategies for health data exchange for secondary, cross-institutional clinical research. Comput Methods Programs Biomed 99:230-51
13. Tsiknakis M, Brochhausen M, Nabrzyski J et al (2008) A semantic grid infrastructure enabling integrated access and analysis of multilevel biomedical data in support of post-genomic clinical trials on Cancer. IEEE Trans Inf Tech Biomed 12:205-17
14. Lenzerini M. (2002) Data integration: a theoretical perspective. ACM SIGMOD-SIGACT-SIGART p. 233-246
15. National Library of Medicine (2009) Chapter 5 - Semantic Networks. UMLS Reference Manual. Bethesda, MD: U.S. National Library of Medicine, National Institutes of Health.

Corresponding Author:

Eleni Kaldoudi
School of Medicine, Democritus University of Thrace
University Campus, Dragana
Alexandroupoli 68100, Greece
kaldoudi@med.duth.gr