Ef-Zin: A hybrid framework for ubiquitous management of comorbidity and multimorbidity in chronic diseases.

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Abstract—The existence of comorbidity and multimorbidity increases the diagnostic uncertainty and has a variety of negative social and economical impacts. This paper proposes the Ef-Zin framework that aims to manage patients suffering from chronic conditions by means of (a) creating collaborative virtual groups through medical and paramedical professionals and (b) delivering the appropriate therapy to the individual patient. Ef-Zin involves two distinct processing phases for parallel evaluation of patient's contextual information. For the evaluation it uses rule-based algorithms and Random Forest (RF) machine learning technique for categorizing patients into groups according to the severity levels, making decisions about the services that will be delivered and notifying the appropriate specialized healthcare professionals for patient's current health status. We have carefully drafted an architecture of the proposed Ef-Zin framework and qualitative evaluation has been conducted in a common use case scenario such as Chronic Obstructive Lung Disease (COPD) and a cardiovascular disease (hypertension) that is the most frequent and significant disease that coexists with COPD.

I. INTRODUCTION

Comorbidity and multimorbidity is very common in the population suffering from chronic diseases. The existence of comorbidities or multimorbidities increases progressively with the age and the existence of a chronic disease [1]. Currently, 125 million persons in the United States suffer from chronic medical conditions while 60 million of them have multiple chronic conditions either comorbidities or multimorbidities. These numbers are expected to increase to 157 million and 81 million respectively, by the year 2020, with a percentage of 95% for adults over 65 years [2]. As a consequence, the existence and effects of comorbidities and multimorbidities are usually a reality in chronic diseases and affects a huge portion of patients. The most significant and vital impact of comorbidities and multimorbidities is the diagnostic uncertainty that causes negative effects in patient's life. Individuals with comorbidities or multimorbidities register a higher mortality and hospital admissions rate, occasion higher healthcare costs [1] and reduce of patient's quality of life.

In response to the emerging challenges posed by comorbidities and multimorbidities, it becomes significant to provide enhanced patient-centric care models which involve collaboration among professions and institutions that have traditionally been separate. These enhanced patient-centric

models aim to provide functionalities for automatic managing and delivering personalized healthcare services. These automated systems aim to have potential benefits to (a) healthcare professionals that can cooperate with each other so as to inform patients about their health severity and therapeutic treatment (b) patients by increasing their quality of life and independency as well as (c) society through the reduce of healthcare costs.

There is a variety of commercial solutions and research efforts related to telemedicine, monitoring, management and assistance to patients suffering from chronic diseases. All these studies [3-6] focus on analyzing extensively the guidelines and reference models for the importance of the management systems. Recently, some works have performed high-level analysis and conceptual design in the field of managing chronic conditions and preventing exacerbations [7-9]. Nevertheless, all these research efforts are oriented toward an acute, episodic care model and there is a lack of meeting the challenges posed by the the long-term and fluctuating needs of patients' suffering from comorbidities and multimorbidities. Additionally, there is a lack of bridging the boundaries between healthcare professionals that belong to different providers and institutions.

Research and literature studies into multimorbidity and comorbidity fields are limited. Most of these studies analyze the risk factors, the intense of these risk factors into the chronic disease and the number of the comorbidities and multimorbidities that may exist in correlation with the age and sex through statistic tools [2]. In study [10], a chronic disease is assessed using the Elixhauser comorbidity measure that is associated with comorbidity affected outcomes such as hospitalization and mortality.

This paper proposes the Ef-Zin framework that provides a more coordinated and integrated approach in order to increase patients' quality of life by delivering personalized services at any time and whenever the patient and doctors are located. Ef-Zin is a hybrid framework based upon the functionality of: (a) the CDME module of the NG-SDP platform [6] that uses rule-based algorithms for evaluating vital bio-signs and making decisions about the existence and the severity level of a disease as well as (b) the u-MCHC [9] predictive model that is based on the Random Forest (RF) machine learning technique for the detection and prediction of exacerbation risks. For the appropriate delivery of services the output of the Ef-Zin framework triggers the P2Care network [11] that establishes collaboration through healthcare professionals with the appropriate expertise for patient's current conditions. Finally, the effectiveness of Ef-Zin is evaluated.

The rest of the paper is organized as follows: in section II the system overview and the proposed Ef-Zin architecture are described. Additionally, in the section III the implementation details and a qualitative evaluation of the proposed Ef-Zin framework is presented and discussed.

II. EF-ZIN FRAMEWORK

Patients that suffer from several diseases usually experience aggravation of one disease by treatment of another [1]. Under this restriction, Ef-Zin is developed as a hybrid framework that aims to manage patients through a collaborative environment of specialized healthcare professional and delivery of the personalized therapeutic services to the individual patient. Its hybrid functionality involves two distinct phases of acquisition and interpretation. The first phase includes measurement analysis and evaluation of the vital bio signals while the second phase involves correlation of these values with other contextual information and parameters so as to identify the patient's health status.

A. System Overview

Fig. 1 shows the salient components of the system. The ubiquitous patient's environment is composed of many sensors, devices and applications that are used for monitoring patient and providing information about his context.
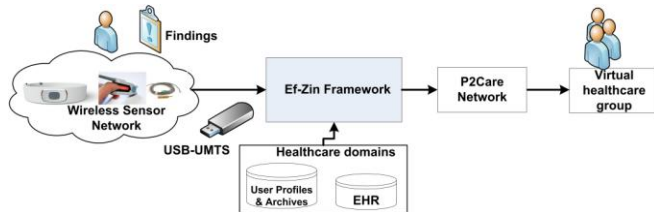

Figure 1. System overview.

The Ef-Zin framework interprets and evaluates the collected contextual information by means of rule based and probabilistic reasoning so as to determine the intensity of symptoms, the diseases that may exist, their severity and their impact on patient's health status. In case of diseases that are evolving quickly in time and jeopardize life (i.e. diabetes, congestive heart failure, etc), the risk of exacerbation or hospitalization is calculated. According to the results of the evaluations, a message is generated by an alarm system with the appropriate services and the healthcare professionals that ought to be triggered.

B. Ef-Zin Architecture

The Ef-Zin has been developed as a general-purpose framework and it is easily extensible and scalable for a variety of healthcare scenarios in the eHealth domain. Fig. 2 depicts the architecture of the Ef-Zin framework.

Context Acquisition Module (CAM) (a) gathers the physiological and non physiological data from sensors and bio-sensors (Fig. 2, step 1a) (b) retrieves contextual information from User Profiles and Electronic Health Records (EHRs) (Fig. 2, step 1b) that are located into the healthcare providers and (c) forwards the collected contextual data into the Decision Making Module (DMM) for evaluation purposes. Additionally, the data is stored temporarily into to a database named Context DataBase for recovery purposes.
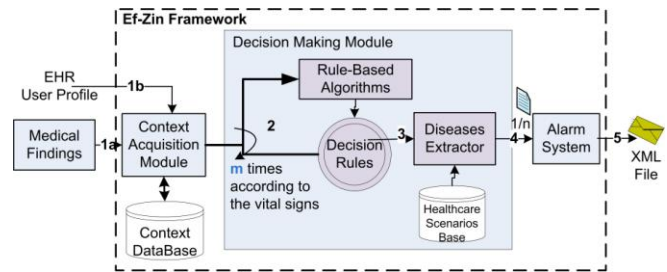

Figure 2. Ef-Zin Framework Architecture

Decision Making Module (DMM) creates the patient's current health status. It evaluates, processes, interprets and integrates acquired information by CAM. The DMM involves two distinct phases. The *first phase* involves parallel analysis of the m series data from the sensors that are vital for someone's life (i.e. heart rate, blood pressure, pulse arterial blood oxygen saturation, pulse rate, etc) based on rule based algorithms. Each disease is represented by different indications; as a consequence, analysis is made by comparing each output value of the m sensor's readings with predefined threshold values. The results of the analysis indicate the divergence of the physiological values of measurements and determine the existence probability of a disease. In this first phase alarm(s) is/are generated with the non physiological values and the actions that will be activated. Nevertheless, the isolated values of a measurement are not certain indications of a disease. The existence, the severity and the impact of a disease in patient's health status are calculated in correlation with environmental parameters and patients' primitive contextual data (i.e. EHR, user's profile, etc). This consists the *second phase*. DMM uses Random Forest (RF) machine learning techniques in order to categorize the severity level of the diseases, the exacerbation risk and calculate the current patient's health status (Fig. 2, step 2). The patient's current health statuses are processed by the Disease Extractor (Fig. 2, step 3) which identifies the number and the type of diseases, and matches type of diseases with healthcare roles through a Healthcare Scenarios Base. An XML event message is created (Fig. 2, step 4) with the delivering services and the appropriate medical and paramedical professionals for treating patient's current health status.

Alarm Module is a notification system that triggers and forwards the XML file to the P2Care network [15]. P2Care Network (i) finds binds and invokes the most available specialized professionals and (ii) establishes a session between them in order to cure patient (Fig. 2, step 5).

At the end of the whole process, the collected information into the Context DataBase is forwarding into the University Hospital and is integrated with the patient's history into User's Profile and EHR for data enhancement.

III. IMPLEMENTATION AND EVALUATION

For the development of the Ef-Zin, we thoroughly studied the COPD disease in conjunction with hypertension and diabetes. Hypertension is likely to be the most frequently occurring comorbidity in COPD and its existence has significant implications [2, 12]. Moreover, hypertension and diabetes are strictly correlated with each other and its existence demands immediate collaboration between

specialists in order to provide efficient therapy without unnecessary hospital admission or aggravation in patient's life. Usually in a COPD patient, hypertension (comorbidity) is more crucial for patient's life and should be treated with high priority. Nevertheless, in case of diabetic patient (multi-comorbidity), the therapeutic guidelines and the blood pressure thresholds are not the predefined. In order to validate the effectiveness and diagnosis certainty of Ef-Zin framework, trials have been conducted in cooperation with specialists of the Pulmonary Department and the Department of Emergency Medicine, Rion University Hospital.

A. System set up

Wearable and ambient sensor technologies have been used to enable seamless monitoring of vital bio-signals. These sensors do not require any interaction with the patients and the healthcare professionals. All sensors are transferring their data wirelessly to the Ef-Zin. In order to achieve adaptation with the sensors into the patient's ubiquitous environment we use a USB-UMTS adapter. For the evaluation we used the portable devices: pulse oximeter, accelerometer, body temperature sensor, airflow sensor, blood pressure sensor and an electrocardiograph ECG. Moreover, a web human-friendly interface was implemented in PHP which allows (a) patients to log in, be monitored and submit questionnaires as well as (b) healthcare professionals to provide their availability and location, find, bind and invoke collected data or information (i.e. EHR, profile). The provided data for processing is stored in a MySQL database.

B. Context Acquisition Module (CAM)

The patient has being monitored on a daily basis two times per day (morning and afternoon). For the evaluation of hypertension, the value of blood pressure sensor by means of systolic and diastolic pressure is used. Nevertheless, the hypertension usually coexists with other diseases [1, 2, 16] such as cardiovascular diseases (coronary heart disease, stroke, kidney failure, etc) and diabetes introduce errors in the evaluation of systolic and diastolic pressure putting in danger patient's life. For this reason, the number of the cardiovascular risk factors (i.e. obesity, smoking, diabetes, cardiovascular failure, etc) and their values are retrieved from patient's EHR and profile. Moreover, for the evaluation of COPD it is demanded a combination of measurements from the portable devices, EHR, the history of the patient, and a set of 8-questions aligned with the COPD Assessment Test (CAT) [13] that indicates the intensity of symptoms.

C. Decision Making Module (DMM)

First Phase of DMM

In this phase the vital bio data is evaluated using rule based algorithms according to the recommendations from [12]. In this case study hypertension is the most significant disease. For this reason the blood pressure data, by means of systolic and diastolic pressure (mmHg), is evaluated. In order to calculate more accurately the severity level (normal, mild, moderate, severe) of hypertension, the number of the cardiovascular risk factors is retrieved through EHR and used in conjunction with (a) the knowledge or heredity from other diseases such as diabetes and chronic kidney disease (user's profile) and (b) bio-data measurements (Table 1).

TABLE I: ASSOCIATION OF BLOOD PRESSURE, RISK FACTORS AND SEVERITY LEVEL

Blood Pres.	Systolic Diastolic	130-139 80-89	140-159 90-99	160-179 100-109	≥180 ≥110
Risk factors	No indications	normal	mild	moderate	severe
	1-2 indications	mild	moderate	moderate	severe
	≥3 or Diabetes or kidney	severe	severe	severe	severe

According to the classification of the hypertension severity levels and the blood pressure measurements, are identified the diseases and are activated the alarms for delivering services and triggering the appropriate medical and paramedical staff for patient's current health condition through the P2Care network [11] as suggested in Algorithm 1 and Table 2.

Algorithm 1 First-phase decision making algorithm

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loop
  get blood pressure measurements
  if severity level not normal **then**
    if severity level is mild **then**
      activate Service 1 and Service 2
    else if severity level is moderate **then**
      activate Service 1 and Service 3
    else if severity level is severe **then**
      activate Service 4 and Service 5
    end if
  end if
  Proceed in second phase

TABLE II: ASSOCIATION OF SERVICES AND ALARMS TO HEALTHCARE PROFESSIONALS AND PATIENT

Service	Actions	Alarms to P2CARE for specialists
1	**SMS** to the **patient** and a **family member** with recommendations for exercise and diet	Patient, Family member, paramedical staff
2	Arrange **2 appointments** with a **cardiologist** during a **year**	Patient, Cardiologist
	If **BMI>25** arrange 1 appointment with a diabetes specialist	Diabetes specialist
3	Arrange **4 appointments** with a **cardiologist** in a **year** Arrange **2 appointments** with a **diabetes specialist** in a **year**	Patient Cardiologist Diabetes specialist
4	Arrange immediately **3 appointments** with a **cardiologist** during a **week** **VoIP** session with **cardiologist and diabetes specialist** **SMS** to a **nurse** for monitoring patient and evaluate the symptoms	Patient Family member Cardiologist Diabetes specialist Nurse
5	**Ambulatory Service Hospitalization**	Ambulance provider Hospital

In order to validate the effectiveness of the first phase of DMM, data has been recorded from 30 patients suffering from COPD and other comorbidities (hypertension) or multimorbidities (hypertension and diabetes). The data has

been acquired on a daily basis during the period of one year. Fig. 3 depicts the success ratio of the decision making module in the two different cases (hypertension, hypertension and diabetes). The results confirm that more parameters and diseases the framework takes into account more accurate (90%) the result tends to be.
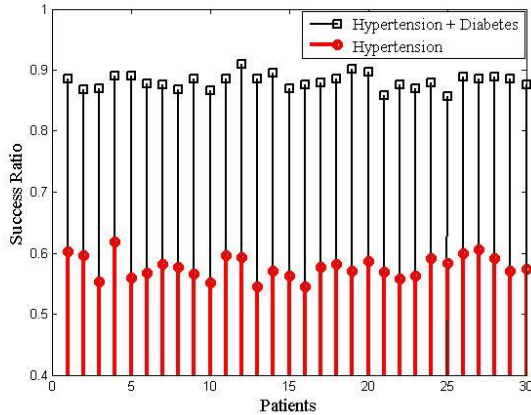

Figure 3.   Evaluation of first phase of DMM

Second Phase of DMM

In this phase data is retrieved from CAM with information related to the measurements of sensors, CAT scores, history of exacerbation and the history of hospitalization during the last 12 months for COPD disease. The COPD severity level is calculated using RF techniques. According to the severity level, CAT scores and history of exacerbation or hospitalization the patient's current health status is identified and the probability of an exacerbation episode is calculated through rule based algorithms. The outcomes present the alarms and actions for the appropriate delivery of services and the involved participants as analyzed in [9]. Fig. 3 depicts the whole process of the second phase.
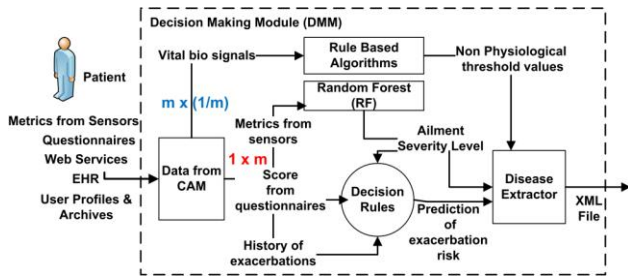

Figure 1.   The whole processes of DMM

The validation of the effectiveness of the second phase of DMM has been confirmed by a doctor in 75.74% success ratio for the Group1 and 50.87% for Group 2 [9].

The final assessment and effectiveness of the Ef-Zin framework is confirmed 78.57% (SD± 6.43%) by a group of collaborative medical professionals. The difference in the success ratio is justified by the lack of sensor data and/or EHR or by false alarms that activate healthcare professionals without any necessity. This occurs due to (i) patients' failure to follow the recommendations, (ii) the use of other medicines of which doctors were not aware and (iii) the existence of anxiety disorders. The final results confirmed the effectiveness of the Ef-Zin for delivering personalized services through a collaborative virtual healthcare team.

IV.   CONCLUSION

In this paper, a hybrid framework, named Ef-Zin, was presented for ubiquitous management of comorbidities and multimorbidities in chronic diseases. The Ef-Zin framework takes into consideration more that a single disease aiming to establish a collaborative environment through expertise healthcare providers and anticipate aggravations in patient's healthcare status. Ef-Zin may serve as a valuable tool for healthcare professionals for providing an integrated diagnosis with no uncertainties. The key feature of the system is the direct communication with the P2Care network [15] in order to trigger the most available and expertise healthcare professionals so as to deliver high level personalized services. Qualitative evaluations of the Ef-Zin verify its effectiveness.

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