

Designing a Patient Monitoring System Using Cloud and Semantic Web Technologies

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Abstract—Moving into a new era of healthcare, new tools and devices are developed to extend and improve health services, such as remote patient monitoring and risk prevention. In this concept, Internet of Things (IoT) and Cloud Computing present great advantages by providing remote and efficient services, as well as cooperation between patients, clinicians, researchers and other health professionals. This paper focuses on patients suffering from bipolar disorder, a brain disorder that belongs to a group of conditions called affective disorders, which is characterized by great mood swings. We exploit the advantages of Semantic Web and Cloud Technologies to develop a patient monitoring system to support clinicians. Based on intelligently filtering of evidence-knowledge and individual-specific information we aim to provide treatment notifications and recommended function tests at appropriate times or concluding into alerts for serious mood changes and patient's non-response to treatment. We propose an architecture as the back-end part of a cloud platform for IoT, intertwining intelligence devices with patients' daily routine and clinicians' support.

Keywords—Bipolar disorder, intelligent systems patient monitoring, semantic web technologies, IoT.

I. INTRODUCTION

IMPROVING the level of health service quality is a primary and constant need in health society. The considerable interest arises in computational methods and tools able to provide assistance to health care services more efficiently, led to the development and implementation of intelligent systems within the medical domain.

In this context, patient monitoring systems have grown substantially for addressing several requirements in early-diagnosis, optimal treatment strategies and disease prevention, as well as analysis, management and communication of medical information [1], [2]. Key factors in this attempt are the integration of medical information from various sources, as well as constant, on-time briefing of patient's health state and behavior. Multi-source patient monitoring evolves into an important service in this domain.

Although mental health is an essential component of the quality of life and a common goal for all individuals, relatively little attention has been paid to the challenges of computer-based assistive technologies in mental health care. Mental illnesses are serious disruptions of behavior, mood, thinking

and/or interpersonal and social relationships. Bipolar disorder (BD) is a severe mental illness characterized by devastating mood swings. Chronicity, episodic nature with several motifs, misdiagnosis, high prevalence (1-2%), risks of suicide attempts and recurrence are the major characteristics of the disease, leading to a massive negative impact on the quality of life of individuals suffering from BD, on their families and on economy [3]. To manage and treat bipolar disorder effectively, we must address different aspects of patient's physical, emotional and social daily status. There is need for patient monitoring systems that can deal with it and support longitudinal follow-up of the disease. More recently, advanced systems are generated to monitoring patients with BD by exploiting the daily mood charting, or by analyzing data from wearable [4], [5] and environmental sensors [5] and Smartphone applications [6].

Long-term monitoring is valuable in patients with BD; we aim to approach the problem of longitudinal follow-up by generating a time-determined ontology based on semantic web and capable of specific reasoning over concepts of BD and on their evolution over time. Relying on well-established clinical guidelines [7] we generate personalized models that can better follow mood changes, recognize early warning signs and facilitate their timely intervention by clinicians. We take advantage of Semantic Web Technologies to provide an intelligent patient monitoring system, which is perceived as the back-end part of a cloud platform for IoT.

Semantic Web [8] and its technologies enable us to manage information and processes. At the heart of Semantic Web technologies are the use of ontologies. An ontology [8] formally specifies the conceptualization of a domain of interest. Ontology's components are concepts (classes), relations (properties), instances and axioms. An ontology is formally expressed in OWL [9], the standard language for publishing and sharing ontologies on the World Wide Web. We derive new knowledge by applying reasoning in the instance semantic data of the ontology. Semantic Web Rule Language [10] (SWRL) is the language for specifying rules, enabling powerful deductive reasoning on Semantic Web ontologies. Application examples of the use of Semantic Web Technologies in health care systems include among others, encoding of clinical practice guidelines [11] and disease management [12], [13]. None of these systems handles temporal information or deal with evolution of a disease in time. OWL's syntax is restricted to binary relations making representation of temporal properties –which are ternary relations-, a complicated task. In this work, the temporal information that is necessary for representing a chronic disease

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such as bipolar disorder is encoded using the N-ary relations approach [14]. Representation and reasoning over temporal information is realized using SOWL [15].

Further to this, provision of health services could be linked with new emerging technologies like Cloud Computing and Internet of Things (IoT) [16], [17]. At a glance, the concept behind Clouds is to provide a platform environment where hardware and software could be delivered on a bespoke manner to users and utilized accordingly to their requests. This is an important cloud computing advantage as it allows the scaling of user resources on demand (a process called elasticity). In parallel, IoT relates users and their smart devices along with sensors used in every day actions (e.g., Smart phones and wearable devices). Using the IoT paradigm, new opportunities are rising where various devices could offer to sensor-embedded healthcare new applications and services. In this study, we focus on monitoring health of bipolar disorder patients where cloud services could offer the means for data analysis and integration.

Aiming at developing an intelligent patient monitoring system: in Section II, (i) we demonstrate our core system implementation based on Semantic Web technologies that has been implemented already and is currently under testing using real patient cases and (ii) we present our design of a cloud deployment model; in Section III, we provide the overall system architecture of the proposed solution for bipolar patient monitoring; and in Section IV, we give a summary and the future research directions.

II. INTELLIGENT PATIENT MONITORING SYSTEM APPROACH

We aim at supporting clinical professionals in the initial evaluation and diagnosis of adults with suspected BD, as well as to providing evidence-based treatment options for a personalized therapeutic approach, notifications for early-warning signs and alerts for crucial mood swings leading to their timely intervention in order to prevent relapse and suicide. It consists of three components namely, a) the core system, b) the front-end system and c) the back-end system.

A. Core System Implementation

The time-determined ontology is the major ingredient of core system by identifying key components of bipolar disorder, while emphasis has been placed on modeling temporal concepts and relationships. Based on well-documented clinical guidelines and algorithms, it aims at developing electronic support to clinicians and health care professionals in BD issues through a suggested sequence, while taking into account patient-specific information (demographic, medical, behavioral) from different heterogeneity sources from the input repository. Both, clinical guidelines and user scenarios for individualized bipolar patients' are used to develop the ontology.

1. Guidelines

Guidelines refer to "systematically derived statements that are aimed at helping individual patient and clinician decisions". Our core system reclaims different aspects of the

treatment and management of bipolar disorder, operating in five selected evidence-based clinical practice guidelines: WFSBP [18], CANMAT [19], NICE [20], Australian and New Zealand [21], British Association for Psychopharmacology [22], and other systematic reviews for BD [7].

2. User Scenarios For Bipolar Disorder

Bipolar I disorder (at least one manic or mixed episode) and bipolar II disorder (hypomania and depression) are the main types of BD, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM). At present, we provide user diagnostic scenarios for bipolar I disorder (BDI) (Fig. 1), taking into account the persons' history, and specific assessments of diagnostic screening instruments (e.g., Mood Disorder Questionnaire, MDQ; structured clinical interview for the DSM-IV, SCID; various Rating Scales) to diagnose bipolar illness by recognizing the symptoms that meet criteria for a mood episode (manic, depressive) and their severity, by evaluating its possible comorbidities (medical, mental), and by preventing its misdiagnosis, particularly with unipolar disorder (depression).

Moreover, using findings from physical examinations, imaging, and laboratory tests, the diagnostic scenarios are designed to support clinicians by a sequential multi-step processing; to reach out the differential diagnosis of these manifestations in the initial evaluation; to re-evaluate diagnosis considering alternate causes (organic disorders or other psychoses) at the outset of treatment; and finally to confirm the diagnostic correctness after repeated failure of patient to respond to treatment strategies.

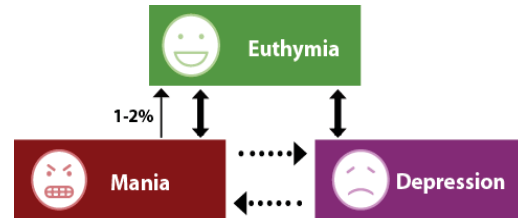


Fig. 1 Possible phase transitions of Bipolar I Disorder

Based on the above evidence-based treatment guidelines, we generated the user scenarios for BDI treatment, following the complex nature of the illness, and address treatment issues specific to the variability in mood swings associated with the acute treatment (mania, depression, rapid cycling and mixed states, electroconvulsive therapy), or to symptom-free intervals (euthymia) related to the maintenance treatment (relapse prevention, treatment discontinuation, rapid cycling). Patient Long-term monitoring is operated by our system to assess the presence or absence of symptoms, medication adherence, psychiatric and medical comorbidities, mortality and medical morbidity, and to track therapeutic drug safety and tolerability. We have placed warnings in decision nodes with supporting annotation from the literature in order to provide the appropriate recommendations and alerts to the clinicians on real-time to address different kinds of

alternations, and early-warning signs, and also to suggest psychotherapy interventions to their patients.

3. BD Ontology

The need of integrating and retrieving data as well as extending interoperability leads into a wide definition of formal approaches in ontology domain, concluding into formalizing domain terminology, categorization described by formal ontologies, such as SNOMED CT [23], ICD [24], ICF [25] etc. Although this formalism offers great advantages such as formal rigor and inference power it also limits expressiveness along design and instance knowledge [26], [27]. User requirements expect not only basic truisms but also full expressiveness in the representation of the domain of the ontology. Formal and general purpose ontologies such as those referred to above offer a vocabulary of terms along with concept definitions and their inter-relationships. They can be regarded as upper level ontologies and as such they can be integrated with our developed ontology which, however, is more specialized and geared around concepts related to the monitoring of patient condition and its evolution in time.

The representation of the domain of bipolar I disorder occurs through the description of the corresponding concepts, the characteristics of these concepts and the correlations between them. The designed ontology that includes all the necessary concepts, attributes and relationships that encodes the disorder as well as patient's diagnosis, treatment, and monitoring. We present this ontology through the class diagram of Fig. 2.

In the diagram static concepts are distinguished from dynamic concepts.

Dynamic entities (entities which evolve in time):

- ❖ *PHR*: The patient's medical record.
- ❖ *Patient State*: Information about the patient's current state (in euthymia or in an episode).
- ❖ *Symptom*: information about the symptom (type, severity).
- ❖ *Function Tests*: Information about the function test a patient is submitted. Function Tests includes various categories of tests. We distinguish tests into imaging tests, laboratory tests, recording tests, which are also subcategorized into subclasses (presented in Fig. 3). Each Function Tests is related with the corresponding class of Standard Tests which keeps information about the general attributes of tests (unit of measurement, normal values). As shown in Fig. 3, Function Tests are based on guidelines provided recommendations for initial baseline assessments (complete medical and laboratory investigations) and follow-up laboratory investigations and monitoring strategies for bipolar patients [7], [18]-[22].
- ❖ *Therapy*: The therapeutic approaches a patient may receive (medication, hospitalization, psychotherapy).
- ❖ *Medicine*: Information about the medicine the patient receives (medicine name, category, dosage etc).

Static entities:

- ❖ *Patient*: Personal information about the patient (first and last name, age, address, sex etc).
- ❖ *Patient History*: Information about patient's medical history. Age of onset, heredity, number of manic or depressive episodes, previous medication.
- ❖ *Episode*: Information about the type (manic or depressive) and severity of an episode.
- ❖ *Initial Evaluation*: Initial evaluation for the diagnosis procedure. Initial evaluation is a combination of:
 - *History*: History record of a patient that collects a clinician through various questions.
 - *Questionnaire*: Mood questionnaires for symptoms evaluation, that a patient is called to answer (MDQ, BSDS, CIDI).
 - *Clinical Evaluation*: The patient is submitted into various functional tests in order to reject other medical causes and ensure psychiatric disorder.
- ❖ *Medical Cause*: If the clinical evaluation suggests other medical cause than bipolar disorder.
- ❖ *Diagnosis*: Information about the type of the disorder (Type I or Type II) and if the patient is suffering from rapid cycling or not.
- ❖ *Standard Test*: Highest and lowest optimal values of each functional test and unit of measurement of the test.
- ❖ *Side Effect*: Possible side effects of a medicine.

The described classes relate with each other as presented in Fig. 2. Relationships Dynamic classes are related with each other during specific intervals. For example class Patient State relates with class Episode during the interval the episode occurs. Main concept in the ontology is class Patient Health Record (PHR). By accessing PHR, we can easily access all the vital information described by the classes which relate with PHR. For example through PHR we can access Patient State and conclude if a patient is in euthymia or not.

We start the design with a static ontology describing the main concepts of the Bipolar Disorder disease scenario. This initial ontology is developed using a common ontology editor such as Protégé Editor [28].

Then, it is converted to temporal using the CHRONOS plugin of Protégé [29].

To issue alerts and recommendations, we implement a reasoning system, using SWRL. We have encoded the clinical guidelines as rules and we apply these rules over patient's information.

For example, the following rule evaluates the mood questionnaires that the patient is called to fill as well as the results from the clinical evaluation.

If there is a positive mood questionnaire, there is a suspicion of BD and in that case, if the clinical evaluation excludes other medical causes from being responsible for the patient's symptoms then, the rule concludes that the clinician needs to continue with assiduous clinical examination. Necessary information for the rule is included in the classes Personal Health Record (PHR), Initial Evaluation, Questionnaire (MDQ, CIDI, BSDS), Clinical Evaluation.

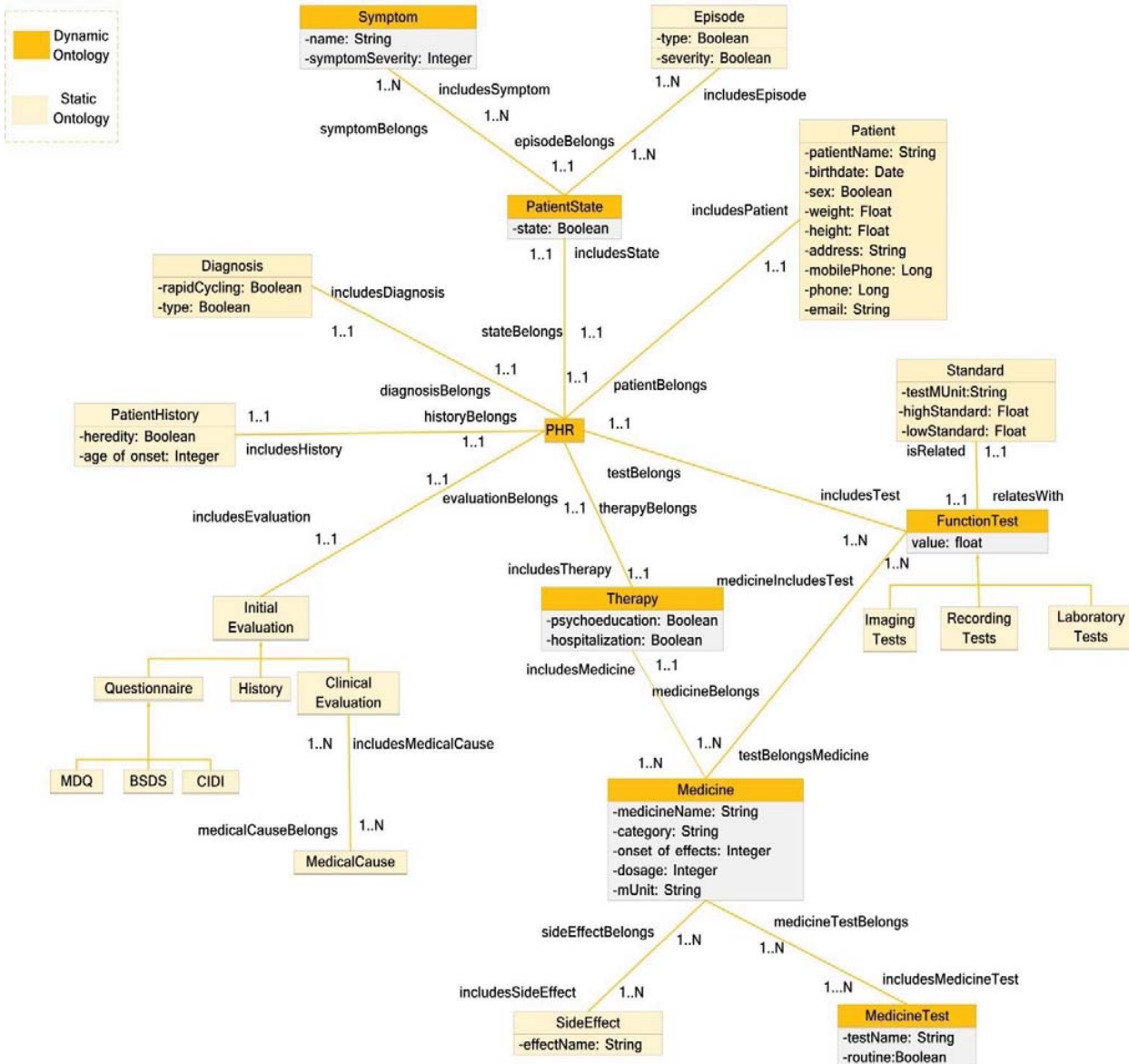


Fig. 2 Class Diagram of the developed ontology in Bipolar I Disorder domain

We present the implemented rules in Description Logics (DLs), a family of Knowledge Representation languages that form the basis for the Semantic Web standards [30].

The rule is expressed in DLs [30] as:

$$PHR \cap \text{Initial Evaluation} \cap (\exists \text{Questionnaire.result} = \text{true}) \cap (\exists \text{Clinical Evaluation.result} = \text{normal}) \rightarrow \text{Recommendation} \text{ (BD existence)}$$

This rule is implemented in SWRL language as presented in Fig. 4.

The next example of a treatment recommendation rule results in the suggestion of medical treatment. It evaluates the medication the patient is receiving and the type of symptoms the patient presents. In the case that the patient is first

diagnosed, receiving no medication and the symptoms suggest existence of a manic episode then the rule directly suggests medical treatment (Lithium, Li; Valproate, VPA; atypical antipsychotic, AAP). Necessary information for the rule is included in the classes Personal Health Record (PHR), PatientState, Episode, Therapy, and Medicine.

The rule is expressed in DLs [30] as:

$$PHR \cap (\exists \text{PatientState.state} = \text{inEpisode}) \cap (\exists \text{Episode.type} = \text{manic}) \cap \text{Therapy} \cap \neg \text{Medicine} \rightarrow \text{Recommendation} \text{ (Start Therapy with Li/VPA/AAP or combination of two medicines)}$$

This rule is implemented in SWRL language as presented in Fig. 5.

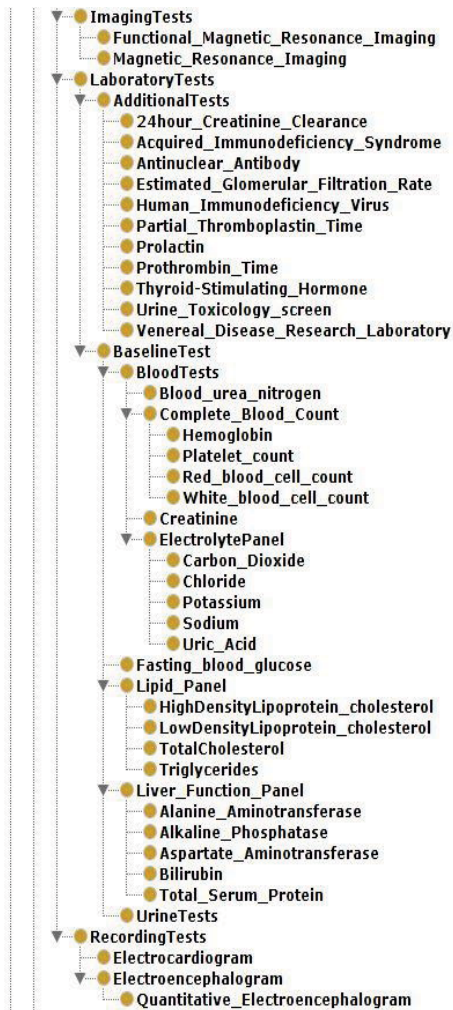


Fig. 3 Subclasses of the Class Function Tests for baseline assessment and follow-up monitoring of Bipolar I Disorder

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MDQ (?mq), PHR(?phr),
Recommendation(?rec), ClinicalEvaluation(?clinicalEval),
includesInitialEvaluation(?phr, ?ev mq),
includesInitialEvaluation(?ev mq, ?mq), Interval(?int mq),
Event(?ev mq), during(?ev mqRes, ?int mqRes),
questionnaireResultOP(?mq, ?ev mqRes),
questionnaireResult(?ev mqRes, ?mqRes), Event(?ev mqRes),
Interval(?int mqRes), during(?ev mq, ?int mq),
booleanNot(?mqRes, ?false),
includesInitialEvaluation(?phr, ?ev clinicalEval),
includesInitialEvaluation(?ev clinicalEval, ?clinicalEval),
Event(?ev clinicalEval), Interval(?int clinicalEval),
during(?ev clinicalEval, ?int clinicalEval),
clinicalEvaluationResultOP(?clinicalEval, ?ev clinicalRes),
clinicalEvaluationResult(?ev clinicalRes, ?c_eval), Event(?ev clinicalRes),
Interval(?int clinicalRes),
during(?ev clinicalRes, ?int clinicalRes), booleanNot(?c_eval, ?false),
equals(?int mqRes, ?int clinicalRes),
text(?rec, ?rec txt), equal(?rec txt, "suspicion of BD"),
intervalEquals(?int clinicalEval, ?int mqRes) ->
recommendationBelongs(?rec, ?phr)

```

Fig. 4 SWRL Rule for Bipolar I Disorder screening

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PHR(?phr), MedicalHistory(?medHist),
Recommendation(?rec),
includesInitialEvaluation(?phr, ?ev medHistory),
includesInitialEvaluation(?ev medHistory, ?medHist),
Event(?ev medHist), Interval(?int medHist),
during(?ev medHist, ?int medHist),
evaluationOP(?phr, ?ev_eval), evaluation(?ev_eval, ?eval), eq
ual(?eval, "mild to severe"),
Event(?ev_eval), Interval(?int_eval), during(?ev_eval, ?int_eval),
intervalBefore(?int_medHist, ?int_eval), text(?rec, ?txt),
equal(?txt, "Recommend Li/VPA/AAP or 2 drug
combination") -> recommendationBelongs(?rec, ?phr)

```

Fig. 5 SWRL rule of medicine recommendation for first diagnosed patient with an acute manic episode

B. Design of a Cloud Deployment Model

We present our vision for a high level architecture of an intelligent patient monitoring system where sensors that are connected to the Internet monitor users' actions and condition. As stated before, IoT and cloud computing highlight new openings, yet, due to health standards, regulations and recommendations health data transferring (such as ISO standards like ISO 80001, security standards like ISO 27000 etc.) and analysis to the cloud has become an issue [31].

To overcome this, the software to data cloud model comes to offer solutions with regards to the deployment of cloud applications that utilize sensitive data. In order to meet the requirements of a global Health industry the FI-STAR project, as described in [31], utilizes such technology to allow software to be transferred near to the data source. It is expected that this model will offer the required framework to allow cloud services to be initiated at clients' sites and to be hosted in a private cloud [31]. The proposed architecture will follow FI-STAR conceptual model by demonstrating a cloud platform architecture wherein no sensitive data will be exchanged but it will reside at the back-end site.

1. Front-End System

Apart from patients' health records, diagnostic examinations, and clinical guidelines, different kinds of paper-based or electronic-based monitoring tools (forms for mood charting, life charting, antipsychotic and lithium monitoring) arise to support different aspects of patients' daily life.

As depicted in Fig. 6, we intend to build a heterogeneous medical information repository, supporting different kinds of input-data, such as data from patient's health records, paper-based monitoring forms, and other advanced computer-based assistive tools, sensors, devices and smartphones [4]-[6] such as:

- **Computer-based Assistive Tools:** Electronic diaries (mood charting, mood, medication and sleep), life charts, self-reporting, weekly text-messaging, antipsychotic monitoring tool, metabolic monitoring.
- **Sensors:** Biofeedback, biomedical sensors, electrodermal activity (EDA) sensor, GPS, accelerometer, Bluetooth scanning, light detector, microphone, infra-red (PIR) motion detectors, door and bed sensors, other sensors (weight, blood pressure, etc.).

- *Portable Devices*: Portable sensing devices, home sleep-monitoring devices, galvanic skin response (GSR) device, fluorescence measurement device.
- *Smartphone Applications*: Wi-Fi access, Self-assessment data, voice analysis.

Attention is given to create a friendly, easily accessible, intuitive and expandable, user interface that enables continuous longitudinal monitoring of patient's progress, provides warnings or alarms for addressing critical situations to their timely response and facilitates communication in real time between doctors, patients and our system. It provides high functionality allowing continuous updating and rapid retrieval of medical data for each patient. The GUI will also highlight the diverse capabilities of the other system modalities and their interaction, resulting in timely availability of data and reliable decisions of clinicians.

2. Back-End System

The back-end system is implemented using the FI-WARE platform, as described in [31] that offers the specifications and the tools to build novel cloud applications and services. The latter offers fundamental functional blocks, named as Generic Enablers (GEs) such as user and application authentication, context data management, storage and others included in the FI-WARE catalogue [31]. In detail, the back-end site will include interfaces to (a) the provider site that offers various modular services (such as GEs) in the concept of the public cloud, (b) the private cloud consumer site(s) that is the back-end of the system and integrates the use case trial software modules (and GEs) installed in the Clinical Monitoring site, and (d) the interoperation network to allow interaction among the front-end that represents the human user (GUI and input-

data repository) and the Clinical site.

III. OVERALL SYSTEM ENVIRONMENT

We presented an intelligent patient monitoring system architecture using Semantic Web and cloud computing technologies to provide clinicians and health professionals with variety of operations. These are treatment notifications, recommended function tests, and alerts for critical mood shifts and patient's non-response to treatment, intelligently assessed and shown at suitable times. We expect that such a system will attract a wide community of users that will utilize their everyday devices and will enhance human mental health monitoring. Fig. 6 shows the high level functionalities of the monitoring system prototype. These are as follows:

- *Data collection* from the user side by utilizing smart-devices and/or sensors in terms of local data retrieval.
- *Interoperability* to the interfaces of the back-end system by allowing connectivity service from the side of the front-end applications and services.
- *Notification services* to push statements and/or warnings to any interested party such as users, doctors or other medical personnel.
- *Data analysis and integration* with regards to the properties of the patients e.g. in our case for patients with bipolar disorder.
- *Secure data storage* within the cloud to ensure data privacy.
- *Legacy system adaptors* for communication to local systems such as the EHR (e.g., tools for diagnosis).
- *Other services* such as semantic analysis tools (Ontology repositories and rules) that might be needed.

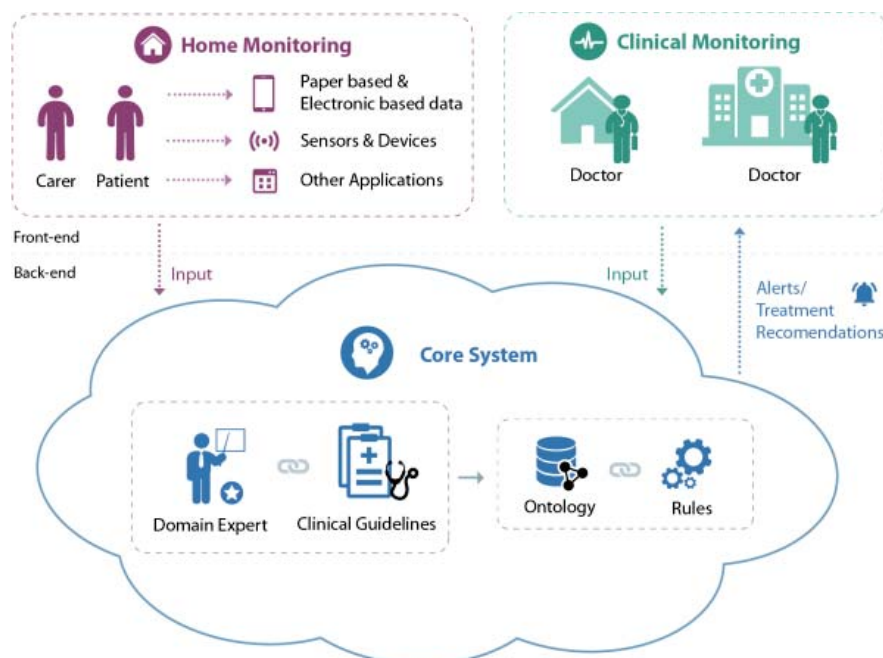


Fig. 6 Overall System Architecture of the designed monitoring system using cloud and semantic web technologies

IV. CONCLUSIONS

We demonstrate that Semantic Web allows systematic knowledge extraction and ontology creation by analyzing patient records and filtering evidence-based guidelines leading to notifications and recommendations for individualized diagnosis and treatment approaches. In addition, we illustrate a cloud deployment model as a perspective for an advanced environment that assists in monitoring of complex chronic pathologies, such as brain disorders including BD.

Moreover, we proposed a fundamental architecture based on a cloud computing framework. Tests and validation performed progressively on the implemented pilot applications to a selected sample of ten real clinical cases of bipolar disorder and three published case reports [32]. A successful longitudinal monitoring for BD patients would also serve to adopt this intelligent system useful for knowledge representation and inference to improve health care services in other mental or neurological disorders.

In the future, we aim to test this cloud-based architecture on a real setting performing data acquisition from sensors and wearable devices, that could be forwarded to the cloud platform for data analysis and patient monitoring based on well-defined standards for exchanging PHR information such as FHIR standard [33].

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REFERENCES

- [1] I. Chiuchisan, and O. Geman, "An Approach of a Decision Support and Home Monitoring System for Patients with Neurological Disorders Using Internet of Things Concepts," WSEAS Transactions on Systems, vol. 13, pp. 460-469, 2014.
- [2] U. Varshney, "A Framework for Wireless Monitoring of Mental Health Conditions," in Conf. Proc. EMBS 2009 IEEE 31st Annual International Conference, pp. 5219-5222.
- [3] B. S. Shastry, "Bipolar disorder: An Update," *Neurochem. Int.*, vol. 46, no. 4, pp. 273-279, 2005.
- [4] G. Valenza, C. Gentili, A. Lanata, and E. P. Scilingo, "Mood Recognition in Bipolar Patients Through the PSYCHE Platform: Preliminary Evaluations and Perspectives," *Artif. Intell. Med.*, vol. 57, no. 1, pp. 49-58, 2013.
- [5] P. Prociow, K. Wac, and J. Crowe, "Mobile Psychiatry: Towards Improving the Care for Bipolar Disorder," *Int. J. Ment. Health. Syst.*, vol. 6, no. 1, pp. 5, 2012.
- [6] J. Alvarez-Lozano, V. Osmani, O. Mayora, M. Frost, J. Bardram, M. Faurholt-Jepsen, and L.V. Kessing, "Tell Me Your Apps and I Will Tell You Your Mood: Correlation of Apps Usage with Bipolar Disorder State," in ACM Proceedings 7th International Conference on Pervasive Technologies Related to Assistive Environments, Rhodes Island, 2014.
- [7] K. R. Connolly, and M. E. Thase, "The Clinical Management of Bipolar Disorder: A Review of Evidence-Based Guidelines," *Prim. Care. Companion CNS Disord.*, vol. 13, no. 4, pp. PCC.10r01097, 2011.
- [8] T. Berners-Lee, J. Hendler, and O. Lassila, "The Semantic Web," *Scientific American*, pp. 28-37, May 2001.
- [9] G. Antoniou, and F. Harmelen, "Web Ontology Language: OWL," *Handbook on Ontologies*, 2004.
- [10] I. Horrocks, P. F. Patel-Schneider, H. Boley, S. Tabet, B. Groszof, and M. Dean, "SWRL: A semantic web rule language combining OWL and RuleML," W3C Member Submission, May 2004.
- [11] S. Hussain, and S. S. R. Abidi, "Ontology Driven CPG Authoring and Execution via Semantic Web Framework," in Proceedings 40th IEEE International Conference on System Sciences, IEEE Computer Society, Hawaii, 2007.
- [12] E. Sanchez, C. Toro, E. Carrasco, P. Bonachela, C. Parra, G. Bueno, and F. Guijarro, "A Knowledge-Based Clinical Decision Support System for the Diagnosis of Alzheimer Disease," in Proceedings 13th IEEE International Conference on e-Health Networking, Application & Services, Columbia, MO, 2011, pp. 355-361.
- [13] J. S. Deogun, and W. Spaulding, "Conceptual Development of Mental Health Ontologies. Advances in Intelligent Information Systems," *Studies in Computational Intelligence*, vol. 265, pp. 299-333, 2010.
- [14] N. Noy, and B. Rector, "Defining N-ary Relations on the Semantic Web," W3C Working Group Note, April 2006.
- [15] S. Batsakis, and E. G. M. Petrakis, "SOWL: A Framework for Handling Spatio-temporal Information in OWL 2.0," in RuleML Europe, ser. Lecture Notes in Computer Science, Springer, 2011, vol. 6826, pp. 242-249.
- [16] Mell P, Grance T, "The NIST definition of cloud computing," *Commun. ACM.*, vol. 53, no. 6, pp. 50, 2010.
- [17] A. M. Kuo, "Opportunities and challenges of cloud computing to improve health care services," *J. Med. Internet Res.*, vol. 13, no. 3, pp. e67, Sep. 2011.
- [18] L. N. Yatham, S. H. Kennedy, S. V. Parikh, A. Schaffer, S. Beaulieu, M. Alda, C. O'Donovan, G. Macqueen, R. S. McIntyre, V. Sharma, A. Ravindran, L. T. Young, R. Milev, D. J. Bond, B. N. Frey, B. I. Goldstein, B. Lafer, B. Birmaher, K. Ha, W. A. Nolen, and M. Berk, "Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2013," *Bipolar Disord.*, vol. 15, no. 1, pp. 1-44, Feb. 2013.
- [19] H. Grunze, E. Vieta, G. M. Goodwin, C. Bowden, R. W. Licht, H.-J. Moller, S. Kasper and WFSBP Task Force on treatment guidelines for bipolar disorders, "The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological Treatment of Bipolar Disorders: Update 2009 on the Treatment of Acute Mania, The World Journal of Biological Psychiatry, vol. 10, no. 2, pp. 85-116, 2009.
- [20] National Institute for Health and Care Excellence, "Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care," National Institute for Health and Care Excellence, NICE clinical guideline 185, Sep. 2014.
- [21] Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for Bipolar Disorder, "Australian and New Zealand clinical practice guidelines for the treatment of bipolar disorder," *Aust. N. Z. J. Psychiatry*, vol. 38, no. 5, pp. 280-305, May 2004.
- [22] G. M. Goodwin, Consensus Group of the British Association for Psychopharmacology. Collaborators: S. Chandler, I. Anderson, F. Colom, D. Coghill, J. Cookson, N. Ferrier, J. Geddes, G. Goodwin, P. Haddad, N. Hunt, N. Kapur, I. Jones, D. Lam, A. Lingford-Hughes, D. Miklowitz, R. Morriss, B. Sahakian, J. Scott, D. Taylor, J. Thakore, A. Thapar, A. Thomas, P. McGuire, S. Cooper, P. Cowen, C. Manning, K. Ebmeier, J. Cavanagh, T. Barnes, and K. J. Aitchison, "Evidence-based guidelines for treating bipolar disorder: revised second edition--recommendations from the British Association for Psychopharmacology," *J. Psychopharmacol.*, vol. 23, no. 4, pp. 346-388, June 2009.
- [23] G. Heja, G. Surja, and P. Varga, "Ontological analysis of SNOMED CT," *BMC Med. Inform. Decis. Mak.*, vol. 8, no. 1 (Suppl), pp. S8, Oct. 2008.
- [24] M. Moller, D. Sonntag, and P. Ernst, "Modeling the International classification of diseases (ICD-10) in OWL," in Second International Joint Conference 2010 Knowledge Discovery, Knowledge Engineering and Knowledge Management, pp. 226-240.
- [25] B. Smith, and P. Grenon, "The Cornucopia of Formal Ontological Relations," *Dialectica*, vol. 58, no. 3, pp. 279-296, 2004.
- [26] S. Schulz, H. Stenzhorn, M. Boeker, and B. Smith, "Strengths and limitations of formal ontologies in the biomedical domain," *Rev. Electron Comun. Inf. Inov. Saude*, vol. 3, no. 1, pp. 31-45, March 2009.

- [27] K. Halland, K. Britz, and A. Gerber, "Investigations into the use of SNOMED CT to enhance an OpenMRS health information system," *South African Computer Journal*, vol. 47, pp. 33-46, 2011.
- [28] J. H. Gennari, M. A. Musen, R. W. Fergerson, W. E. Grosso, M. Crubezy, H. Eriksson, N. F. Noy, and S. W. Tu, "The evolution of Protege: an environment for knowledge-based systems development," *Int. J. Hum. Comput. Stud.*, vol. 58, no. 1, pp. 89-123, 2003.
- [29] A. Preventis, E. Petrakis, and S. Batsakis, "Chronos Ed: A Tool for Handling Temporal Ontologies in Protege," *International Journal of Artificial Intelligence Tools (IJAIT)*, 2014.
- [30] F. Baader, "Theory, Implementation and Applications," in *The Description Logic Handbook*, Cambridge Univ. Pr., 2003.
- [31] S. Sotiriadis, E. G. M. Petrakis, S. Covaci, P. Zampognaro, E. Georga, and C. Thuemmler, "An Architecture for Designing Future Internet (FI) Applications in Sensitive Domains: Expressing the Software to Data Paradigm by Utilizing Hybrid Cloud Technology," in *Proceedings IEEE 13th International Conference, Bioinformatics and Bioengineering (BIBE)*, Chania, 2013, pp. 1-6.
- [32] M. B. SoaresdeM, R. A. Moreno, and D. Hupfeld-Moreno, "Electroconvulsive therapy in treatment-resistant mania: case reports," *Rev. Hosp. Clin.*, vol. 57, no. 1, pp. 31-38, 2002.
- [33] D. Bender, and K. Sartipi, "HL7 FHIR: An Agile and RESTful approach to healthcare information exchange," in *26th IEEE International Symposium, Computer-Based Medical Systems*, Porto, 2013, pp. 326-331.